REDISPLACEMENT OF DISTAL RADIUS FRACTURES
INSIGHTS FROM PREDICTION TO PRACTICE

BRITT BARVELINK

Redisplacement of distal radius fractures

Insights from prediction to practice

Britt Barvelink

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Redisplacement of Distal Radius Fractures
Insights from prediction to practice

Secundaire dislocatie van distale radiusfracturen
Inzichten van voorspellingen tot de kliniek

Proefschrift

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Erasmus Universiteit Rotterdam
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PROPOSITIONS

1. The type of cast does not affect the risk of redisplacement in reduced distal radius fractures in adults. (*this thesis)*

2. It is reasonable to monitor the stability of well-aligned distal radius fractures and to reserve surgery for fractures that develop secondary displacement. *(this thesis)*

3. Even a perfectly moulded cast cannot prevent redisplacement of reduced distal radius fractures. *(this thesis)*

4. It is important to manage patient expectations early in the treatment of reduced distal radius fractures, particularly regarding pain and discomfort during the first weeks of immobilisation. *(this thesis)*

5. Big data can enable a shift from experience-based predictions about distal radius fracture instability to scientifically grounded, patient-specific predictions. *(this thesis)*

6. Within a decade, the execution of a clinical trial will take half the time thanks to the implementation of artificial intelligence. *(inspired by Hutson, Nature, 2024)*

7. Orthopaedic trauma teams function better when they include female surgeons, leading to stronger teamwork and potentially improved patient outcomes. *(supported by Green et al., Bone and Joint Journal, 2025)*

8. The societal romanticization of cold winters enabling natural ice skating in the Netherlands obscures the fact that it is a major seasonal source of fractures. *(inspired by Melian et al., Journal of Orthopaedic trauma, 2025)*

9. The efficiency of current orthopedic residency training is questionable when a fellowship is a necessity to become a fully qualified specialist. *(supported by Daniels, J Grad Med Educ, 2014)*

10. It is not only about the imaging; fracture displacement alone does not predict future outcomes. *(inspired by Abraham Colles, 1814)*

11. Vake bi'j te bange *(papa)*

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Chapter 1

General introduction

Distal radius fractures (DRFs) are one of the most common types of fractures.[1] Often, a DRF is the result of a low-energy simple fall on the outstretched hand with the wrist in extension. Although DRFs can occur across all age groups, there is a significant increase in their incidence in post-menopausal women.[2-4] In 1814, Abraham Colles was the first to describe the most common type of DRF, which he identified by a characteristic deformity of the wrist (Figure 1). Today, this fracture type is radiographically associated with characteristic dorsal comminution, dorsal angulation, radial shortening and not necessarily an associated ulnar styloid fracture. A DRF with these fracture characteristics is eponymously referred to as a 'Colles fracture'. Multiple eponyms like the Smith fracture, the Barton (or reverse Barton) fracture have subsequently followed, each describing different fracture patterns of the wrist. Nowadays, DRFs are most commonly classified according to the AO classification system, which is based on radiographic fracture characteristics.[5]

Postero-anterior (PA) and lateral radiographs are typically taken to adequately assess the injury. When assessing a wrist radiograph, specific radiographic parameters should be considered. On PA radiographs, this includes radial inclination, radial height and articular congruence. On lateral radiographs, radial sagittal tilt and articular congruence should be assessed. An additional CT scan is sometimes indicated to further explore intra-articular fracture patterns and/or provide additional insight for surgical planning. Two- and three-dimensional CT images improve both the reliability and the accuracy of fracture characterization and frequently alter the treatment plan towards surgical fixation.[6, 7] Based on (inter)national guidelines, the decision is made as to whether a fracture is acceptably aligned or not. The Dutch Guideline for DRFs states that a DRF is considered unacceptably aligned if one or more of the following criteria are met: ≥ 10° dorsal angulation, ≥ 20° volar angulation, ≤ 15° radial inclination, ≥ 3 mm radial shortening and ≥ 2 mm intra-articular step-off or gap.[8] In case a DRF is displaced (e.g. unacceptably aligned), closed reduction is advised to realign the fracture.

In 2018, our research group carried out an online questionnaire amongst all emergency rooms in the Netherlands, to gain insight into national treatment differences for displaced DRFs.[9] We found that closed reduction is most often performed by a resident (not) in training, followed by immobilization of the fracture with a plaster splint.[9] When conservative treatment is initiated, there is a significant risk of fracture redisplacement while in the cast. Redisplacement rates in reduced DRFs range between 32% and 64%.[10-12] To date, no modifiable factors have been identified that might reduce the risk of redisplacement. Yet there are several non-modifiable patient and fracture characteristics associated with an increased risk of redisplacement. These include female sex, age over 60 years and the presence of certain fracture characteristics, namely dorsal fracture comminution, dorsal angulation >20° at presentation, intra-articular incongruence and an associated ulnar fracture.[12-15]

The high rate of fracture redisplacement in conservatively treated DRFs, substantially contributes to the emerging tendency to opt for surgical treatment. However, complicating the decision-making process whether to operate or not, doubts exist regarding the long-term benefit of surgical treatment, particularly in patients over 65 years of age.[16] Multiple randomized controlled trials have recently been performed to determine the most effective treatment. Their conclusions often favor surgery over conservative treatment on the short term but after a follow-up of longer than one year no large differences have been found.[17-19] While wrist range of motion and patient-reported outcomes often show better results on the short term, no clinically relevant differences have been found in any of these studies one year after the fracture occurred. Surgical treatment is more costly compared to cast immobilization[20, 21] and is associated with more major complications such as nerve lesions, tendon ruptures and infection.[16] Identifying the specific patient who would truly benefit from surgery instead of casting remains challenging. Also, it is unclear whether outcomes are adversely affected by postponing the decision for surgery. If postponement does not affect outcome, it may be justified to start with non-operative treatment and proceed with surgery only if redisplacement occurs.

This thesis focuses on unraveling the mystery of fracture redisplacement occurrence and comparing treatment options for displaced DRFs. Improving our understanding of redisplacement and its impact on patients' functioning could facilitate more personalized decision-making regarding the appropriateness of non-operative treatment. In the **first part** of this thesis, our aim was to explore the possibility of predicting which fractures are displaced or will redisplace over time. We investigated the value of additional CT imaging in assessing fracture displacement. Next, we aimed to deploy machine learning to help us predict, based on trauma- and post-reduction radiographs, whether a DRF is stable or likely to redisplace during conservative treatment. In the **second part** of this thesis, we investigated whether cast immobilization influences the redisplacement risk. It is unclear whether there is a difference in redisplacement incidence between DRFs treated with a plaster splint versus a circumferential cast. We conducted a large multicentre randomized controlled trial to reliably answer this question. Additionally, we investigated whether the quality of cast molding affects DRF stability. Nowadays, different casting materials are available and we suspected that the experience of cast applicants might influence the cast molding quality. The **third part** of this thesis compares non-operative treatment versus direct plate fixation or delayed plate fixation. We compared patient-reported outcomes between two groups: patients who started non-operative treatment but later were operated (because of fracture redisplacement) and patients treated directly with volar plate fixation. If results between groups are comparable, starting with cast immobilization and observing fracture alignment changes during follow-up would be justified. Moreover, when differences in patient-reported outcomes between current treatment options are small, it is important to consider factors such as financial burden on society. We therefore conducted a detailed cost-analysis.

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PART I

Predicting (re)displacement

Chapter 2

Traditional radiography versus computed tomography to assess reduced distal radius fractures

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ABSTRACT

Introduction: This study compares computed tomography (CT) with plain radiography in its ability to assess distal radius fracture (DRF) malalignment after closed reduction and cast immobilization.

Methods: Malalignment is defined as radiographic fracture alignment beyond threshold values according to the Dutch guideline encompassing angulation, inclination, positive ulnar variance and intra-articular step-off or gap. After identifying 96 patients with correct alignment on initial post-reduction radiographs, we re-assessed alignment on post-reduction CT scans.

Results: Significant discrepancies were found between radiographs and CT scans in all measurement parameters. Notably, intra-articular step-off and gap variations on CT scans led to the reclassification of the majority of cases from correct alignment to malalignment. CT scans showed malalignment in 53% of cases, of which 73% underwent surgery.

Conclusion: When there is doubt about post-reduction alignment based on radiograph imaging, additional CT scanning often reveals malalignment, primarily due to intra-articular incongruency.

INTRODUCTION

Distal radius fractures (DRF) that heal non-anatomically could result in functional impairment in the short term and degenerative changes on the long run. Malalignment of a DRF is defined as radiographic fracture alignment beyond threshold parameters by the Dutch guidelines: ≥ 10° of dorsal angulation, or ≥ 20° of volar angulation, ≤ 15° of inclination, ≥ 3 mm of positive ulnar variance and ≥ 2 mm intra-articular step-off. The question of to which extent fracture displacement can be accepted remains open. Traditionally, fracture displacement is measured on plain radiographs, but the use of computed tomography (CT) scans to guide treatment has increased [1, 2]. A CT scan has the potential to provide more details on the fracture alignment but is less easily available and more expensive, and radiation exposure is increased compared to plain radiographs. Therefore, it is relevant to determine in which specific cases a CT scan adds value to the radiographic parameters used to asses malalignment.

While radiographs are standardly used to determine the existence of a fracture [3-10], additional CT scanning is advised when doubting the alignment or involvement of the articular surface and consequently doubting the necessity for surgical reduction and fixation, according to the Dutch guidelines [11]. Compared to conventional radiographs, additional CT scanning is more accurate in determining the degree of angulation and the involvement of the distal radioulnar joint [4, 12-14]. The treatment choice is adjusted from conservative to operative in 23% to 46% of DRFs after additional CT scanning, and a CT scan improved the intraobserver reproducibility in the choice of surgical treatment [1, 2, 4, 12-20]. However, most of these studies are based on relatively small sample sizes [1, 2, 16, 17, 19-21], evaluated by a limited number of observers, and not evaluating all five fracture characteristics (angulation, inclination, positive ulnar variance, step-off and gap) that are used to guide the treatment modality [11]. Thus, the differences in assessment of all relevant fracture alignment characteristics, measured on radiographs versus CT scans in a large cohort, have yet to be investigated.

The aim of this study is to unravel whether an additional CT scan compared to conventional radiographs will result in different alignment measurements that might cross the border from correct to malaligned in DRFs. In addition, the agreement and reliability between radiographs and CT scans are assessed, with a subanalysis to confound for secondary displacement.

METHODS

Study Population and Data Selection

According to the local Medical Ethics Committee approved protocol (MEC-2020-0258), cases were selected from a retrospective cohort. This cohort consists of patients who sustained a DRF and were presented at our academic level 1 trauma centre between January 2011 and July 2020. Inclusion criteria were: 1) age ≥ 18 years, 2) reduced DRF, 3) pre- and post-reduction posterior-anterior (PA) and lateral radiographs available, and 4) additional post-reduction CT scans available, taken within seven days after trauma. Exclusion criteria were: 1) no, incomplete or inadequate radiographic follow-up, 2) re-fracture of the distal radius, 3) malalignment post-reduction according to the Dutch Guidelines for DRFs [11], 4) fracture not reduced within 24 hours after trauma and 5) initial treatment with external or internal fixation.

Baseline and fracture characteristics

The following baseline characteristics were collected: age at the time of injury (years), sex, AO fracture classification (A/B/C, according to the trauma radiograph), the interval between trauma and additional CT scanning (days), and – in case of surgical reduction and fixation – the interval between trauma and surgery.

On all radiographs and CT scans, fracture alignment was measured to define whether the fracture was correctly aligned or not. The fracture characteristics that were measured DRFs comprise radial inclination (degrees), positive ulnar variance (mm) and intra-articular step-off and gap (mm) on PA views, and dorsal or volar angulation (degrees) and intra-articular step-off and gap (mm) on lateral views on radiographs (Figure 1A). Four trained and experienced researchers conducted these alignment measurements according to the same measurement guidelines by Medoff et al. [22]. When doubting measurements, radiographs and CT scans were reviewed by a senior orthopaedic surgeon (JC).

Angulation was measured on the sagittal CT scan, on the slide where the line could be drawn between the uppermost (dorsal and volar) point of the articular surface of the distal radius [23, 24]. Inclination and positive ulnar variance were measured on the coronal CT view, on the slide where the distal-most point of the radial styloid and the midpoint between the dorsal and palmar radial cortical margins was shown [4] (Figure 1B). Intra-articular step-off or gaps were measured on the slide with the largest step-off or gap [4] (Figures 1A and B). Measurements were performed using a DICOM viewer, Synedra View Personal, version 20.0.0.4. In case of multiple step-offs or gaps, the largest was described. When a step-off or gap was measured on a CT and could not be seen on radiographs, it was valued as '0' on the radiograph.

Figure 1. Examples of measurements on radiographs and CT scans: A. (1) Angulation, (2) inclination, and (3) positive ulnar variance on radiographs; B. (1) Angulation, (2) inclination, and (3) positive ulnar variance on CT scan.

Data presentation

The primary outcomes involved the difference in angulation, inclination, positive ulnar variance, intra-articular step-off, and gap on post-reduction radiographs and additional CT. We assessed each parameter individually to determine if correct alignment or malalignment was seen on CT. Overall, fractures were labelled for all imaging as correctly or malaligned according to the Dutch guideline threshold values. The Dutch guidelines for DRFs state that a fracture is malaligned when one or more of the following threshold values are exceeded: ≥ 10° of dorsal angulation, or ≥ 20° of volar angulation, ≤ 15° of inclination, ≥ 3 mm of positive ulnar variance and ≥ 2 mm intra-articular step-off [11]. The median time between trauma and CT scan and the median time to surgical intervention was calculated. As a secondary outcome, the agreement between the two imaging techniques, radiographs versus CT, and the reliability of the agreement was calculated. In addition, a separate assessment was performed on the subgroup, for which the CT scan was made the same day as the post-reduction radiographs to minimize the change for early secondary displacement.

Statistical analysis

Data distribution was assessed using the Shapiro-Wilk test, with a p-value <0.05 indicating non-normal distribution. Missing data were not imputed, and a p-value <0.05 was deemed significant for all analyses.

Descriptive statistics summarized patient characteristics and radiographic measurements. Continuous data are reported as mean with standard deviation (SD) for normal distributions or median with interquartile range (IQR) for non-normal distributions. Categorical data are presented as counts with percentages.

CT scan analyses included calculating percentages for correct alignment versus malalignment, with 95% confidence intervals (CIs) derived via the modified Wald method. Statistical significance was inferred when the 95% CIs did not encompass 0. The Wilcoxon Signed-Rank test evaluated differences in fracture alignment measured on radiographs and CT scans.

Agreement between imaging methods and their clinical relevance was examined through Bland-Altman analysis, plotting mean measurements against their differences. Points scattered above 0 with a 95% CI above 0 indicated that the CT scan measurements were larger than those on radiographs. This analysis, along with Intra Class Correlation (ICC) for reliability (categorized by Koo and Li, 2016 as "poor" <0.5, "moderate" 0.5-0.75, "good" 0.75-0.90, and "excellent" >0.90), highlighted systematic biases and agreement levels. Both analyses extended to acute CT scans.

RESULTS

Study population

We included 96 patients with 96 DRFs from our database from 2011 to 2020. A flowchart of the inclusion process is shown in Figure 2. Baseline characteristics are demonstrated in Table 1. According to the AO classification, most fractures concern AO type C (68%). The median interval from presentation at the emergency room to CT scanning was three days (IQR 2-4 days), and in 55% of cases, the CT scan was performed on the day of reduction. A total of 63 patients (66%) were treated surgically; the median time from trauma to surgical fixation was five days (IQR 3-9 days).

Table 1. Baseline patient- and fracture characteristics.

Characteristic	**n = 96**
Age in years, mean (SD)	52 (SD 17.5)
Female, n (%)	60 (63%)
AO classification, n (%)	
A Extra-articular	19 (20%)
B Partial articular	12 (12%)
C Complete articular	65 (68%)

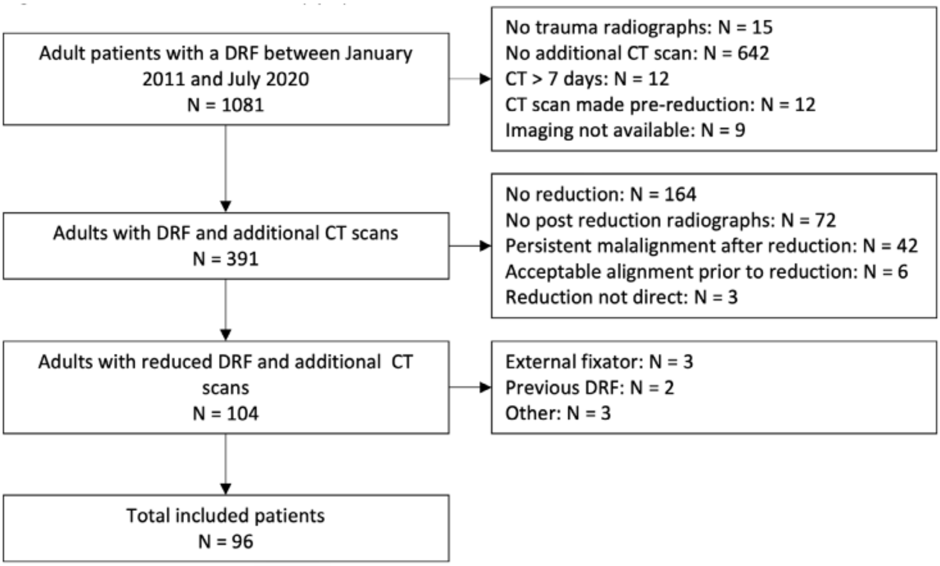

Figure 2. Flowchart of the study population
DRF: Distal radius fracture; CT: Computed tomography

Primary outcome

The median measurements on all parameters differed significantly when comparing radiographs and CT scans (Table 2). Radiograph measurements and CT scans agreed that after reduction, 68 (71%) of DRFs were dorsally angulated and 28 (29%) volarly. In contrast with the acceptable sagittal angulation on radiographs, measurement on CT scan revealed unacceptably dorsal angulation in 20 (29%) patients and unacceptably volar angulation in 3 (11%) patients. Inclination was measured in all cases, revealing malalignment in 17 cases (18%), only indicated by CT scans. Positive ulnar variance was measured in 36 (38%) cases, of which in 3 (8%) cases, a positive ulnar variance ≥ 3mm was measured on CT only. An intra-articular step-off or gap was measured in 28 (29%) and 76 (79%) DRFs, respectively, resulting in malalignment in 20 (71%) and 69 (91%) of the cases on CT.

In 53% of cases, the fracture was labelled correctly aligned on post-reduction radiographs, while additional CT scanning revealed a malalignment. In the other cases (47%), there was an agreement on both radiographs and CT scans on correct fracture alignment. Divided by fracte morphologies according to the AO classification (A/B/C), CT scans revealed malalignment in 52%, 41%, and 58% of the cases, respectively. The DRF was surgically treated in 73% of cases in which radiographs and CT disagreed. The remaining 27% with malalignment conform CT scan measurements were conservatively treated. In addition, surgery was chosen in 13% of DRFs that were correctly aligned conform the guideline.

The number needed to treat (NNT), or as in this study, 'the number needed to diagnose', was 1.89. This indicated that approximately two patients would need to be assessed using CT scans instead of radiographs to correctly identify one additional case of malalignment that was misdiagnosed by radiographs.

Table 2. Fracture alignment measured on post-reduction radiographs and CT.

	Cases n = 96	Post-reduction alignment on radiographs	Post-reduction alignment on CT-scan	P-value[b]	Malalignment conform CT imaging[c]
Angulation					
Dorsal, °	68[a]	5.0 (2.0–8.0)	6.0 (3.5-11.0)	0.002	20 (29%, 0.19-0.42)[d]
Volar, °	28[a]	6.0 (1.0-10.8)	8.5 (3.3-14.0)	0.015	3 (11%, 0.03-0.28)[d]
Inclination, °	96[a]	22.0 (18.0-23.7)	20.5 (17.0-23.0)	0.016	17 (18%, 0.11-0.27)[d]
Positive ulnar variance, mm	36[a]	1.7 (1.0-2.0)	2.1 (1.5-2.4)	0.007	3 (8%, 0.05-0.30)[d]
Step-off, mm	28[a]	1.0 (0.0-1.6)	2.1 (1.5-2.3)	<0.001	20 (71%, 0.51-0.86)[d]
Gap, mm	76[a]	1.4 (1.0-2.0)	4.1(2.4-5.8)	<0.001	69 (91%, 0.81-0.95)[d]

If not noted differently, information is presented as median with interquartile range between parentheses.
[a.] Includes the number of DRFs in which this fracture parameter was measured.
[b.] Wilcoxon Rank Sum test was used.
[c.] Number of cases in which fracture alignment was not acceptably aligned on the CT scan.
[d] The 95% confidence intervals were calculated using the modified Wald method.

Secondary outcome

The agreement and reliability for all measurements between radiographs and CT scans were calculated (Table 3). Figure 3 shows the Bland-Altman plots assessing the agreement, showing that the differences vary systematically for all measurements. CT scans showed significantly increased angulation severity, loss of inclination, positive ulnar variances and intra-articular incongruences (Figure 3).

The intraclass correlation (ICC), which indicates reliability between the two imaging techniques, showed that the radiographs and CT scans were in poor agreement for all alignment measurements. The ICC also showed poor reliability for all measurements (Table 3).

In 55% of the included cases, the CT scan was obtained immediately after reduction. The separate ICC and Bland-Altman analysis for these cases showed differences in angulation, inclination, step-off and gap measurements. Only measurements of positive ulnar variance showed a negative ICC and did not vary systematically on the Bland-Altman plots (Table 4 and Figure 4).

Table 3. Correlation between alignment measurements performed on radiographs versus CT-scan.

	Cases n = 96	Intraclass Correlation[b]	95% Confidence Interval	Reliability
Angulation, °				
Dorsal	68[a]	0.19	-0.03-0.40	Poor
Volar	28[a]	0.35	0.01-0.63	Poor
Inclination, °	96[a]	0.44	0.26-0.59	Poor
Positive ulnar variance, mm	36[a]	0.05	-0.23-0.34	Poor
Step-off, mm	28[a]	0.11	-0.09-0.37	Poor
Gap, mm	76[a]	0.09	-0.07-0.27	Poor

[a.] Includes the number of DRFs in which this fracture parameter was measured.
[b.] Type A intraclass correlation coefficients using an absolute agreement definition. Values < 0.5 indicates poor reliability.

Table 4. Sub analysis for correlation between alignment measurements on radiographs versus CT-scan, performed on same day.

	Cases N = 53	Intraclass Correlation[b]	95% Confidence Interval	Reliability
Angulation, °				
Dorsal	42[a]	0.15	-0.12-0.42	Poor
Volar	11[a]	0.27	-0.16-0.69	Poor
Inclination, °	53[a]	0.52	0.30-0.69	Poor
Ulnar positive variance, mm	14[a]	-0.03	-0.27-0.30	Poor
Step-off, mm	16[a]	0.11	-0.10-0.43	Poor
Gap, mm	44[a]	0.11	-0.08-0.33	Poor

[a.] Includes the number of DRFs in which this fracture parameter was measured.
[b.] Type A intraclass correlation coefficients using an absolute agreement definition. Values < 0.5 indicates poor reliability.

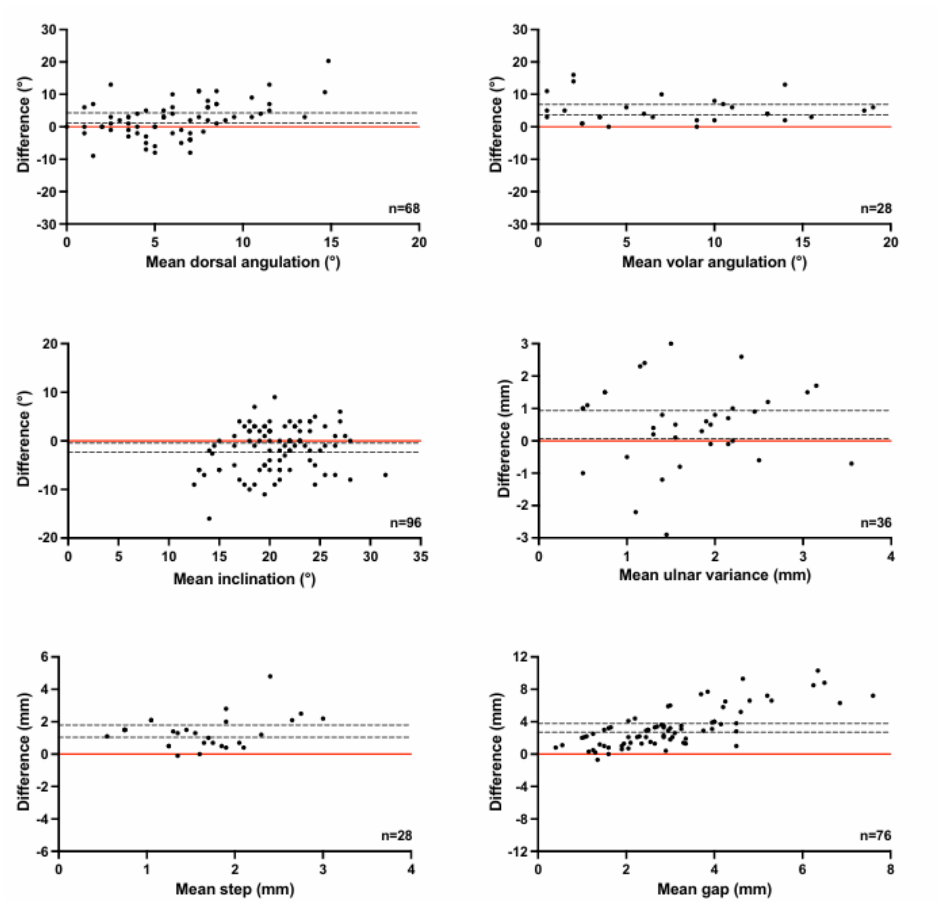

Figure 3. Bland-Altman Plots of the differences between radiographs versus CT scans. The CT measurements were subtracted from radiograph measurements. Horizontal black lines display the limits of agreement (95% CI). Points scattered above 0 with a 95% CI above 0 (red line) indicated that the measurements on the CT scan were larger than the measurements on radiographs

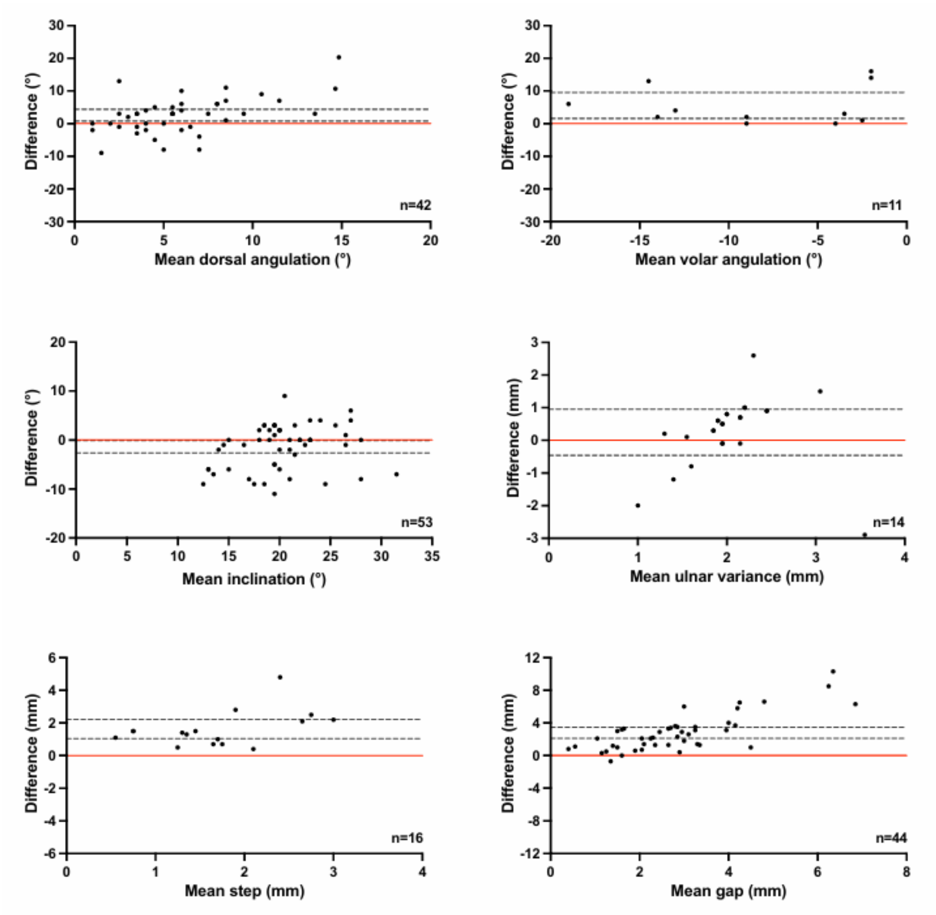

Figure 4. Sub analysis of radiographs versus CT scans made on the same day. Bland-Altman Plots of the differences between radiographs versus CT scans. The CT measurements were subtracted from radiograph measurements. Horizontal black lines display the limits of agreement (95% CI). Points scattered above 0 with a 95% CI above 0 (red line) indicated that the measurements on the CT scan were larger than the measurements on radiographs.

DISCUSSION

This study shows that conventional radiographs consistently underestimate reduced DRFs' severity compared to CT scans based on volar and dorsal angulation, loss of inclination, positive ulnar variance and intra-articular incongruence. In 53% of cases, additional CT scanning showed malalignment, while they appeared correctly aligned based on radiograph measurements. The ICC and Bland-Altmant plots showed a clear discrepancy between the two imaging techniques on all measurement parameters, whereas CT scans showed significantly increased severity on all alignment measurements compared to radiographs.

In line with our findings, previous studies reported that radiographs tend to underestimate intra-articular incongruence concluding that the CT scan is more reliable for the measurement of intra-articular involvement in DRFs [4, 12-15]. Furthermore, previous research has shown that CT scans increase inter-surgeon agreement on the need for surgical intervention [2, 14-18]. Additional CT scanning changes the indication from conservative treatment to surgery in 23% to 46% of cases [2, 15, 19, 21]. Therefore, in cases of uncertainty regarding the alignment after reduction, especially concerning the intra-articular incongruence, a CT scan may offer additional value. Future studies need to asses if this consideration would contribute to eventually improved clinical outcomes.

Although the Dutch guideline for DRFs advises operative treatment for malaligned fractures [11], approximately a quarter of malaligned DRFs in this cohort were treated conservatively. Potential reasons can be patient-related (e.g., age or concomitant health problems being a risk for surgery in general), fracture-related (e.g., alignment was close to threshold values), or surgeon-related (e.g., reluctance to operate on severely comminuted fractures). Due to the retrospective nature of this study, the exact reasons for the chosen treatment modality remain unknown.

Before advocating surgical intervention to prevent malunion, one has to realize that previous studies showed a poor correlation between malunion and clinical outcomes, especially in older patients [11]. Studies report malunion rates of 35% in non-surgically treated fractures and 10% in surgically treated fractures [25, 26]. Malunion might result in chronic pain, reduced function, decreased grip strength and impaired ability to perform daily activities [27-29]. Secondary invalidating osteoarthritis can also be initiated due to uneven force distribution across the radiocarpal joint surface [30]. Further studies are needed to accurately determine the level of malalignment that leads to clinically unacceptable outcomes.

We decided to define the acceptability of fracture alignment conform the Dutch guidelines for DRFs. Simply because retrospective cases were used that were treated conform this guideline. Secondly, the Dutch guideline comprises a broad assessment of alignment. Volar angulation and inclination are not encountered in the American Academy of Orthopaedic Surgeons guidelines

[31]. However, both guidelines agree on the threshold values for dorsal angulation, positive ulnar variance, and step-off or gap. Our analysis revealed that shifts from correct to malalignment primarily occurred in measurements step-off or gap, parameters recognized by both guidelines.

This study needs interpretation in light of its strengths and limitations. To date, this study is the first to evaluate all these characteristics on radiographs and CT scans based on a large cohort of DRFs. Previous studies either only assessed intra-articular involvement [4, 14, 15] or only the extra-articular radiographic parameters [17]. Furthermore, we consciously chose only to include cases in which the CT scan was made shortly after (within seven days) reduction. Additionally, the subgroup analysis on cases where the CT scan was performed immediately after reduction, which minimized the risk of secondary displacement, showed similar results. Therefore, it can be concluded that the discrepancies between the radiograph and CT are not attributed to secondary displacement.

As the first limitation, there was a potential for selection bias. According to the guidelines, a CT scan is made when doubting the alignment of a DRF and for pre-operative planning. Due to the retrospective design of this study, the exact reason behind the physician's decision to perform a CT scan is unknown. Therefore, conclusions should be carefully interpreted and are only applicable on cases in which post-reduction fracture alignment is doubted. Secondly, the measurements were not repeatedly executed by different observers, which might have resulted in undetected measurement errors. Consequently, inter- and intra-observer reliability of measurements is not presented. However, Watson et al. showed that the intra-observer reliability is high for angulation measurements and moderate for inclination and positive ulnar variance measurements on radiographs [32]. Lastly, in some cases, it was difficult to determine the axis of the radius on CT scans due to the truncation of the radial shaft. This might have influenced the angulation and inclination measurements since these are based on the radial shaft axis. However, the suboptimal radiology results depict more of the daily clinical situation than the optimal scientific situation, enabling extrapolation of the results.

This study suggests that additional CT scanning often shows DRF malalignment. According to our findings, the differences between radiographs and CT scans on step-off and gap measurements might have clinical implications because these measurements appeared beyond the guideline’s threshold in 71% and 91% of the cases, respectively. In patients with any uncertainty about the articular congruency, a CT scan can provide valuable insights into fracture alignment. Therefore, a CT scan might help to plan a surgical approach. However, it is essential to consider the additional costs and the radiation exposure associated with additional CT scans, while the clinical impact remains unknown. Future research should assess the cost-benefits of additional CT scans of reduced DRFs. Furthermore, it should be taken into account that DRF treatment is not only based on radiological parameters. More aspects of the patient's condition and preferences should be considered when deciding on the optimal treatment for a DRF.

In conclusion, our study consistently demonstrates an underestimation of DRF alignment on radiographs compared to CT scans. According to the guideline, this leads to a shift from correct alignment to malalignment in over half of the cases, mainly underestimating intra-articular step-off and gap measurements. Our finding emphasizes the clinical significance of incorporating CT scans in evaluating and managing displaced DRFs in which post-reduction alignment is doubted. Further evaluation is needed to assess the effect of the implications of these findings, and it is essential to extend our focus on the importance of patient preferences beyond radiographic parameters.

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3

Chapter 3

A Deep Learning model to predict distal radius fracture instability on injury radiographs

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Submitted

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ABSTRACT

Importance: Shared decision making for patients with wrist fractures is challenging. Treatment decisions are partly based on whether the distal radius fracture will lose threshold alignment, or will remain stable in a cast. Surgery is offered to patients with high probability of instability, while cast treatment is reserved for patients with a stable fracture. Estimating fracture stability remains challenging for surgeons, hindering shared -surgical- decision making.

Objective: An -open-source- interpretable Deep Learning algorithm (Convolutional Neural Network – CNN) was created with the aim to accurately predict DRF loss of threshold alignment based on trauma and post-reduction radiographs to ultimately facilitate shared decision making.

Design: In this study a CNN algorithm was created and validated.

Setting: Patients with DRFs were included from a ten-center prospective database, and two retrospective databases from two hospitals.

Participants: Patients were required to: 1) have complete longitudinal follow-up including radiographs to determine the label 'stable' or 'unstable'; 2) be primarily treated non-operatively; and 3) no surgery while still in acceptable alignment (i.e. 'stable'). Trauma- and reduction-radiographs, both postero-anterior (PA) and lateral, were collected including sex and age of the patient. These were annotated with 21 landmarks to augment CNN training.

Main outcomes and measures: Accuracy, sensitivity, specificity, and area under the receiver operator characteristics curve (AUC) were calculated as a measure of the algorithm compared to the testset. Interpretability is facilitated by automated landmark annotations as output on radiographs.

Results: The algorithm was trained on 2136 radiographs (583 cases), and tested on 563 radiographs (150 cases). Our model achieved an AUC of 0.82, with 76% accuracy, 68% sensitivity and 84% specificity.

Conclusions and relevance: Half of DRFs treated in a cast will ultimately become unstable during follow-up, while surgeons' accuracy to predict such loss of threshold alignment was only 54% in an international online experiment. This open-source interpretable DL model outperforms surgeons, and may augment the shared decision-making process. Contrary to previous models developed to detect pathoanatomy, this is the first CNN used in surgery to make a prediction about clinical outcomes based on plain radiographs.

INTRODUCTION

Patients with traumatic fractures contribute significantly to years lived with disability, and this global problem is on the rise: increasing with 65% since 1990, to 25.8 million years with disability in 2019 worldwide.[1] For context, the disability burden among surviving oncology patients is one-tenth of that caused by traumatic fractures.[2] Distal radius fractures (DRFs) are the most common fractures in the USA with over half a million new cases annually.[3]

In general, treatment of DRFs is either non-operative in a cast; or surgery; most often by open reduction and internal fixation (ORIF) with plate and screws.[4] Treatment decisions vary significantly per country, hospital or even surgeon: "what you get depends on where you live, and who you see".[5–7] In Australia, surgery is offered for up to 80% of DRFs, compared to 26% in the USA and 10% in the Netherlands.[8–10] One could argue such variation is undesired: some patients may be overtreated, while some may go undertreated. Unnecessary surgical treatment may lead to both preventable surgical complications, and avoidable treatment costs.

In general, surgical decision making is as follows: a DRF that is not displaced (i.e. within threshold alignment according to local guidelines) is considered stable, and patients are generally offered cast immobilization.[11,12] DRFs that are displaced (i.e. beyond threshold alignment) will undergo a closed manual reduction, followed immediately by cast immobilization. In the shared decision-making process, a patient might be offered surgery if: a) attempted closed reduction was not sufficient (DRF is not within threshold alignment); or b) if the surgeon predicts that cast immobilization will "fail" and therefore deems the fracture to be unstable (i.e. future fracture redisplacement beyond threshold alignment). The latter prediction is the surgeons' estimation of the probability for a DRF to lose threshold alignment. However, studies have shown that human estimation of the probability for future loss of threshold alignment of a DRF is fallible. An international online experiment via the Science of Variation Group (Boston, USA) showed that surgeons accurately predicted re-displacement of a DRF based on plain injury radiographs in only 54% of patients with a reduced DRF; a guesstimation. In a subsequent experiment, surgeons evaluated both radiographs as well as injury CT-scans of reduced DRFs: accuracy improved up to 70% with the use of CT.[13–15] The difficulty of this clinical challenge is displayed in figure 1, with the actual outcome displayed in figure 2.

Approximately half of reduced DRFs lose threshold alignment, leading to malunited DRFs, while non-union is rare.[15–17] The resulting clinical problem is that such posttraumatic deformity of the wrist may lead to functional impairment, and potentially requires (complex) reconstructive surgery, with arguably less favorable outcomes than early surgical management.[18,19]

Previously, studies have focused on discovering factors associated with loss of threshold alignment (i.e. DRF instability) leading to prediction tools such as the Edinburgh Wrist probability Calculator (EWC) based on quantification of injury alignment. Unfortunately, the diagnostic performance characteristics of the EWC was unsatisfactory upon external validation studies in the USA and the Netherlands.[20–22]

To date, AI driven computer vision research in the field of radiology has focused on automated detection of pathoanatomy on plain radiographs, CT and MRI. For orthopedic trauma, the number of deep learning models made available for fracture detection and classification is rapidly increasing. For DRF detection, such AI algorithms have been successfully trained and validated as well. To date for DRF alone, fifteen studies have published deep learning algorithms to detect and/or classify DRFs on radiographs or CTs, including some that are now commercially available as part of a software package.[23] However, the prediction of clinically much more relevant outcomes, such as DRF stability has not been the focus of any studies in this field to date.

We argue that for relatively “simple” pathoanatomy such as a DRF, the diagnostic performance characteristics of radiologists and surgeons are already excellent. The clinical challenge is rather the early prediction of future loss of threshold alignment, which is our main driver to offer surgery. Thus, in order to facilitate -timely- shared surgical decision-making and avoid delayed surgery, it is clinically relevant to accurately predict the probability of loss of threshold alignment at the time of injury (i.e. predict instability). A patient with a fracture with a high probability of remaining aligned can more confidently be offered definitive non-operative treatment without the need for delayed surgical intervention; while for patients with a fracture that is deemed “unstable” (i.e. high chance of loss of threshold alignment) an operative fixation can be discussed in a shared surgical decision-making process between patient and surgeon. In this common clinical scenario, there is a significant opportunity for automated AI-driven probability calculations to minimize human biases.

We aimed to develop a deep learning model that is able to accurately predict DRF loss of threshold alignment based on trauma and post-reduction radiographs in order to facilitate shared decision-making. The hypothesis is that this DL model outperforms surgeons’ predictions of instability.

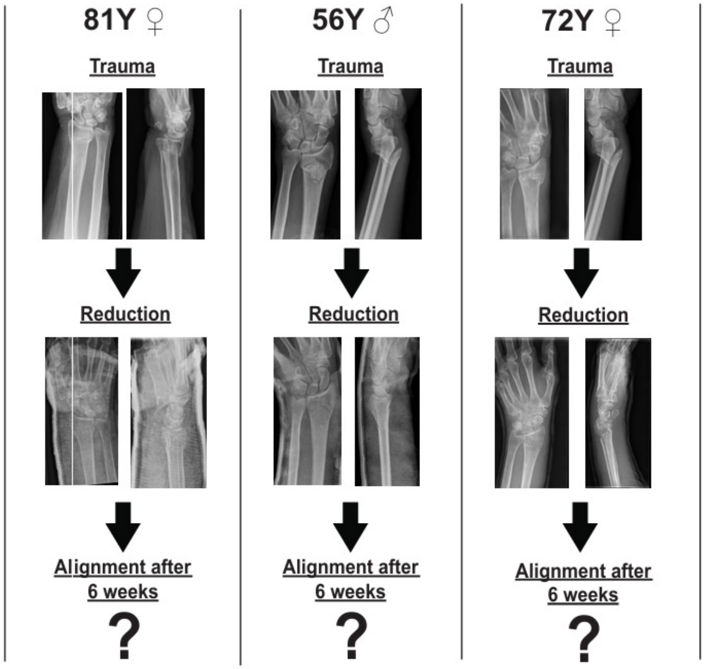

Figure 1. Showcase of clinical problem with 3 patient cases.

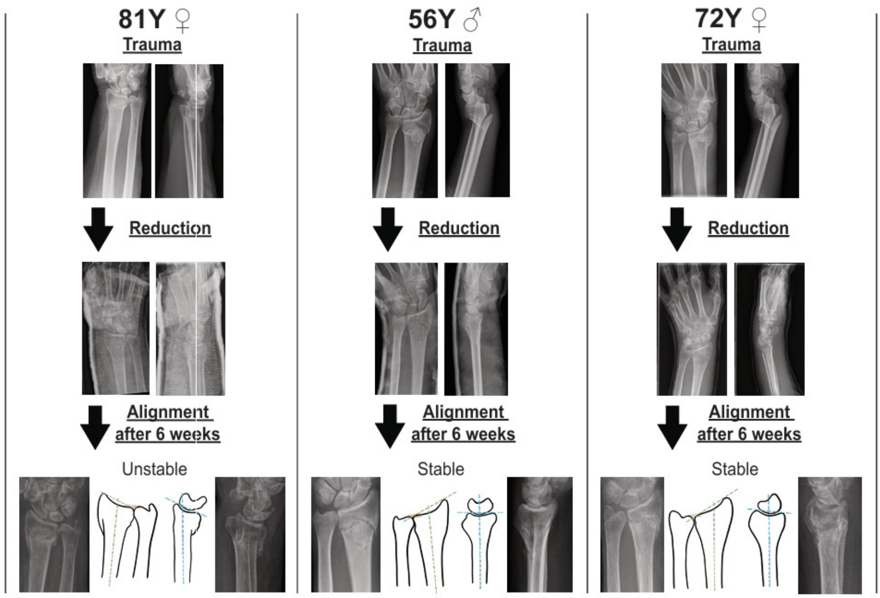

Figure 2. Clinical problem with 6 week follow-up. A schematic overview of alignment of the fracture has been provided.

METHODS

Study design and participants

This study is a diagnostic accuracy study developing and validating AI methodology (Convolutional Neural Network - CNN). For algorithm development and training, cases of DRFs were included from one multicenter prospective cohort study in the Netherlands, and two retrospective cohorts from two other hospitals in order to improve generalizability. Concerning the two retrospective cohorts, data collection has been approved by the Medical Research Ethics Committee of two participating university hospitals, the University Medical Center Groningen, (202200114) and the Erasmus MC, Rotterdam (MEC-2020-0258). The need for informed consent was waived by the ethics committees for the use of anonymized imaging data in these retrospective cohorts according to the Declaration of Helsinki. The prospective cohort contains a subset of patients from the CAST study, a multicenter, cluster-randomized trial comparing circumferential casting and plaster splinting in reduced DRFs (MEC-2019-0528). [24] All patients gave their consent prior to the start of the CAST study.

A flowchart of patient selection process is shown in eFigure 1. For the retrospective cohorts, the picture archiving and communication systems (PACS) were searched for adult patients with a DRF. All radiographic imaging of the patients' wrists was derived from the PACS and pseudo-anonymized. After radiographic evaluation, patients were excluded in the following situations: 1) Incomplete radiographic follow-up, 2) fracture other than solitary DRF with or without styloid ulnae fracture, 3) polytrauma patients, 4) primarily surgically treated DRFs and 5) previous ipsilateral DRF. If a DRF was unacceptably aligned (according to the guidelines below) immediately after (or without) reduction, the patient was also excluded.[12] Finally, some patients were excluded during the annotation process (56 patients in total), most often due to poor quality radiographs. The final DRF dataset contains 2699 plain radiographs (733 DRF cases), 492 and 886 radiographs (128 and 279 DRFs) from the retrospective cohorts respectively, 1321 radiographs (326 DRFs) from the prospective cohort.

Procedures

1. Ground truth: Alignment measurements and labelling

Alignment measurements were carried out on all trauma, post-reduction and follow-up radiographs. Acceptable fracture alignment was defined as per the Dutch Orthopedic Society (NOV) guidelines for DRFs, similar to the American Academy of Orthopaedic Surgeons (AAOS).[11,12] This guideline states that a fracture is unacceptably aligned if one of the criteria is met, as listed in eTable 1. These guidelines have recently been revised in 2021 to contain the most current evidence. The Dutch guidelines are similar to the AAOS guidelines, and contain volar angulation and radial inclination thresholds, in addition to dorsal angulation, radial shortening and intra-articular step-offs.

UMCG, EMC and CAST radiographs were measured by three, four and two different independent observers, respectively, conform to standardized guidelines.[25] All independent observers were clinician-scientists who received in depth radiologic training prior to the start of measurements. Cases that were so called 'bordeline-cases' (i.e. arguably just below-, on- or just above threshold alignment depending on manual measurement) were checked by a second observer and supervised by Fellowship trained Orthopedic (Trauma) Surgeons with experience in treating DRFs.

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Cases were labeled according to the reference standard (i.e. Ground Truth): 1) cases that remained acceptably aligned on all radiographs during longitudinal follow-up were labeled as "stable"; and 2) fractures were labeled as "unstable" when loss of threshold alignment occurred at any subsequent follow-up radiograph according to the Guidelines in Supplement - Table S1.

If a patient underwent surgery while the DRF was still within threshold alignment (i.e. stable according to the Guidelines), the case was excluded. Both trauma- and post-reduction radiographs were collected, however, to reflect clinical practice, cases with only trauma radiographs were not excluded.

2. Interpretable deep learning: Landmark annotation and detection

To augment CNN training, a method called landmark annotation was used. Landmark annotation is a way of gathering attention of the algorithm to relevant points of the radiographs. Eleven landmarks were annotated on postero-anterior (PA) radiographs and ten were annotated on the lateral (LAT) radiographs (see eFigure 2 and eTable2). These landmarks are defined consistently with specific points of interest used in the clinical guidelines to determine fracture alignment.[11,12,25] All available trauma- and post-reduction radiographs were annotated by two independent trained researchers.

A landmark detection model to automatically and accurately detect all 21 pre-defined landmarks was created. To make our framework easily reproducible, a widely used landmark detection model HRNet-v2 was adopted.[26] Two models have been trained separately; one for PA radiographs and one for LAT radiographs. To optimize the landmark detection model, we employ Mean Squared Error (MSE) loss function to compare the predicted landmarks with the ground-truth (manually annotated) landmarks.

3. Final deep learning model: predicting loss of threshold alignment

After acquiring the landmark coordinates, we use all radians and distance features of those landmarks to train the XGBoost predictive classification model. In our experiments, the stable DRFs are defined as the positive class whereas the unstable DRFs are defined as the negative class. The features used to train the model are radians features, distance features and available demographic features (age and sex). We use XGBoost and Scikit-Learn libraries for model creation, training and performance measurements.[27,28] Figure 3 shows an overview of the process to create the algorithm.

4. Statistical analysis

For the loss of threshold alignment algorithm, accuracy (defined as the percentage of cases correctly predicted by the XGBoost model based on CNN produced landmark features), sensitivity, specificity, and area under the receiver operator characteristics curve (AUC) were calculated. The AUC reflects the ability of the algorithm to predict loss of threshold alignment, where an AUC of 1 shows perfect prediction capabilities, and 0.5 indicates a random prediction capability.

The accuracy of the landmark detection (as given above) is determined by the average Euclidean distance between the predicted landmark locations and their corresponding ground-truth radius landmark locations.

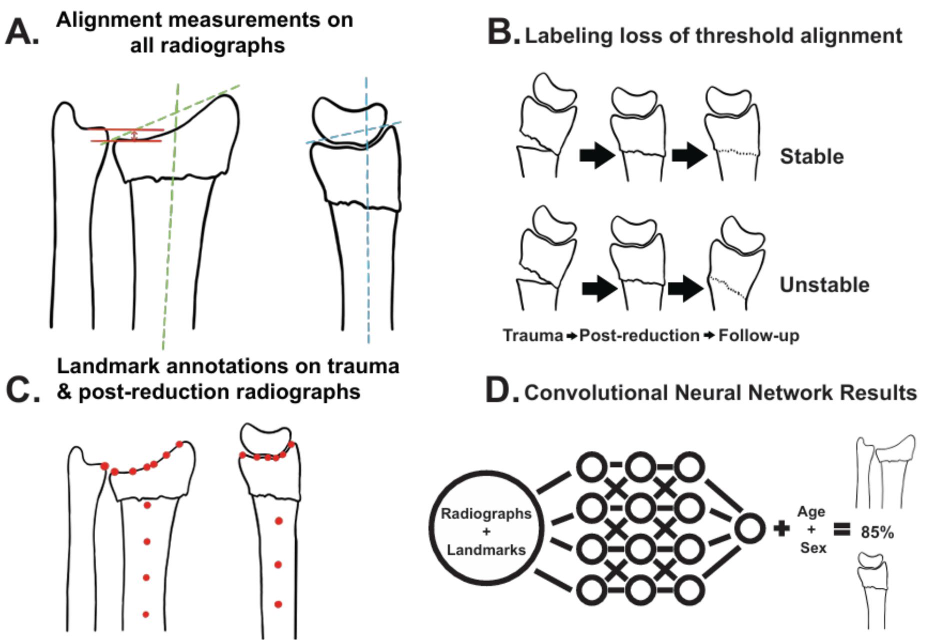

Figure 3. The process of determining loss of threshold alignment and training the algorithm step by step.

RESULTS

Based on a CNN algorithm, we developed a new prediction pipeline, based on DRF trauma and post-reduction radiographs, combined with annotated landmarks and patient age and sex. The complete dataset included 2699 plain radiographs (733 DRF cases, 424 stable and 309 unstable). Of these, 2136 radiographs (583 cases) were used as training set and 563 radiographs (150 cases) were used as test set, taking 50 patients from each cohort, with 1:1 distribution of stable and unstable cases. The best model produced was selected based on accuracy and AUC in predicting loss of threshold alignment.

1. Landmark annotation and detection

eTable 3 demonstrates the mean error of the landmark detection model. On PA radiographs the algorithm achieved a mean error 0.05. On LAT radiographs a mean error 0.07. Figure 4 shows the landmark annotations as given by the algorithm, compared to the manual annotations.

2. Predicting loss of threshold alignment algorithm

eTable 4 shows the performance of our model on the test-set. Our model achieved 0.82 AUC, 76% accuracy, 68% sensitivity and 84% specificity in predicting future DRF loss of threshold alignment when combining PA- and LAT radiographs. The results on PA radiographs are worse compared to LAT radiographs. The algorithm provides physicians with multiple ways of interpretation, coined interpretable AI: 1) landmark visualization; and 2) a percentage-based confidence grade, stating the certainty of its decision.

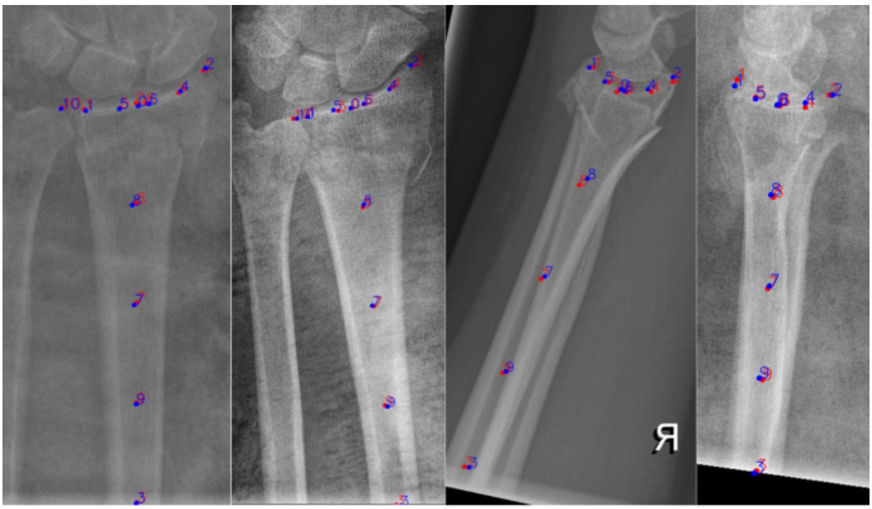

Figure 4. Visualization of landmark detection results on the testing set on postero-anterior view and lateral view, in trauma and post-reduction radiographs. The predicted landmarks (blue), and the corresponding manual landmarks (red) are overlaid to show accuracy.

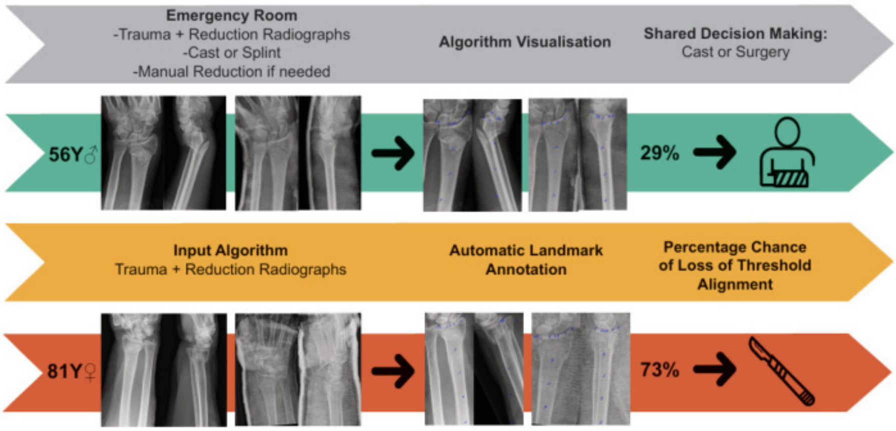

Figure 5. Practical application of the algorithm: patients arrive at the emergency room where radiographs will be made, followed by visualization of the landmarks by the algorithm with a percentage chance of loss of threshold alignment, allowing for shared decision making.

DISCUSSION

This study presents an open-source CNN-based pipeline using trauma and post-reduction radiographs, along with patient age and sex, to predict loss of threshold alignment in DRFs. This CNN outperforms surgeons with an AUC of 0.82 and an accuracy of 76%. As DRF instability is the main driver for surgery this automated CNN probability calculator may enhance the shared decision-making process of patients and surgeons to minimize human biases. Such an AI-driven prediction, combined with surgeon training and empathy, can empower patients to choose for non-operative or operative treatment, based on their personal values and preferences.

In the field of Computer Vision in surgery to date, CNNs have been deployed to detect pathoanatomy. But in the clinical scenario of a DRF, one could argue that mere detection of the fracture is not the real clinical challenge.[29] Surgeons' ability to detect wrist fractures is already satisfactory, however prediction of loss of fracture alignment by surgeons is flawed; with an accuracy of only 54% when evaluating plain radiographs. Therefore, the current results are promising because this is the first CNN used in surgery to make a prediction about an expected clinical outcome that drives surgical treatment.

In addition, this algorithm can provide accurate landmark detection for DRFs, faster than manual annotation. This landmark detection model might be of use for automated measurements of fracture alignment, expediting the manual annotation of large datasets, which takes substantial time. Additional training, in the form of federated learning, of this open-source CNN is facilitated with this.

This study should be interpreted in light of its strengths and weaknesses: First, it was decided to only use patient factors; namely sex and age.[20,30] Other potentially relevant factors, such as osteoporosis and dorsal comminution, were not added, since these are detectable on radiographs and may be part of the CNN's discriminating decision tree. Additionally, the algorithm is trained on radiographs from 11 hospitals, either Dutch university or regional hospitals to enhance future external validation studies, which was a problem with previous wrist instability calculators. Moreover, to increase applicability, we trained the CNN using plain radiographs, instead of more advanced imaging techniques such as computed tomography (CT). It is known that CT provides more accurate assessment of fracture details (e.g. degree of comminution, articular involvement) in comparison to standard radiographs, but radiographs are the golden standard for diagnosing DRFs in Emergency Departments around the world, being fast and inexpensive.[31] Future computer vision studies will include CT.

This study has a number of limitations. First, the number of DRF cases is limited for CNN training standards, even though the added landmark detection algorithm improved diagnostic performance. We therefore consider the results promising and encourage other groups to further train our -open source- CNN in order to find plateau in diagnostic performance characteristics. Another limitation is that both the fracture alignment measurements and the landmark annotations were carried out manually by separate independent observers. Although no accurate alternatives were available to date, manual measurements and annotations are susceptible for human mistakes. Finally, different countries or hospitals might use diverse criteria for fracture malalignment. For instance, the AAOS guideline does not contain volar angulation and radial inclination thresholds, but our algorithm is indeed trained with these strict criteria of instability.[11]

The impact of this predictive algorithm in daily clinical practice is promising because almost 50% of successfully reduced DRFs will lose threshold alignment during non-operative treatment, and we do not know which fractures.[15] Half of these fractures can be treated conservatively whilst the others would most probably benefit from surgery. A recent online experiment objectified the performances of surgeons in predicting future loss of threshold alignment in DRFs.[13] A total of 116 surgeons from several countries were provided with trauma- and post-reduction radiographs, sex and age.[13] Human accuracy was 54% with a sensitivity and specificity of 56% and 31% respectively, compared to Machine accuracy of 76% and sensitivity and specificity of 84% and 68%. Upon evaluation of DRF CT scans, surgeons' predictive performances improved to 74% accuracy. The superior performances of our CNN confirms that AI-driven probability calculations can help to minimize human biases. A more objective probability of patient's DRF stability as visualized in a decision making dashboard -rather than the treating surgeon's guesstimation- with landmarks represented on trauma and reduction radiographs to increase explainability (eFigure 3). This will greatly facilitate the shared decision making process, and will empower patients with their personalized probabilities of outcome to choose a treatment strategy that represents their values.[26,27]

CONCLUSION

Our study presents a CNN algorithm capable of predicting loss of threshold alignment in DRFs with a promising accuracy based on a limited number of radiographs. This algorithm might aid clinicians and patients in their shared decision-making process. Simultaneously a landmark prediction algorithm was created, capable of automatically detecting DRF features with high accuracy for explainability of the CNN. We encourage other groups to further train our open source model using additional datasets to find the plateau of peak diagnostic performance, and subsequently validate this decision tool in clinical practice.

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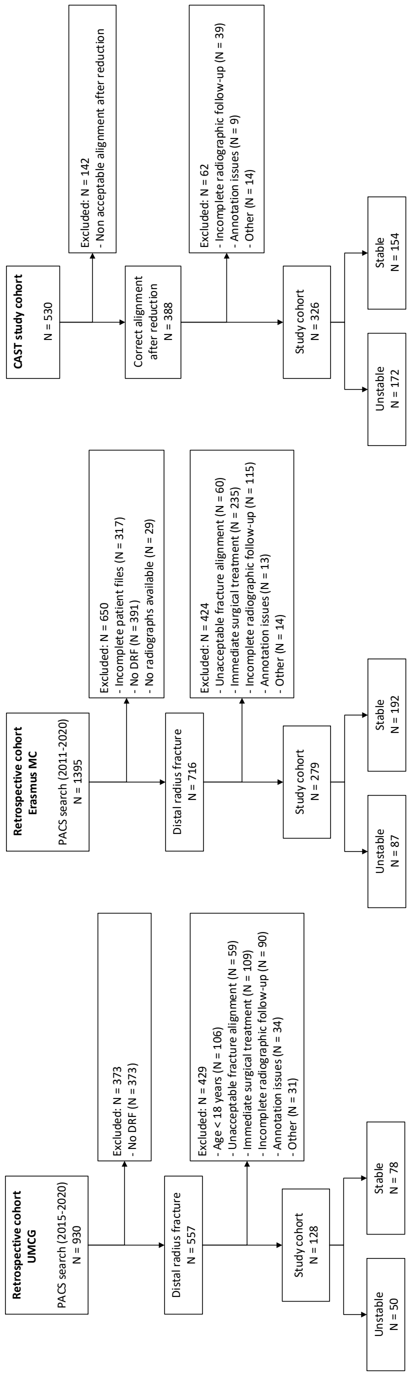
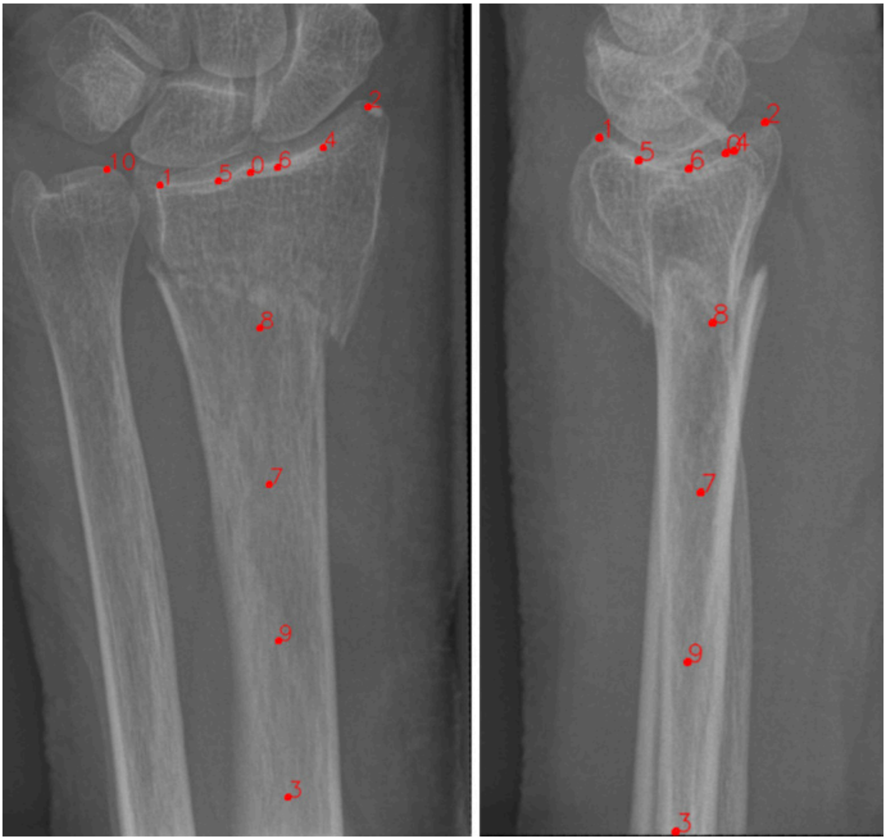
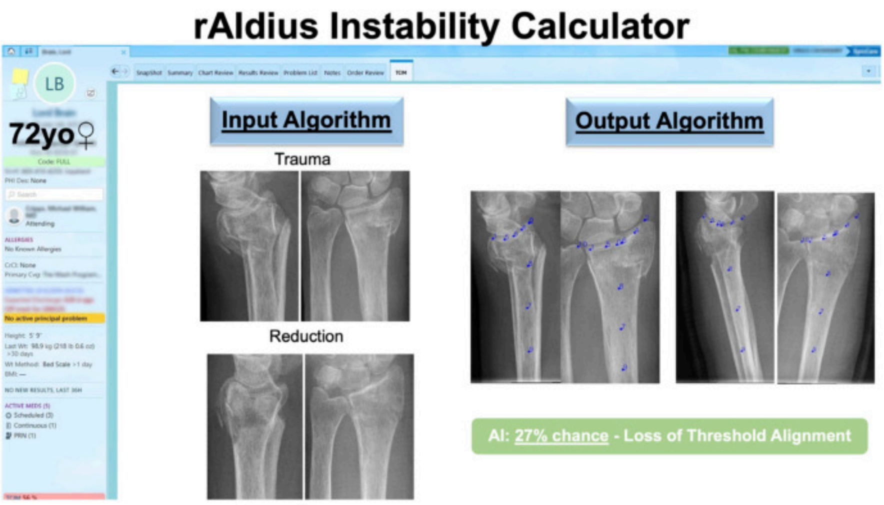
SUPPLEMENTAL MATERIALS



eFigure 1. Flowchart of patient cohort selection.



eFigure 2. Manual landmark annotation on both the postero-anterior and lateral radiograph.



eFigure 3. Future vision: application of the algorithm in electronic patient files.

eTable 1. Alignment criteria for DRFs conform the Dutch Guideline.

Measure parameter	Not acceptable
Dorsal angulation	≥10°
Volar angulation	≥20°
Radial inclination	≤15°
Radial shortening/ulnar variance	≥3 mm
Intra-articular step-off	≥2 mm

eTable 2. Instructions for manual landmarks as annotated in radiographs. Landmarks 0 to 6 and 10 for PA-radiographs, and 0 to 6 for lateral radiographs were manually annotated. Landmarks 7, 8 and 9 for PA-radiographs, and 7, 8 and 9 for lateral radiographs were automatically created by the algorithm based on manual landmarks.

PA radiographs landmarks:		Lateral radiographs landmarks:	
0	Most distal point of radial axis	0	Most distal point of radial axis
1	Most ulnar point of radial articulate surface	1	Most dorsal point of radial articulate surface
2	Most radial point of radial articulate surface	2	Most volar point of radial articulate surface
3	Most proximal point of radial axis, or the middle of the radius at the isthmus	3	Most proximal point of radial axis, or the middle of the radius at the isthmus
4	Point between landmark 2 and 6 on radial articulate surface	4	Point between landmark 2 and 6 on radial articulate surface
5	Point between landmark 1 and 6 on radial articulate surface	5	Point between landmark 1 and 6 on radial articulate surface
6	Middle of the radial articulate surface	6	Middle of the radial articulate surface
7	Point halfway between most proximal and distal point of radial axis.	7	Point halfway between most proximal and distal point of radial axis.
8	Point halfway between landmark 0 and 7	8	Point halfway between landmark 0 and 7
9	Point halfway between landmark 3 and 7	9	Point halfway between landmark 3 and 7
10	Most radial point of ulnar articulate surface		

eTable 3. Mean error of landmark detection on test set.

Radiograph	Mean error
PA view	0.05
Lateral view	0.07

PA: postero-anterior

eTable 4. Predictive performances of the model on the test-set.

Radiograph	Accuracy (%)	AUC	Sensitivity (%)	Specificity (%)
PA + lateral view	76	0·82	68	84
PA view	61	0·72	32	91
Lateral view	69	0·78	53	85

PA: postero-anterior, AUC: area under the receiver operator characteristics curve

PART II

Influence of casting techniques on redisplacement

Chapter 4

Does circumferential casting prevent fracture redisplacement in reduced distal radius fractures? A retrospective multicentre study

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ABSTRACT

Background: This study evaluates whether a circumferential cast compared to a plaster splint leads to less fracture redisplacement in reduced extra-articular distal radius fractures (DRFs).

Methods: This retrospective multicenter study was performed in four hospitals (two teaching hospitals and two academic hospitals). Adult patients with a displaced extra-articular DRF, treated with closed reduction were included. Patients were included from a 5-year period (January 2012 – January 2017). According to the hospital protocol, fractures were immobilized with a below elbow circumferential cast (CC) or a plaster splint (PS). The primary outcome concerned the difference in the occurrence of fracture redisplacement at one-week follow-up.

Results: A total of 500 patients were included in this study (PS n=184, CC n=316). At one week follow-up, fracture redisplacement occurred in 52 patients (17%) treated with a CC compared to 53 patients (29%) treated with a PS. This difference was statistically significant (p=0.001).

Conclusion: This study suggests that treatment of reduced DRFs with a circumferential cast might cause less fracture redisplacement at 1 week follow-up compared to treatment with a plaster splint

INTRODUCTION

Distal radius fractures (DRFs) are the most common fractures seen in the emergency room. Despite its high incidence, a worldwide diversity in treatment strategies exists. This is especially true for displaced DRFs in the adult population [1, 2].

Displaced DRFs are generally reduced and immobilized in either a plaster splint (PS) or a circumferential cast (CC). Unfortunately, 30-40% of reduced DRFs are unstable which results in fracture redisplacement during the cast immobilization period [3-5]. To prevent fracture redisplacement, the choice for early surgical reduction and plate fixation is gaining popularity [5]. Concerning functional outcome and complication risks, the clinically relevant benefit of surgery in comparison to cast immobilization is not convincing. For a large group of patients, especially elderly people, cast immobilization is therefore still the first choice of treatment [6].

It would be ideal to predict fracture redisplacement of DRFs in an early stage to aid physicians in their decision making whether to perform surgery or not. The scope of many studies in displaced DRFs is focused on defining fracture characteristics predicting fracture instability (e.g. age, degree of initial displacement and metaphyseal comminution of the fracture)[4, 7, 8]. However, good quality evidence concerning the influence of the type of casting (PS or CC) on fracture redisplacement is lacking.

The choice for a CC or PS is usually based on the hospitals protocol and preference of the treating physician [6, 9]. A potential benefit of circumferential casting is more stability during fracture immobilization [3]. A possible benefit of splinting is the allowance of soft-tissue swelling which may reduce pain and the risk of a compartment syndrome [10].

No evidence exists yet that shows superiority of one technique above the other regarding fracture redisplacement in reduced DRFs [9, 11]. This study aims to evaluate whether a circumferential cast compared to a plaster splint reduces the risk of fracture redisplacement in reduced extra-articular distal radius fractures in adults during the first treatment week.

METHODS

This manuscript is written according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [12].

Study design

This retrospective multicenter study was conducted in the Netherlands. Patient selection took place in four hospitals (two teaching hospitals and two academic medical centers). Eligible patients who visited the emergency room of one of the participating hospitals between January 2012 and January 2017 were included.

Data collection

Adult patients (≥18 years) with a displaced extra-articular distal radius fracture (AO/OTA classification 23-A.2 (simple) and 23-A.3 (metaphyseal comminution)) treated with a below elbow CC or below elbow PS were included [13]. The decision for a CC or a PS was mostly based on the hospitals protocol and preference of the treating physician. Exclusion criteria comprised: no reduction performed, type of cast unknown, other types of immobilization than below elbow CC or PS, registered cast modifications during the first week of follow-up (e.g. cast cleavage), concomitant fracture of the ulna (except ulnar styloid process' fractures), no radiographs available at one-week follow-up and failed reductions with unacceptable fracture displacement after reduction. Unacceptable fracture displacement is defined according to the Guidelines of the American Academy of Orthopaedic Surgeons [6]. This guideline defines displacement as radial shortening >3 mm, or dorsal angulation >10 degrees. General patient data (age, gender and fracture type) and treatment-related data (the type of cast and radiographs) were retrospectively reviewed.

Outcomes

The primary outcome concerned the occurrence of fracture redisplacement at one-week follow-up, opting operative fixation as defined by the Guidelines of the American Academy of Orthopaedic Surgeons [6]. A subanalysis was performed for simple fractures and fractures with metaphyseal comminution. Furthermore, we analyzed fracture angulation and radial length separately.

Measurements

The degree of volar or dorsal angulation was measured on the lateral view radiographs. This value represents the angle between a line along the distal radial articular surface and a line perpendicular to the longitudinal axis of the radius (Figure 1a)[10]. Radial shortening was measured on the posteroanterior radiograph and refers to the distance between the carpal joint surface of the radius and the most distal part of the ulnar articular surface (Figure 1b) [14]. These measurements were performed 3 times; before reduction (T0), post-reduction (T1) and at 1-week follow-up (T2). Radiographic measurements were carried out digitally in the locally available picture archiving and communication systems (PACS). To determine the direction of fracture redisplacement, the difference in angulation at T1 and T2 was used.

All measurements were performed by one researcher (AB). To evaluate inter-and intra-observer variability, 50 measurements were repeated and compared to one another by an orthopaedic surgeon (JC) and the researcher (AB).

Statistical analysis

Statistical analyses were performed using SPSS (version 24; IBM). A *p*-value of <0.05 was considered significant. There was no missing data. Mann-Whitney U tests were used to describe baseline characteristics since they were all non-normally distributed. The Pearson Chi-Square test was used to compare the appearance of fracture redisplacement after one-week follow-up between both groups. Differences in radial shortening and angulation were assessed using the independent samples Mann-Whitney U test. An Intraclass Correlation Coefficient (ICC) was calculated to assess inter-and intra-observer variability in radiograph measurements. A two-way mixed-effects model was used, based on a single measurement with an absolute agreement definition. Values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 are indicative of poor, moderate, good, and excellent respectively [15].

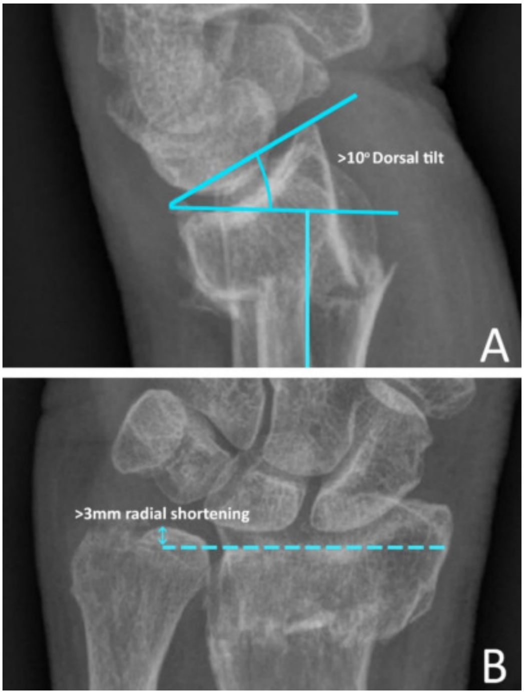

Figure 1. Fracture displacement measured according to the AAOS guideline.
Figure 1a. The degree of angulation (volar or dorsal) was measured on the lateral view radiographs. This value represents the angle between a line along the distal radial articular surface and the line perpendicular to the longitudinal axis of the radius [10].
Figure 1b. Radial shortening was measured on the posteroanterior radiograph and refers to the distance between the carpal joint surface of the radius and the most distal part of the ulnar articular surface [14].

RESULTS

Patient selection

The patient selection workflow is displayed in Figure 2. The initial selection contained 4.013 patients treated in four hospitals. A total of 500 cases remained after eliminating patients meeting the exclusion criteria.

Baseline characteristics

Baseline characteristics are displayed in Table 1. The PS group consisted of 184 patients and the CC group of 316 patients. Patients were predominantly female in both groups, namely 85% in the PS group and 91% in the CC group. The age distribution was similar in both groups. No between group differences were observed concerning the severity of fracture displacement at admission. The PS group consisted of relatively more fractures with metaphyseal comminution (AO/OTA 23-A.3) compared to the CC group, respectively 16% versus 9%. In both groups several DRFs were minimally displaced before reduction, meaning ≤3 mm radial shortening and ≤10 degrees of dorsal angulation. There was no significant difference concerning the distribution of minimally displaced fractures.

Fracture displacement

At 1-week follow-up, fracture redisplacement occurred in 29% of patients treated with a PS compared to 17% in patients treated with a CC ($p = 0.001$). Similar results were found in subgroup analyses for simple fractures as well as fractures with metaphyseal comminution ($p = 0.009$ and $p = 0.02$, Table 2).

At 1 week follow-up, radial shortening occurred in 30% of fractures treated with a PS versus 15% of fractures treated with a CC (p=0.038). Re-angulation was seen more often in fractures treated with a CC (75% vs 43%, p=0.001). These results are displayed in Table 3.

Inter- and intra-observer variability

Intraclass correlation coefficients (ICCs) of 0.88 (95% C.I. 0.75-0.94) and 0.88 (95% C.I. 0.79-0.93) were determined for respectively inter- and intra-observer variability regarding the measurement of radial shortening. Regarding fracture angulation measurements ICCs of 0.67 (95% C.I. 0.49-0.80) and 0.66 (95% C.I. 0.47-0.79) were found for respectively inter- and intra-observer variability.

Table 1. Baseline characteristics

	Splint n=184	Circumferential cast n=316	P value
Female, n (%)	157 (85)	289 (92)	**0.033**
Age, years	66 (56;79)	67 (56;75)	0.738
Fracture displacement at T0			
Angulation*, degrees	21 (13;27)	23 (14;31)	0.055
Radial shortening, mm	-2(-3;0)	-1 (-3;0)	0.622
Fracture classification (AO/OTA)			**0.008**
Simple (AO/OTA 23-A.2), n (%)	154 (84)	289 (91)	
Metaphyseal comminution (AO/OTA 23-A.3), n (%)	30 (16)	27 (9)	
Minimally displaced fracturesΩ, n (%)	30 (16)	41 (13)	**0.304**

Data is presented as medians with the interquartile range between parentheses
n = number of patients
T0 = at admission to emergency room
*** =** Dorsal angulation is referred to as a positive number. In case of volar angulation, this is referred to as a negative number.
Ω = Minimally displaced fractures concern fractures with ≤3 mm radial shortening and ≤10 degrees of dorsal angulation

Table 2. Radiographic results

	Before reduction			At 1 week follow-up		
	Splint (n=184)	Circumferential (n=316)	P-value	Splint (n=184)	Circumferential (n=316)	P-value
Displaced fractures, n (%)	184	316	0.30	53	52	**0.001**
Simple fractures, n (%)	154	289	0.21	43	50	**0.009**
Fractures with metaphyseal comminution, n (%)	30	27	0.89	10	2	**0.023**

n = number of patients

Table 3. Radial shortening and angulation in redisplaced fractures at 1-week follow-up

Displaced fractures	Splint (n=53)	Circumferential (n=52)	P-value
Radial shortening*, n (%)	16	7	0.038
Angulation Ω, n (%)	23	39	0.001
Radial shortening* and angulation Ω, n (%)	14	6	0.052

n = number of patients
*** =** radial shortening >3mm
Ω = dorsal angulation >10 degrees

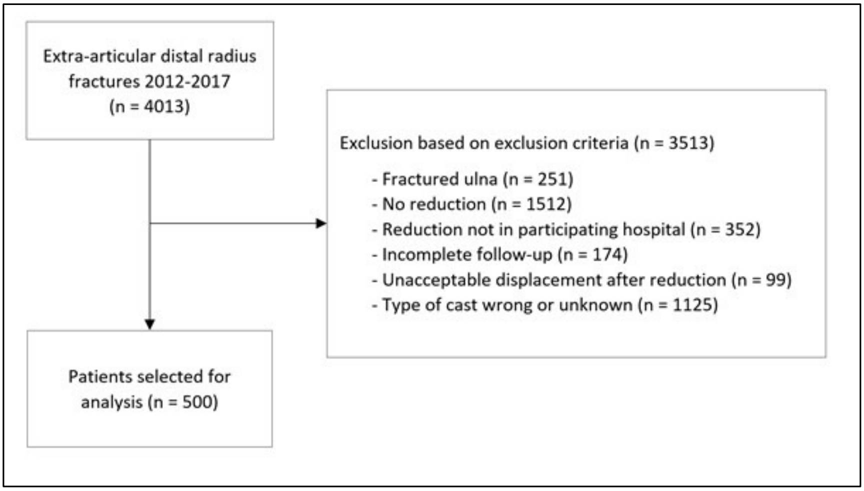

Figure 2. Flowchart of the selection process

DISCUSSION

This study showed that one week post-reduction, fracture redisplacement occurred almost twice as often in reduced DRFs immobilized with a below elbow PS compared to those treated with a below elbow CC (29% versus 17%). Amongst fractures with metaphyseal comminution (AO/OTA 23-A.3), almost five times as much redisplacement occurred in fractures treated with a PS compared to those treated with a CC (33% versus 7%).

A unique advantage of this study is the large number of patients included (n=500). Patient selection took place in four hospitals, both academic and teaching hospitals, yielding a representative image of the patient population and treatment differences [16].

Concerning existing literature on this topic, only few articles focus on the influence of immobilization techniques on reduced DRFs. A systematic review by Handoll et al. (n=4215) and more recent prospective studies by Grafstein et al. (n=101), Wik et al. (n=72) and O'Connor et al. (n=66) compared circumferential casting (above-and below-elbow), plaster splints (dorsal and volar splints), synthetic splints (sugar-tong fibreglass splints, volar and dorsal fibreglass splints) and braces [9, 11, 17, 18]. In these studies, no significant differences were found between immobilisation types regarding the occurrence of fracture redisplacement. Above mentioned studies have different setups which makes it hard to adequately compare outcomes. Grafstein et al. reported the loss of reduction in 16% of splinted DRFs versus 20% of circumferential casted DRFs [17]. However, in this study, loss of reduction was defined as the occurrence of radiologic slippage (based on radiographs of the complete casting period) or surgical fixation performed during the immobilization period. The definition of radiologic slippage is not further clarified in the article. O'Connor et al. performed a randomised controlled trial (n=66) comparing a plaster cast with a lightweight removable splint [18]. In both groups, one patient suffered fracture displacement. Unfortunately, radiographic details and the type of plaster casting used, either splint or circumferential, is not mentioned.

Interestingly, loss of radial length occurred twice as much in fractures treated with splinting compared with fractures treated with circumferential casting. The outcome is conform to previous research by Wik et al. [11]. Better preservation of radial length in reduced DRFs treated with a CC might be explained by more equal pressure distribution, both volarly and dorsally. This minimizes potential shearing and migration of the fracture. This theory is supported by a study of Alemdaroglu et al. They studied the impact of casting technique-related indices and found the three-point index to be useful in predicting fracture redisplacement (sensitivity of 96%, specificity of 96%)[3]. It makes sense to hypothesize that flattening a wet circumferential applied cast at the level of the wrist before it has hardened is essential to prevent redisplacement. Noteworthy to mention is that radial shortening seems to have the most significant negative impact on patient-reported outcomes during follow-up, making this parameter a potentially important factor in predicting outcome [19].

This study has its limitations. First, because of the retrospective design, patient-reported outcomes (e.g. pain scores, the comfort of casting) are not registered. However, multiple previous studies found no significant difference in pain severity when comparing circumferential casting to splinting [9, 11, 17, 18]. Second, we have no data available concerning the occurrence of adverse events. We consciously chose to focus on radiographic outcome alone. In our opinion, there is a high risk of bias searching for adverse events retrospectively. Especially patient complaints and minor adverse events are not always reported consistently. A potential disadvantage of applying a CC directly after fracture reduction is the assumed higher risk of pressure-related problems, in ultimo reflected in a higher incidence of compartment syndrome of the forearm [20]. The occurrence of this serious complication is often used as an argument against the circumferential casting. However, the reported prevalence of compartment syndrome in unstable DRFs is very low (0-0.25%) and current knowledge of the prevalence in extra-articular DRFs is lacking [21, 22].

Third, we chose to include a select group of patients. Only extra-articular DRFs were included because the inter-observer variability of radiograph measurements in extra-articular fractures is lower compared to intra-articular fractures [23, 24]. We only included patients who did not encounter cast modifications during the first week of treatment to diminish the number of external factors that could possibly influence the reduction.

There was a difference regarding the distribution of extra-articular fractures with metaphyseal comminution. Relatively more fractures with metaphyseal comminution were found in the PS group. These fractures are considered to be more unstable compared to simple DRFs [7]. However, when excluding these fractures from the analysis, fracture redisplacement still occurred almost twice as much in the PS group.

Finally, this study focused on a limited timeframe of treatment, namely the first week. This point was chosen to minimize confounding by other factors that might influence the process of redisplacement (e.g. cast alterations or cast replacement). Thereby the included hospitals have different follow-up protocols which could influence the outcome. The results of this study should therefore be carefully interpreted as a first insight in the effect of immobilization on reduced DRFs.

Conclusion

This study suggests that circumferential casting in reduced extra-articular distal radius fractures might cause less fracture redisplacement during the first treatment week compared to treatment with a plaster splint. Fracture redisplacement occurred twice as much in patients treated with a plaster splint compared to treatment with a circumferential cast. Important questions about functional outcome, complication risks and patient reported outcomes are still to be answered. Therefore, a randomized controlled trial will be conducted to confirm the current findings, taking functional outcome, complication risks and patient-reported outcome into account[25].

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Chapter 5

The CAST study protocol: A cluster randomized trial assessing the effect of circumferential casting versus plaster splinting on fracture redisplacement in reduced distal radius fractures in adults

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ABSTRACT

Background: There is no consensus concerning optimal casting technique for displaced distal radius fractures (DRFs) following closed reduction. This study evaluates whether a splint or a circumferential cast is most optimal to prevent fracture redisplacement in adult patients with a reduced DRF. Additionally, the cost-effectiveness of both cast types will be calculated.

Methods/Design: This multicenter cluster randomized controlled trial will compare initial immobilization with a circumferential below-elbow cast versus a below-elbow plaster splint in reduced DRFs. Randomization will take place on hospital-level (cluster, n=10) with a cross-over point halfway the inclusion of the needed number of patients per hospital. Inclusion criteria comprise adult patients (≥ 18 years) with a primary displaced DRF which is treated conservatively after closed reduction. Multiple trauma patients (Injury Severity Score ≥ 16), concomitant ulnar fractures (except styloid process fractures) and patients with concomitant injury on the ipsilateral arm or inability to complete study forms will be excluded. Primary study outcome is fracture redisplacement of the initial reduced DRF. Secondary outcomes are patient-reported outcomes assessed with the Disability Arm Shoulder Hand score (DASH) and Patient-Rated Wrist Evaluation score (PRWE), comfort of the cast, quality of life assessed with the EQ-5D-5L questionnaire, analgesics use, cost-effectiveness and (serious) adverse events. In total, 560 patients will be included and followed for one year. The estimated time required for inclusion will be 18 months.

Discussion: The CAST study will provide evidence whether the type of cast immobilization is of influence on fracture redisplacement in distal radius fractures. Extensive follow-up during one year concerning radiographic, functional and patient reported outcomes will give a broad view on DRF recovery.

Trial registration: Registered in the Dutch Trial Registry on January 14th 2020. Registration number: NL8311. https://www.trialregister.nl/trial/8311

BACKGROUND

Displaced distal radius fractures (DRF's) are very common in the adult population and their incidence is still increasing because of the ageing population [1, 2]. In the Netherlands, the incidence of DRFs is estimated at 20 per 10.000 persons per year [3]. Two-thirds of DRFs in adults are displaced and require closed reduction [4]. After successful reduction, DRFs are generally immobilized using a non-circular splint or a circumferential cast. Unfortunately, a large number of reduced DRF's (32%-64%) redisplace during cast immobilization in the first treatment weeks [5-7]. Whereas redisplacement of DRFs was previously accepted or reduced in a second attempt, nowadays these redisplaced fractures are generally treated surgically [8, 9].

Although surgical reduction and fixation generally results in a satisfying outcome, preventing fracture redisplacement and thereby preventing surgery would be the preferred scenario. Therefore, it is important to discover factors that could predict or prevent fracture redisplacement. Studies focusing on this topic are mostly assessing non-modifiable factors predicting fracture redisplacement [5-7, 10]. Known factors enhancing the risk on fracture displacement are female gender, age > 60 years and fractures with dorsal comminution [10]. However, it is unknown if type of cast immobilization is of influence.

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Existing literature concerning the role of cast immobilization on fracture re-displacement is scarce and inconclusive [11]. Recently, Caruso et al. (2019) performed a randomized controlled trial comparing the effect of above-elbow casting and below-elbow casting on maintaining reduction and found similar results in both groups [12]. Patient-reported outcome after 1-year follow-up did not differ amongst both treatment groups. A randomized controlled trial by Wik et al. (2009) evaluated fracture alignment during 5 weeks follow-up in 72 patients with displaced DRF's treated with dorsal splinting versus circumferential casting [13]. The circumferential casting group showed a significantly better result for radial length at 5 weeks but no difference concerning dorsal angulation. Recently, our research group conducted a retrospective study in 500 patients with reduced DRFs and found significantly less fracture redisplacement in fractures treated with circumferential casting compared with splinting, namely 17% versus 29% [14].

The choice for a splint or circumferential cast is often based on the treating physician's preference [11]. A splint could be considered easy and quick to apply which is favorable at busy emergency departments, but it can loosen easily. One argument for not applying a circumferential cast initially after reduction is the risk of pain and comprised circulation due to swelling. Several studies however found none or mild differences in pain complaints comparing circumferential casting with splinting [13, 15, 16].

This study aims to clarify if type of cast immobilization influences maintaining fracture alignment in reduced adult distal radius fractures. A cluster randomized controlled trial is designed to compare the treatment of reduced DRFs with a splint or a circumferential cast. Radiological, functional and patient-reported outcomes are studied during a one-year study period.

METHODS/DESIGN

This manuscript is written according to the Consolidated Standards for Reporting Trials (CONSORT statement) and Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT guidelines [17, 18]).

1. Objectives

The primary objective is to assess which type of cast, a splint versus a circumferential cast, is most optimal to prevent fracture redisplacement in adult patients with a reduced DRF.

As secondary objectives, we assess which type of casting results in fewer surgical interventions and complications. Thereby we will assess cost-effectiveness, the comfort of the cast, pain scores, functional outcome, patient-reported outcome and quality of life.

2. Design, participants, interventions and outcomes

Study design and randomization

For this study, a multicenter cluster randomized design is used. All participating hospitals are located in the Netherlands and include the following 10 centres; Alrijne hospital (Leiderdorp), Elisabeth-Tweesteden hospital (Tilburg), Erasmus MC University Medical Center (Rotterdam), Franciscus hospital, location Gasthuis and Vlietland (Rotterdam and Schiedam), Haga Teaching hospital (Den Haag), Haaglanden Medical Center (Den Haag), IJsselland hospital (Capelle aan den IJssel), Maasstad hospital (Rotterdam), Reinier de Graaf Gasthuis (Delft) and St. Antonius Hospital (Utrecht and Nieuwegein).

Two types of cast immobilization will be compared in this trial. Randomization at patient level will be challenging because of the 24/7 availability of the Emergency Department (ED), leading to a high number of treating physicians. To overcome the potential of many protocol violations, we chose to randomise on hospital-level with a cross-over point halfway the needed inclusions per hospital (i.e. after 31 inclusions). This means all patients in one hospital will receive the same intervention, which will change after half of the number of patients are included. This cross-over design is used to overcome potential non-eligibility of both groups because patient populations can differ amongst hospitals. Secondly, possible bias due to existing experience with one of the techniques in each hospital will be diminished. Before the start of the study, an independent researcher not involved in the study, randomly allocated the starting treatments amongst the participating hospitals.

Study population

Participants and recruitment

The study population will consist of adult patients who visit the ED of participating hospitals with a distal radius fracture needing reduction. Fractures who should be reduced conform to the Dutch guideline meet one or more of the following criteria: > 15° of dorsal angulation, > 20° of volar angulation, < 15° of radial inclination, > 3 mm of radial shortening and > 2 mm intra-articular step-off or gap.

Patients that match the inclusion criteria are informed about the study by the treating physician before closed reduction. All patients receive written information, namely the patient information folder (PIF) and a short information folder containing the study aim, contact information of the local hospital and general information about cast immobilization. Because of the acute status of a sustained fracture, patients will be asked for participation in the study directly after diagnosis of a displaced DRF. Written informed consent is obtained before the study procedure starts.

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Inclusion criteria

- Age ≥ 18 years
- Distal radius fracture requiring closed reduction

Exclusion criteria

- Concomitant ulnar fracture (styloid process fracture not encountered)
- Multiple trauma patients (Injury Severity Score (ISS) ≥ 16)
- Concomitant injuries to the ipsilateral extremity, interfering with the treatment of the DRF
- Inability to complete study forms due to any mental status or insufficient understanding of the Dutch language

Study procedures and timeline

Measurements will take place at 7 time points as shown in table 1. These time points are: baseline (T0), 1 week (T1), 2 weeks (T2), 5 weeks (T3), 3 months (T4), 6 months (T5) and 1 year (T6) after inclusion in the study. At T0, baseline characteristics will be gathered. An inclusion form will be filled in by the treating physician providing fracture and treatment-specific information. Second, patients receive a questionnaire, providing predominantly patient and injury-specific information. The list of baseline characteristics is shown in table 2. Patients receive questionnaires at T1 to T6. These questionnaires are carried out by email with the use of data capture system GemsTracker [19]. GemsTracker (GEneric Medical Survey Tracker) is a secure web-based application for distribution of questionnaires and forms during clinical research and quality registrations. Receiving questionnaires on paper is optional, as well as telephone interviews. Reminders will be automatically sent. When the patient does not respond to emails, we will contact the patient by telephone. Posterior-anterior (PA) and lateral radiographs of the wrist will be taken at T0 (before and after reduction) and during follow-up at T1 –T3. Physical examination of the wrist will take place at T4 and will be performed by the researcher. If patients are not able to visit the hospital, a home visit will be offered to improve the follow-up.

Interventions

We will compare two casting options that are applied directly after reduction: a plaster of Paris envelope splint (further called splint) versus a below-elbow forearm cast (further called circumferential cast). Both interventions are shown in figure 1 and 2. The splint or circumferential cast will be applied by an ED nurse, a cast technician, the physician or a physician assistant. Both interventions will be implemented by education and training. Education will be available at the ED's at all times by means of an instruction video and an instruction poster. The need for training of both casting techniques is evaluated before the start of the study and differs amongst participating hospitals. We chose hospital individualized training instead of a general training program because participating hospitals differ in: the currently used treatment, the experience of ED nurses with both casting techniques and the availability of cast technicians at the ED. In case extra training is needed, training is organized by local cast technicians, in accordance with the research group.

Figure 1. Plaster splint

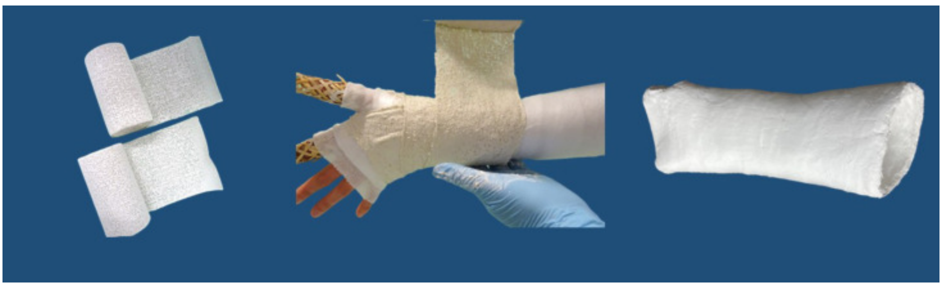

Figure 2. Circumferential cast

Outcome

Primary outcome

The primary outcome of this study is the occurrence of fracture re-displacement of the initial reduced DRF assessed on PA and lateral radiographs at 1, 2 and 5 weeks after reduction. Displacement of the radius is defined by the Dutch guideline: > 15° of dorsal angulation, > 20° of volar angulation, < 15° of radial inclination, > 3 mm of radial shortening and > 2 mm intra-articular step-off or gap. Measurements will be digitally carried out in the Picture Archiving and Communication System (PACS) on standard PA and lateral radiographs of the wrist. PA and lateral radiographs will be taken conform standardised procedures. An Intraclass Correlation Coefficient (ICC) will be calculated to assess inter- and intra-observer variability in radiograph measurements. For this, 50 radiographs will be measured twice by BB and NS.

Secondary outcomes

An overview of measurements is shown in table 1.

- Comfort of the cast assessed using a self-developed questionnaire at T1 and T2.
- Severity of pain evaluated with the Numeric Rating Scale (NRS) at T1 to T6.
- Patient-reported recovery of function assessed using the Quick Disabilities of the Arm, Shoulder and Hand questionnaire (Q-DASH) and the Patients-Rated Wrist Hand Evaluation questionnaire (PRWHE). Both questionnaires are validated for assessing functional outcome in patients with a DRF (20-22). Questionnaires will be carried out at T3 to T6.
- Quality of life will be assessed using the 5-level EuroQol (EQ-5D-5L)[23] scoring questionnaire at T1 (pre- and postfracture state) and T3 to T6.
- Cost-effectiveness will be measured using the Medical Consumption Questionnaire (iMCQ) and the Production Consumption Questionnaire (iPCQ)[24]. Questionnaires will be sent at T3 to T6.
- Recovery of function will be evaluated by physical examination at T4.
    - ◊ Range of motion (ROM) of the wrist will be measured with a goniometer. ROM concerns dorsal flexion, volar flexion, radial deviation, ulnar deviation, pronation and supination.
    - ◊ Grip strength will be measured with a Jamar hydraulic hand dynamometer. Patients get three attempts on both sides. The maximum score for each side is used in the analyses.
    - ◊ Specific testing of the wrist and hand will be performed namely:
        - distal radioulnar joint (DRUJ) stability tested with the DRUJ ballottement test [25]
        - opposition of the thumb using the Kapandji score [26]
        - finger stiffness will be measured with finger-to-palm distance, tested from the tip of the finger to the distal palmar crease when the fingers are in maximal active flexion [27]
        - ROM and grip strength on the injured side will be compared with the uninjured side.
- Number of conversions to surgical treatment and other (serious) adverse events will be monitored and are listed at 1.9.

5

Modified follow-up by partial exclusion

Patients are recruited before fracture reduction because immobilization takes place immediately after reduction. A part of included patients will receive surgical fixation in the first treatment week, due to unsuccessful fracture reduction. Consequently, it is unavoidable to include patients who will eventually be unsuitable to answer the primary research question. Patients receiving surgical fixation before the first follow-up appointment (T1) will not be encountered in the needed patient numbers. Recovery of these patients will be evaluated by questionnaires only (figure 3).

(Serious) Adverse events reporting

All adverse events reported by the patient or observed by the treating physician or researcher will be recorded. Serious adverse events (SAE) will be reported through the web portal *ToetsingOnline* of the Central Committee on Research Involving Human Research (Dutch CCMO) to the Medical Research Ethics Committee of Erasmus Medical Center in Rotterdam, which approved the protocol. SAE reporting will take place within 7 days after the sponsor has first knowledge of a serious adverse event resulting in death or is life-threatening. All other SAE will be reported within 15 days.

Adverse events are defined as:
- Cast or splint related problems
- Fracture redisplacement treated with surgical reduction and fixation
- Complex regional pain syndrome (CRPS) defined conform the Budapest criteria
- Disabling fracture mal-union or non-union

Study related serious adverse events are defined as:
- Compartment syndrome

Sample size

The sample size calculation is based on the results of our recent retrospective study [14]. We hypothesize that fracture redisplacement occurs in 10% of circumferential casted patients versus 20% in splinted patients. A total of 500 patients is needed to detect superiority of a circumferential cast. The sample size calculation is based on a mixed-effects logistic regression, to account for clustering using a random intercept for the hospitals. The intra-class correlation coefficient between the different hospitals for the proportion of fracture redisplacement is assumed to be 0.06, which is generally reported in the literature for hospital processes. From the expected proportions of redisplacement in the two groups, we calculated the hospital-specific log odds of secondary displacement in the circular cast group, equal to -2.275 and log odds ratio of redisplacement between the two groups equal to 0.84. This calculation is based on the formula that links the cluster-specific coefficients in the mixed-effects logistic regression with the population coefficients averaged over the hospitals. With a power of 93%, 50 patients per hospital need to be included, resulting in a total number needed of 500 (10 participating hospitals). Additionally, we also calculated the needed number of patients using a two-sample test for proportions. Using the same assumptions, namely difference between groups, a significance level of 0.05 and a power of 90%. This resulted in 490 needed patients in total. Accounting for a 10% loss to follow-up, a total of 560 (280 patients per group) are required.

To improve awareness of the study in all participating centers and thereby advert for reaching targeted sample size, a local investigator is appointed in each hospital. This local investigator is a physician who supervises the study. This person is easily accessible and will promote the study on a regular base. We send a newsletter every two months to inform about the study progression.

DATA ANALYSIS

General descriptive statistics will be performed on baseline patient and fracture characteristics. Patients will be analyzed according to the intention-to-treat principle.

Primary outcome

The primary outcome, fracture re-displacement, will be analyzed using a mixed-effects logistic regression. To account for clustering, a random intercept for the hospitals will be used. Fixed effects will be the covariates we adjust for as reported in the literature, namely age, presence of osteoporosis, and fracture characteristics. If new prognostic factors will be identified and reported in the literature, these factors will also be added as covariates.

Secondary outcomes

For secondary outcomes, trends between baseline and follow-up time points (T0-T6) will be assessed using linear mixed models for repeated measures. This accounts for comfort of the cast, recovery of function and grip strength, pain severity (NRS), Q-DASH scores, PRWHE and EQ-5D-5L scores. The number of conversions to surgical fixation and complications will be determined using Fisher Exact or Chi-square test, depending on the magnitude of results.

Cost-effectiveness analysis

Both cost-effectiveness (CEA) and cost-utility (CUA) analysis will be performed from a societal perspective. For the calculation of medical costs, we will use charges as published in Dutch guidelines as a proxy of real costs. The unit per price of the cast and splint application in patients with DRF will be calculated with the micro-costing method. Intramural costs (i.a. additional diagnostics, number of hospital visits, in case of hospital admission the length of stay etc.) are collected from the electronic health record. Productivity costs will be registered in detail by the iPCQ. The iMCQ and the iPCQ are validated by the Institute of Medical Technology Assessment (Erasmus University, Rotterdam, The Netherlands).

The difference in costs and effects of a circumferential cast instead of a splint will be calculated as incremental cost-effectiveness ratio (ICER). The primary effect outcome measures will be the number of re-displacements for the CEA and quality-adjusted life years (QALY) for the CUA. QALYs will be measured, based on the Dutch tariff for the EQ-5D-5L.

The sensitivity analysis will assess the robustness of the results to changes in costs and effect parameters. Bootstrapping with 5000 replications will be used to estimate 95% confidence intervals around cost differences and the uncertainty surrounding the ICERs. This will be graphically presented on cost-effectiveness planes and acceptability curves using the net benefit framework [28, 29]. For the time horizon of 1 year, discounting is not necessary.

DATA MANAGEMENT

All data are handled confidentially and anonymized in compliance with the Dutch Personal Data Protection Act. Personal data of participants will be changed by a study number. This number is used for all study documentation, study reports and publications. The key of this study number will be handled by an independent researcher. During the study period, all data will be collected and managed using GemsTracker electronic data capture tools hosted at Erasmus Medical Center [19]. Paper case report forms are entered in GemsTracker by the researcher and the original paper case forms will be filed in the investigator site file at the recruiting hospital. All data is stored for 15 years.

Data monitoring

Since the study is labelled as low risk, a data safety monitoring board is not required. However, the study will be monitored at least once a year by an independent monitoring board. A written report will be available from all monitors.

The investigator will submit a progress report to the accredited Medical Research Ethics Committee of Erasmus Medical Center in Rotterdam throughout the clinical trial annually. This will consist of the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, SAEs, other problems and amendments.

Dissemination

We plan to present the study results at (inter)national conferences and submit the manuscript to general peer-review journals. We aim to implement the study results in the Dutch guideline for DRFs.

DISCUSSION

This study is an open-label trial. Allocated treatments are visually different for the treating physician and the patient. Randomization status will therefore not be blinded.

Heterogeneity of the study population concerning fracture characteristics and age could be pointed out as a limitation. However, this pragmatic study tries to represent the actual patient population.

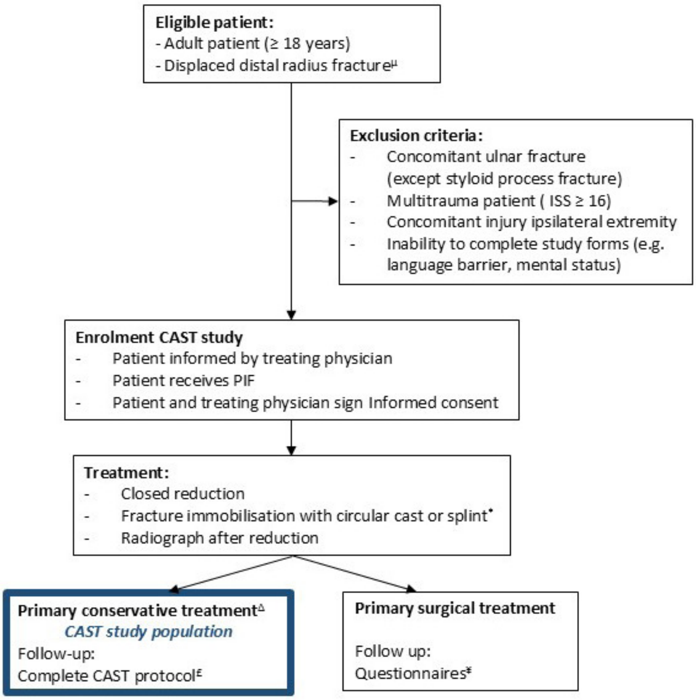

Figure 3 CAST study follow-up flowchart.

*Type of treatment depends on randomization status of the hospital

µ Unacceptable alignment conform the Dutch guideline: > 15° of dorsal angulation, > 20° of volar angulation, < 15° of radial inclination, > 3 mm of radial shortening and > 2 mm intra-articular step-off or gap.

Δ Cast immobilization, at least until the first control radiographs are taken

£ All measurements encountered in table 1

¥ All questionnaires encountered in table 1

Table 1. Overview of measurements.

	T0	T1	T2	T3	T4	T5	T6
	Baseline	**1 week**	**2 weeks**	**5 weeks**	**3 months**	**6 months**	**1 year**
Inclusion form	x						
X-rays[α]	x	x	x	x			
Function tests [β]					x		
NRS		x	x	x	x	x	x
Comfort of cast		x	x				
Analgesic use		x	x	x	x	x	x
EQ5D5L		x[Ω]		x	x	x	x
QDASH				x	x	x	x
PRWHE				x	x	x	x
MCQ-iMTA				x	x	x	x
PCQ-iMTA				x	x	x	x

[α] X-rays before and one after reduction
[β] Concerning ROM, grip strength and specific tests
[Ω] EQ5D5L status pre-fracture and post-fracture sustainment
Questionnaires are written in italics

Table 2. Baseline characteristics

Inclusion form	Questionnaire
Date of emergency room visit	Sex
Affected wrist	Date of birth
Method of reduction	Length
Reduction executed by:	Weight
(e.g. specialist, resident, intern, nurse, cast technician)	Hand dominance
Number of reduction attempts	Mechanism of injury
Type of cast applied	Smoking status
Application of cast executed by:	General medical history
(e.g. specialist, resident, intern, nurse, cast technician)	Previous injuries of the affected extremity
Neurovascular status of fractured hand/wrist	

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Chapter 6

Redisplacement of reduced distal radius fractures in adults; does casting type play a role? The CAST study, a multicenter cluster randomized controlled trial

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ABSTRACT

Aims: It is unclear which casting type provides the best fracture support in distal radius fractures (DRFs). Given that 32–64% of adequately reduced DRFs redisplace during cast immobilisation, preventing redisplacement and thereby preventing a disabling malunion or belated surgery is preferred. We investigated whether circumferential casting (CC) leads to fewer fracture redisplacements and better one-year outcomes compared to plaster splinting (PS).

Methods: In a pragmatic, open-label, multicenter, two-period cluster-randomised superiority trial, we compared two casting types (CC versus PS). Recruitment took place in ten hospitals. Eligible participants (age ≥ 18 years) had a displaced DRF that was acceptably aligned after closed reduction. The primary outcome was incident radiographic redisplacement within five weeks of cast immobilisation. Secondary outcomes were cast complaints, clinical outcomes at three months, patient-reported outcomes (numeric rating of pain scale [NRS], Quick Disabilities of the Arm, Shoulder and Hand [QDASH] and Patient-Rated Wrist/Hand Evaluation [PRWHE] questionnaires), and adverse events (e.g. compartment syndrome) during one-year of follow-up. We used multivariable mixed-effects logistic regression for the primary outcome analysis.

Results: The study sample comprised 420 patients. No significant difference existed in incident redisplacement between interventions (CC 49%, PS 47%, p = 0.85, OR = 1.05, 95% CI 0.65–1.70). PS patients reported more pain than the CC group during the first week of treatment (NRS 4.7 vs. 4.1, p = 0.014). Cast complaints, clinical outcomes and patient-reported outcomes did not differ between groups (p > 0.05). Compartment syndrome did not occur.

Conclusions: Circumferential casting did not result in fewer fracture redisplacements compared to plaster splinting. Both casting techniques resulted in comparable outcomes.

TAKE HOME MESSAGE

- It is unknown if casting type affects the redisplacement risk of reduced adult distal radius fractures and if casting type influences patient-reported outcomes.

- The CAST study found that circumferential casting was not superior to plaster splinting in reducing the fracture redisplacement risk.

- No statistically significant differences in clinical outcomes, patient-reported outcomes or adverse events up to one year were found.

INTRODUCTION

Optimal management of displaced distal radius fractures (DRFs) in adults remains a matter of controversy.[1, 2] The high fracture redisplacement rate in reduced DRFs, reported to be 32–64% in literature, substantially contributes to the emerging tendency to manage DRFs with surgery.[3-5] Preventing fracture redisplacement during cast immobilization and, thereby, a disabling malunion or belated surgery would be preferred to improve clinical outcomes and reduce the need for costly surgical interventions.

In current clinical practice, a plaster splint or a circumferential cast is used to stabilise the fracture. Plaster splinting is often preferred initially, mainly because of its easy application and allowance for soft tissue swelling. Circumferential casting, in theory, provides better three-point fixation and thereby prevents redisplacement.[6] However, it might be associated with higher intracast pressures, potentially increasing the risk of developing compartment syndrome syndrome as studied in a biomechanical model in the lower limb.[7] Results from studies focusing on cast complications in DRFs are inconclusive on that matter.[8, 9]

Although our research group recently concluded from a retrospective multicenter study that circumferential casting might reduce the risk of fracture redisplacement in comparison to plaster splinting[10], an earlier meta-analysis found insufficient evidence to determine the best cast type and duration of immobilisation to manage DRFs.[11] Furthermore, it is unknown if the type of casting influences patient-reported and clinical outcomes. Also, no clinical trials report on patient experiences and cast complaints in different casting types.

This trial aimed to determine whether circumferential casting resulted in a lower incidence of radiographic fracture redisplacement in reduced DRFs in adults, when compared to plaster splinting. We hypothesized that circumferential casting would provide superior fixation and, therefore, would result in lower risk of fracture redisplacement. We also aimed to compare cast complaints and clinical outcomes at three-months follow-up, and patient-reported outcomes and adverse during one-year follow-up.

METHODS

Trial design

The CAST study was a pragmatic, open-label, multicenter, two-period cluster-randomised superiority trial to compare the incidence of fracture redisplacement in displaced and reduced DRFs treated with circumferential casting versus plaster splinting. The rationale and design of the CAST study have been published previously.[12] The medical ethical board of the Erasmus Medical Center approved the trial in 2019 (MEC-2019-0528). Enrollment took place from 30 May 2020 until 11 November 2021. Trial administration, data management and analyses were conducted at the Erasmus MC University Medical Center.

Patient involvement

Patients were involved in several stages of the trial. Prior to the start, a panel of DRF patients was formed to think along with our study. Structured interviews were conducted with a subgroup of participants, to ask for their preferred method of communication about the study results. Results will be disseminated through a newsletter sent by email and main results will be published on a dedicated web page.

Patient population

Patient recruitment and inclusion took place in ten hospitals (one university hospital, nine teaching hospitals) located in the Netherlands (details in Supplementary Appendix). Adult patients (age ≥ 18 years) admitted to the Emergency Department (ED) with a displaced DRF requiring closed reduction were invited to participate. Both extra- and intra-articular fractures were included. Exclusion criteria included both-bone fractures (solitary ulnar styloid process fractures were accepted), concomitant injuries to the ipsilateral extremity affecting DRF treatment, polytrauma (Injury Severity Score ≥ 16), or inability to complete study questionnaires due to cognitive impairment or insufficient understanding of the Dutch language. Written informed consent was obtained at the ED before closed reduction of the DRF. Post-reduction alignment was therefore unknown at the moment of inclusion. When the treating physician decided, based on post-reduction alignment, to conservatively treat the DRF, the participant was included in our study cohort. During data management we discovered that numerous conservatively treated DRFs had an unacceptable post-reduction alignment conform the Dutch guideline for DRFs. We decided to refine the inclusion criteria to only include DRFs that were adequately reduced.

Interventions

Patients were randomised between immobilisation using a below-elbow plaster of Paris volar-dorsal splint (PS) or a below-elbow complete circumferential cast (CC) as shown in Figure 1A and B. Casting is applied directly after reduction.In case one of the interventions was not frequently used in a participating hospital, staff applying the casts were trained and provided with instructional videos and posters. Circumferential casts could be made with either plaster of Paris or synthetic material (e.g. fiberglass), based on availability of materials or preference of the cast applicant.

Randomization and masking

Randomization took place with clustering at the hospital level, with a cross-over to the other treatment arm halfway the needed inclusions per hospital. Prior to the start, an independent researcher randomly allocated the starting treatments amongst the participating hospitals. Treatment started directly after randomisation. Treating physicians and patients were not blinded since casting types are visualy different from each other. During the data analysis, the interventions were masked.

Figure 1. Study interventions

Figure 1A. Plaster splint.

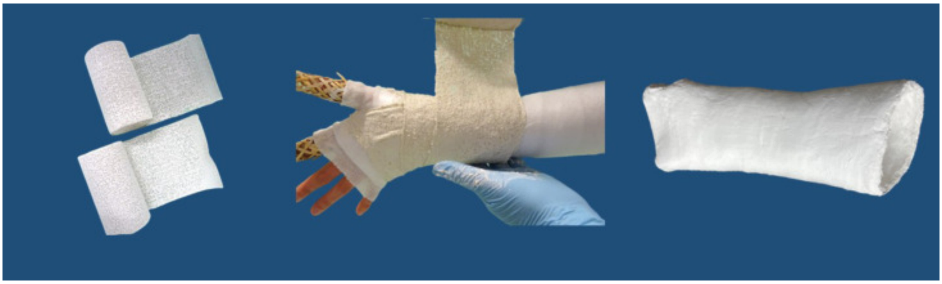

Figure 1B. Circumferential cast. Synthetic casting was also accepted instead of plaster of Paris.

Primary outcome

Our primary outcome was incident fracture redisplacement during cast immobilisation (five-week follow-up). Fracture redisplacement is defined by the Dutch guideline for DRFs. A fracture is unacceptably aligned or redisplaced when it meets one or more of the following criteria: ≥ 15° of dorsal angulation, ≥ 20° of volar angulation, ≤ 15° of radial inclination, ≥ 3 mm of radial shortening and ≥ 2 mm intra-articular gap or step-off. We labelled a DRF as redisplaced when it was no longer acceptably aligned conform these criteria during follow-up. Radiographic measurements were performed on all radiographs (trauma, post-reduction and at one, two, and five weeks of follow-up) and carried out by two trained investigators (BB and SS). An intraclass correlation coefficient ([ICC], two-way mixed and absolute agreement) was calculated to assess inter- and intra-observer reliability in radiograph measurements. These analyses showed almost perfect inter- and intra-observer reliability for all measurements (ICC 0.84–0.99). Only gap/step-off measurements on lateral radiographs showed moderate intra-rater reliability (ICC 0.56).

Secondary outcomes

Secondary outcomes included clinical outcomes, patient-reported outcomes and adverse events. The clinical outcomes included: wrist range of motion (ROM), grip strength, sensory nerve testing, thumb opposition using the Kapandji score, distal radio-ulnar joint (DRUJ) stability, and complex regional pain syndrome (CRPS) analyses with the Budapest criteria. The research team, which was not involved in the treatment, performed this clinical examination at three months of follow-up. Detailed information about clinical outcome assessments is described in the design paper.[12] Patient-reported outcomes comprised of cast complaints, pain severity measured using the numeric rating scale (NRS) and function measured with the Quick Disabilities of the Arm, Shoulder and Hand (QDASH) questionnaire and Patient-Related Wrist/Hand Evaluation (PRWHE) questionnaire. Cast complaints questions are described in the design paper.[12] Patients received questionnaires at several time points: one week, two weeks, six weeks, three months, six months and twelve months. Cast complaints and NRS scores were questionned at weeks one and two. The QDASH and PRWHE questionnaires were measured from three months to twelve months. Adverse events were scored during twelve months.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 28.0.1.0 and R version 4.2.2 (packages lme4 v1.1.31 and nlme v3.1.162). We considered a two-sided p-value of less than 0.05 to be statistically significant. A detailed description of the sample size calculation is available in the design paper.[12] We hypothesized that fracture redisplacement would occur in 10% of DRFs treated with CC versus 20% of those treated with PS. To detect a significant between-group difference with 93% power at a 0.05 significance level, 500 patients were needed. Accounting for 10% loss to follow-up, we required 560 patients (280 per group).

All outcomes were analysed as randomised (intention-to-treat). We analysed all participants that were initially treated conservatively (at least one follow-up appointment after one week, including radiographs). Patients who were immediately planned for surgical fixation, with or without an acceptable fracture alignment after reduction, were excluded since no assumptions can be made about fracture stability when the fracture is surgically fixated.

For the primary outcome analysis, we performed multivariable logistic mixed-effects regression. The following variables were included in the model to correct for potential confounding: baseline age, sex, diagnosed with osteoporosis, severity of angulation (°), inclination (°), radial shortening (mm), and intra-articular incongruence of the fracture. Age, angulation, inclination and radial shortening were treated as continuous variables. Sex, osteoporosis and articular incongruence were added as dichotomous variables. Intra-articular incongruence is defined as the presence of an intra-articular gap or step-off. We included a random intercept at the hospital level to account for within-hospital correlation.

Clinical outcomes at three months, cast complaints, and adverse events were reported as relative frequencies and tested using an independent-samples t-test for normally distributed data and a Mann–Whitney U test for non-normally distributed data. We analysed the NRS, QDASH and PRWHE questionnaires using linear mixed-effects models. To evaluate between-group differences during the follow-up period, we included an interaction between the visit moment and randomisation group. Baseline age and sex were included in the models as independent variables to correct for potential confounding. We considered an unstructured covariance matrix to account for both the within-subject correlation of repeated measurements and the between-subject variability accross different hospitals. We assessed the model's underlying assumptions, particularly regarding the normality and homoscedasticity of the residuals. The proportions of loss to follow-up and evaluated patterns of missingnes, based on individual and fracture characteristics are reported.

RESULTS

Study population

A total of 752 patients with a displaced DRF agreed to participate and were enrolled (Figure 2). From this cohort, 183 patients were immediately planned for surgery and were thus excluded. Of 567 conservatively treated DRFs, 110 were excluded from the analyses since these fractures were unacceptably aligned after reduction. The final trial sample comprised 420 patients (PS: 213 patients, CC: 207 patients). Table 1 shows the baseline characteristics of the trial sample and the excluded sample of unacceptably reduced fractures.

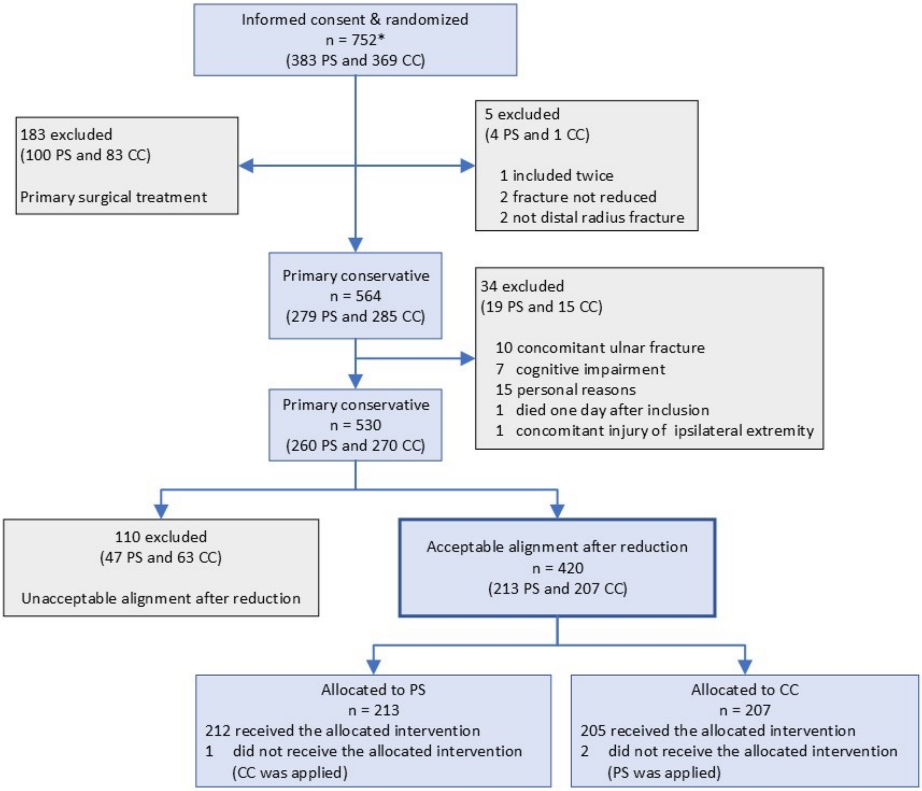

Figure 2. Flowchart of patient enrollment.
* According to Dutch privacy law, it is forbidden to screen electronic patient reports for eligible patients who did not participate in our study. Cases were analyzed according to the intention-to-treat principle. n: number of patients, PS: plaster splint, CC: circumferential cast.

Table 1. Patient and fracture characteristics of the main study cohort and the unacceptably reduced cohort.

	Main study cohort		**Unacceptably reduced**
	Plaster splint n = 213	Circumferential cast n = 207	n = 110
Patient characteristics			
Women, n (%)	177 (83)	174 (84)	94 (86)
Age, years	62.2 (15.4)	62.9 (15.7)	69.9 (4.5)
BMI, kg/m²	25.5 (5.0)	24.3 (3.8)	25.3 (4.2)
Osteoporosis, n (%)	44 (21)	35 (17)	26 (24)
Diabetes, n (%)	16 (8)	12 (6)	9 (8)
Current smoker, n (%)	25 (12)	22 (11)	9 (8)
Fracture characteristics			
Dominant side affected, n (%)	108 (51)	110 (53)	47 (43)
Ulnar styloid fracture, n (%)	98 (46)	109 (53)	58 (53)
Dorsal angulation, n (%)	201 (94)	194 (96)	103 (95)
Angulation, °	21.7 (11.4)	21.1 (10.5)	24.4 (13.3)
Radial inclination, °	16.7 (5.5)	16.7 (6.3)	11.1 (6.6)
Radial shortening, n (%)	102 (48)	101 (50)	75 (70)
If yes, ulnar variance, mm	2.5 (1.4)	2.9 (2.3)	3.9 (2.4)
Intra-articular, n (%)	85 (40)	95 (46)	76 (69)
Post reduction fracture alignment			
Dorsal angulation, n (%)	101 (47)	106 (51)	88 (80)
Angulation, °	5.3 (3.8)	5.4 (4.0)	11.4 (7.5)
Radial inclination, °	21.8 (3.5)	22.3 (3.5)	16.5 (5.3)
Radial shortening, n (%)	25 (12)	30 (15)	48 (44)
If yes, ulnar variance, mm	1.6 (0.7)	1.4 (0.6)	2.7 (1.3)

If not noted differently, information is presented as mean with standard deviation between parentheses. BMI: body mass index, ^{0}: degrees, n: number of patients.

Primary outcome

Fracture redisplacement occurred in 47% (n = 88) of PS patients versus 49% (n = 90) of CC patients, and this difference was not significant (p = 0.85, adjusted OR = 1.05, 95% CI 0.65–1.70). A flowchart of fracture redisplacement during follow-up is shown in Figure 3. Of the 420 patients, 49 (12%) were not included in the primary outcome analysis. These dropouts were due to missing follow-up radiographs or fractures being surgically fixated while not redisplaced. The baseline and fracture characteristics of these 49 individuals were found to be similar to completers (Supplementary Appendix, Table S1). Therefore, missingness was assumed to be independent of the outcome to be measured and it was thus disregarded in the analysis.

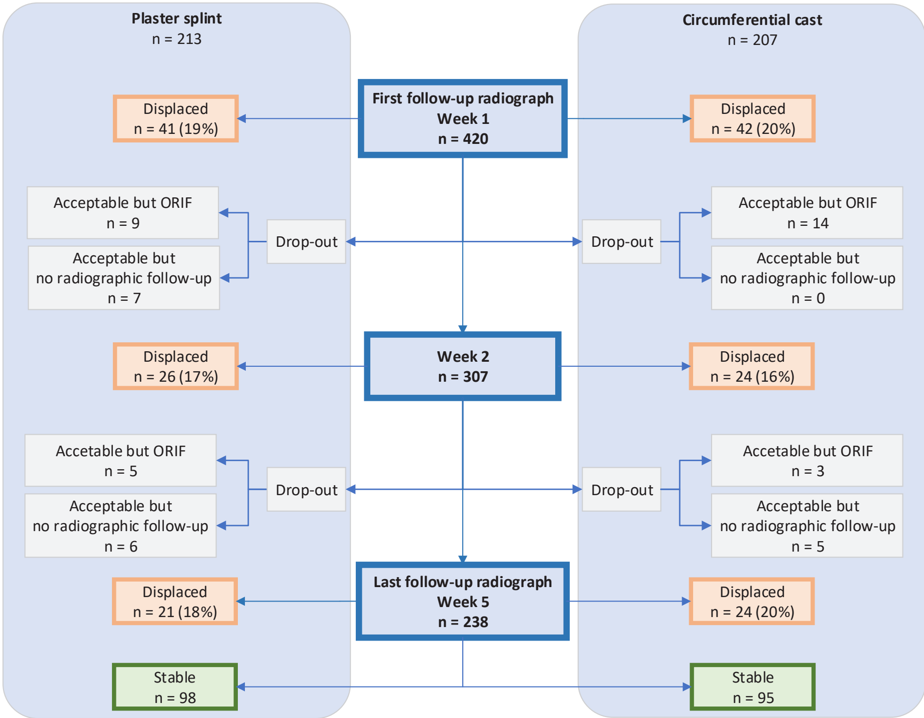

Figure 3. Flowchart of redisplacement incidence per intervention during follow-up.
ORIF: open reduction and internal fixation, n: number of patients

Secondary outcomes

Clinical outcomes

Physical examination at three months of follow-up was attended by 387 patients (PS: 92%, CC: 93%). The mean interval between trauma and this appointment was 98 days (range 74–184, SD 15.7). There were no significant between-group differences in ROM, grip strength, thumb opposition or DRUJ stability (Table 2).

Patient reported outcomes

During the first week of treatment, pain during rest was significantly worse for PS patients compared to CC patients (NRS 4.7 vs. 4.1, p = 0.014) (Table 3). During the second week, there were no significant between-group differences in all pain score subdomains. Analgesic use in the first two weeks was comparable for both groups (week 1 PS: 86%, CC: 89%, p = 0.40 and week 2 PS: 71%, CC 62%, p = 0.06). Regarding reported cast comfort, there was no between-group difference in the first treatment week. At two weeks, 12.5% of PS patients reported their cast to be very uncomfortable, compared to 5.1% of CC patients, though this was not significant (p = 0.073). There were no between-group differences concerning cast complaints, such as tightness, swollen fingers, insufficient support, tingling or itchiness. At two weeks follow-up, PS patients reported severe complaints of swollen fingers more often, though this was not significant (15.1% vs. 9.6%, p = 0.08). The patient-reported outcomes QDASH and PRWHE demonstrated no significant between-group differences at any time points (Table 4).

(Serious) Adverse events

Adverse events are listed in Table 5. The number of unplanned extra hospital visits during cast immobilisation did not differ between groups. The reason for an additional visit was because of cast complaints in 70% of CC patients and 88% in PS patients. No cases of compartment syndrome occurred. Seven patients died during the one-year follow-up period (PS: 4, CC: 3).

Table 2. Range of motion and grip strength at three months follow-up.

	Plaster splint n = 195		Circumferential cast n = 192		
	Mean	Percentage compared to uninjured side	Mean	Percentage compared to uninjured side	P value*
Palmar flexion, °	43 (13.1)	69 (19.5)	45 (13.8)	72 (20.4)	0.18
Dorsal flexion, °	48 (15.1)	79 (22.4)	49 (13.1)	81 (24.2)	0.77
Radial deviation, °	16 (6.1)	89 (45.2)	16 (6.6)	90 (33.8)	0.24
Ulnar deviation, °	23 (8.6)	77 (31.6)	23 (8.6)	73 (21.4)	0.47
Pronation, °	71 (13.4)	92 (14.3)	71 (13.0)	91 (14.3)	0.81
Supination, °	67 (15.8)	84 (18.2)	67 (15.0)	83 (17.6)	0.65
Grip strength, kg	14 (8.4)	54 (23.0)	14 (8.0)	55 (24.1)	0.73

Information is presented as mean with standard deviation between parentheses.
*: Mann Whitney U, n: number of patients, ^{0}: degrees.

Table 3. Estimated pain NRS scores

	Week 1	Week 2
Response rate		
Plaster splint	91%	87%
Circumferential cast	92%	91%
Pain at rest		
Plaster splint	4.7 (4.3 to 5.1)	3.3 (2.9 to 3.7)
Circumferential cast	4.1 (3.7 to 4.4)	3.1 (2.7 to 3.4)
Between-group difference	-0.6 (-1.2 to -0.1)*	0.4 (-0.1 to 0.9)
Pain during activity		
Plaster splint	6.6 (6.2 to 6.9)	5.5 (5.1 to 5.8)
Circumferential cast	6.2 (5.8 to 6.5)	5.3 (4.9 to 5.6)
Between-group difference	-0.4 (-0.9 to 0.1)	0.2 (-0.3 to 0.6)
Worst pain this week		
Plaster splint	7.6 (7.3 to 8.0)	6.3 (5.9 to 6.6)
Circumferential cast	7.4 (7.1 to 7.8)	6.1 (5.8 to 6.5)
Between-group difference	-0.2 (-0.7 to 0.2)	0.1 (-0.4 to 0.6)
Frequency of pain this week		
Plaster splint	6.1 (5.8 to 6.5)	5.1 (4.7 to 5.4)
Circumferential cast	5.7 (5.3 to 6.0)	4.7 (4.4 to 5.1)
Between-group difference	-0.5 (-1.0 to 0.0)	0.1 (-0.3 to 0.6)

Estimated NRS scores, corrected for baseline age and sex, with associated 95% confidence intervals.
The NRS score ranges from 0 to 10, with higher scores indicating more pain. *: P value < 0.05

Table 4. Estimated QDASH and PRWHE scores during follow-up.

	6 weeks	3 months	6 months	12 months
Response rate				
Plaster splint	92%	94%	86%	87%
Circumferential cast	89%	93%	86%	91%
QDASH				
Plaster splint	46 (44 to 49)	29 (27 to 32)	18 (16 to 21)	16 (13 to 18)
Circumferential cast	47 (44 to 49)	28 (25 to 31)	19 (16 to 21)	16 (13 to 18)
Between-group difference	0.2 (-3.3 to 3.8)	-1.6 (-4.7 to 1.5)	0.2 (-3.7 to 4.0)	-0.5 (-4.5 to 3.6)
PRWHE				
Plaster splint	61 (58 to 64)	39 (36 to 42)	24 (21 to 27)	19 (16 to 22)
Circumferential cast	60 (57 to 63)	37 (34 to 40)	23 (20 to 26)	19 (16 to 22)
Between-group difference	-0.6 (-4.9 to 3.8)	-1.6 (-5.4 to 2.2)	0.1 (-4.6 to 4.8)	0.5 (-4.4 to 5.4)

Estimated QDASH and PRWHE scores, corrected for baseline age and sex, with associated 95% confidence intervals.
The scores range from 0 to 100, with higher scores indicating a greater level of disability, pain and functional disability.

Table 5. (Serious) Adverse events

	Plaster splint n = 213	Circumferential cast n = 207
Serious adverse events		
Redisplaced and ORIF[ß]	25 (28)	24 (27)
Acceptably aligned and ORIF[¥]	17 (17)	18 (19)
Implant removal	1 (0.5)	2 (1)
Malunion surgery	4 (2)	2 (1)
CTS release surgery	-	4 (2)
Compartment syndrome	-	-
Adverse events		
Unplanned extra hospital visits	42 (20)	48 (23)
Additional cast replacement	14 (7)	8 (4)
Dysaesthesia[ɸ]	48 (25)	53 (28)
CRPS[ɸ]	1 (0.5)	5 (2)
CTS	4 (2)	8 (4)

Information is presented as frequency with percentages between brackets. [α]Dropouts are excluded from this count. [ß]Frequency in redisplaced sample (PS: 88, CC: 90). [¥]Frequency in acceptably aligned sample (PS: 98 CC: 95). [ɸ]Concerns subset of sample who participated in physical examination (PS: 195, CC: 192). n: number of patients, CTS: carpal tunnel syndrome, CRPS: complex regional pain syndrome, ORIF: open reduction and internal fixation

DISCUSSION

The type of casting—circumferential versus plaster splinting—did not influence the incidence of fracture redisplacement in reduced DRFs in adults. Clinical outcomes were comparable between interventions after three months follow-up, and QDASH and PRWHE outcomes did not differ at any time point. Cast complaints were also similar between groups, although the PS group reported slightly more pain during the first week of treatment, a difference that was likely not clinically relevant.

In this large cohort, nearly half of DRFs redisplaced. This incidence is comparable with previous literature, which reported redisplacement in 32% to 64% of reduced DRFs.[3-5] Interestingly, redisplacement often occurred during the second week or later in the present study. This emphasizes the need for regular radiographic follow-up during immobilization.[3, 4, 13]

No clinically relevant differences were found in terms of pain or cast experience. However, some findings are noteworthy to point out. The rate of extra hospital visits due to cast complaints was high in both groups and casts are generally experienced as uncomfortable. Future research should focus on designing more comfortable immobilization options. Circumferential casted patients reported significantly less pain in the first week, and less severe complaints of finger swelling in the second week. These findings were notable because it is generally believed that circumferential casting increases pain and finger swelling due to the limited allowance available in the cast to permit soft tissue swelling. Overall, these results imply that circumferential casting may be as safe and effective as splinting, supported by a recent retrospective trial.[8] Lastly, higher incidents of CRPS and carpal tunnel syndrome were seen in the CC group. These incidents are serious, but too few to assume a causal relation with casting type based on this cohort. Future research should further explore this possible relationship.

The clinical outcomes at three months were generally good and in line with previous studies in conservatively treated DRFs.[14, 15] ROM results varied between 69% and 92% of the unaffected side. Grip strength was most affected in both groups with mean results of 54% and 55% of the unaffected side respectively. These results are comparable to previous smaller studies in which grip strength varried between 57% and 68%.[14, 16, 17]

PRWHE and QDASH scores did not differ between groups at any time visit. Questionnaire scores were relatively high after six weeks, comparable with previous randomised trials.[14, 18] These high scores represent a large burden for patients. This finding, combined with the high pain scores in the first weeks, imply the importance to manage patient expectations at the beginning of the treatment, as previously suggested.[19] Patient-reported outcomes improved most during the first six-months in the present study, but slight improvements were seen beyond six months. This pattern has been reported previously.[14, 18, 20] To determine whether patients are satisfied with the final outcome, results can be compared with the patient acceptable symptom state (PASS) of both QDASH and PRWHE. The QDASH PASS is estimated to be below 15.9 and for PRWHE this is below 22.[21, 22] Results from the present study showed that QDASH and PRWHE scores were below PASS thresholds at the one-year follow-up, suggesting that patients were satisfied with their treatment.

This trial has some notable strengths. First, this trial is, to our knowledge, the largest RCT performed in conservatively treated reduced DRFs. Second, due to the cluster randomisation at the hospital-level and the large number of participating hospitals (n = 10), this study offers a reliable and generalizable representation of the patient population and fracture characteristics of reduced DRFs. It could be argued that randomisation at patient level is more appropriate, but we consciously decided not to do so. Because of the 24/7 availability of the ED, leading to a high number of treating physicians, many protocol violations could be expected. Cluster randomisation at the hospital-level is beneficial since it corrects for confounding by casting experience with one of the two interventions and secures a comparable case-mix in both interventions. Third, since the CAST study was a pragmatic trial, the results are applicable to daily practice. Lastly, our trial had very little missing data. Only 4% of patients were lost to follow-up for the primary outcome analyses, 92% participated in physical examination, and the response rate on questionnaires was 86-94% across different time visits.

This trial has some limitations. First, we underestimated the incidence of redisplacement in our sample size calculations. Our calculations were based on the incidence of redisplacement in our previously performed retrospective study (CC 17%, PS 29%).[10] However, follow-up in that cohort was limited to one week. In retrospect we should have searched the literature for studies with comparable follow-up, since follow-up in this prospective design was extended to cast removal at five weeks. Around 20% of DRFs redisplaced during the first week, in line with previous results, but a large number of DRFs redisplaced later which we did not take into consideration. As second limitation, due to many non-acceptably aligned DRFs after reduction that had to be excluded, we did not reach our target sample size. All radiographs were anonymously retracted from electronic patient files after the inclusion phase was completed to secure patient anonymity and reduce workload of all radiology departments. We never considered beforehand that this many patients would be lost due to incorrect reductions and we did not account for this in our study protocol. It would have been logistically impossible to prevent these exclusions beforehand, since the study intervention is applied immediately after closed reduction, before post-fracture alignment is radiographically established. However, the between-group differences for main outcomes were small and non-significant. It is unlikely that a larger sample would result in significant and clinically important differences between casting types. A third limitation is that the Dutch guideline for DRFs was updated at the end of the inclusion phase of this trial.[23] Unacceptable dorsal angulation sharpened from ≥ 15° to ≥ 10°. We decided to analyse results according to the previous guideline because these thresholds were used by clinicians at the time of inclusion. Lastly, according to Dutch privacy law, it is forbidden to screen electronic patient files of non-included patients. Therefore, we cannot confirm the total number of potentially eligible patients. The decision to invite a patient to participate could therefore have been subject to treatment bias.

In this large prospective RCT, we found that circumferential casting was not superior to plaster splinting in reducing fracture redisplacement incidence in adults with reduced DRFs. Furthermore, we found no differences in clinical outcomes after three-months, or in patient-reported outcomes or adverse events up to one year after fracture sustainment. We conclude that both casting techniques are comparable and that the decision to use either technique should be based on the preference of the cast applicant. The high redisplacement rates, in combination with the high number of extra hospital visits and cast complaints, should be taken into consideration during shared decision making in whether choosing conservative or primary surgical treatment. Further research should focus on identifying modifiable risk factors that predict fracture redisplacement, and optimizing treatment to reduce the large incidence of failed fracture reductions.

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SUPPLEMENTAL MATERIAL

This appendix has been provided by the authors to give readers additional information about their work.

Table of contents

RCT Recruitment Hospitals

Hospital Erasmus MC – Rotterdam, The Netherlands

36 cases included in 18 months

Hospital Franciscus Gasthuis and Vlietland – Rotterdam and Schiedam, The Netherlands

108 cases included in 18 months

Hospital Haaglanden Medisch Centrum – The Hague, The Netherlands

84 cases included in 18 months

Hospital Antonius – Utrecht and Nieuwegein, The Netherlands

97 cases included in 8 months

Hospital Haga – The Hague, The Netherlands

69 cases included in 16 months

Hospital IJsselland – Rotterdam and Schiedam, The Netherlands

74 cases included in 17 months

Hospital Maasstad – Rotterdam, The Netherlands

69 cases included in 18 months

Hospital Reinier de Graaf Gasthuis – Delft, The Netherlands

44 cases included in 16 months

Hospital Alrijne – Leiderdorp, The Netherlands

92 cases included in 14 months

Hospital Elisabeth Tweesteden Ziekenhuis – Tilburg, The Netherlands

69 cases included in 12 months

Table S1. Descriptives of drop-out population

	Drop outs n = 49
Patient characteristics	
Women, n (%)	40 (82)
Age, years	62 (11)
BMI, kg/m^2	25 (3.8)
Osteoporosis, n (%)	2 (4)
Diabetes, n (%)	2 (4)
Current smoker, n (%)	8 (16)
Fracture characteristics	
Dominant side affected, n (%)	27 (55)
Styloid ulnae fracture, n (%)	20 (41)
Dorsal angulation, n (%)	46 (94)
Angulation, °	23 (10)
Radial inclination, °	17 (7)
Radial shortening, n (%)	24 (49)
If yes, ulnar variance, mm	0.8 (1.0)
Intra-articular, n (%)	18 (37)
Post reduction fracture alignment	
Dorsal angulation, n (%)	21 (43)
Angulation, °	5 (4)
Radial inclination, °	23 (3)
Radial shortening, n (%)	4 (8)
If yes, ulnar variance, mm	2 (0.7)

Chapter 7

The influence of casting techniques on the redisplacement risk of reduced distal radius fractures in adults

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ABSTRACT

Introduction: Successfully reduced distal radius fractures (DRFs) often redisplace while casted. Poor cast moulding might be a risk factor for redisplacement of DRFs. This study aims to assess whether cast moulding quality, as determined by casting indices, impact the risk of redisplacement. Also, we assessed the influence of the cast applicant and the material used on the redisplacement risk.

Materials and Methods: We retrospectively reviewed cases from a prospective cohort (trial registration NL8311). We included 172 adequately reduced and circumferentially casted DRFs with a complete two-week radiographic follow-up. Fracture alignment was measured on all radiographs (trauma, post-reduction and follow-up) in accordance with the Dutch guideline for DRFs. When unacceptably aligned after 2 weeks, the DRF was labelled as redisplaced. Cast moulding quality was measured using the Three Point Index (TPI), Cast Index (CI) and Gap Index (GI). A TPI > 0.8, CI > 0.7 and GI > 0.15 implicates poor cast moulding. Multivariable logistic regression was used to examine the influence of cast moulding quality, cast applicant and casting material on the redisplacement risk. We corrected for patient age, intra-articular involvement, the degree of radial inclination and radial shortening.

Results: Redisplacement occurred in 40% of DRFs. The mean index scores were poor (TPI 0.94, CI 0.85, GI 0.22), indicating generally suboptimal cast moulding quality. None of the cast indices were significantly associated to redisplacement (OR [95% CI]: TPI 1.2 [0.6 to 2.5], CI 2.4 [0.7 to 15.7], GI 1.6 [0.7 to 4.0]). DRFs casted by nurse practitioners had significantly lower odds of redisplacement compared to those casted by emergency room nurses. Type of casting (synthetic versus plaster of Paris) was not associated with redisplacement.

Conclusions: Cast moulding quality, measured using cast indices, is not associated with redisplacement of reduced DRFs. Casts applied by nurse practitioners redisplaced significantly less often.

INTRODUCTION

A significant proportion—32 to 64%—of reduced distal radius fractures (DRFs) in adults will redisplace during non-operative treatment[1-4]. Preventing redisplacement would be ideal as it would lead to less surgical interventions with benefit for both patient and healthcare costs. In the field of paediatric fractures, it is suggested that cast moulding quality affects the redisplacement risk[5-8]. This association is only scarcely investigated in the adult population. Three studies in adults have been published on this topic, reporting contradictory conclusions[9-11]. Cast moulding quality can be described to as the quality of plaster moulding and padding in a way it provides best support to the fracture zone. Several cast indices are described to measure cast moulding quality, including the Cast Index (CI) [12], the Gap Index (GI) [5] and the Three-Point Index (TPI)[6]. The TPI has shown highest specificity and sensitivity in predicting redisplacement in both paediatric and adult forearm fractures.[6, 11] In a retrospective cohort, a promising sensitivity of 96% and specificity of 96% was found for the TPI[11].

In addition to cast moulding quality, the influence of the occupation of the healthcare provider applying the plaster—casting technician, emergency room nurse or nurse practitioner—on the redisplacement risk is unknown. Also, different types of casting material are available these days. The influence of plaster of Paris versus synthetic casting on redisplacement has not yet been investigated.

This study aims to investigate if cast moulding quality, as determined by the TPI, CI and GI, is associated with redisplacement in a prospective cohort of adult patients with adequately reduced DRFs. In addition, we investigate whether the cast applicant (casting technician, emergency room nurse or nurse practitioner) and the choice of casting material (plaster of Paris or synthetic cast) are of influence on the redisplacement risk.

METHODS

Study design

This observational follow-up study retrospectively reviews prospectively collected radiographs from a subset of patients who participated in the CAST study, a pragmatic multicentre cluster-randomised controlled trial (METC 2019-0528, registered at ClinicalTrials.gov [NL8311])[4, 13]. Patients were included in ten hospitals in the Netherlands from May 2020 to November 2021. In the CAST study, a total of 752 patients (age ≥ 18 years) with reduced DRFs that started conservative treatment were included and randomized between immobilization using plaster splinting and circumferential casting. Exclusion criteria comprised: both-bone fractures (a solitary ulnar styloid process fracture was accepted), trauma patients with an injury severity score above 16, concomitant injury to the ipsilateral extremity and the inability to complete questionnaires due to a language barrier or cognitive impairment. Written informed consent was obtained for every patient.

Participants

For the current study, cases from the CAST study cohort were selected with an acceptable fracture alignment after reduction, conform the Dutch guideline for DRFs, published in 2010 [14]. The Dutch Guideline for DRFs stated that a DRF is unacceptable aligned if one or more of the following criteria are met when measuring alignment on the radiographs: ≥ 15° dorsal angulation, ≥ 20°, palmar angulation, ≤ 15° radial inclination, ≥ 3 mm radial shortening and ≥ 2 mm intra-articular step-off or gap. We only included patients that received a circumferential cast after reduction in this manuscript since casting indices are not applicable, neither measurable on splinted fractures. In all included cases, a below-elbow circumferential cast was applied with the hand in neutral position, conform instructions that were available in all participating hospitals by means of instructional videos and posters[13]. Circumferential casts could be made with either plaster of Paris or synthetic material (e.g. fiberglass), based on availability of materials or preference of the cast applicant. Radiographic follow-up took place at one week, two week and five weeks post-inury. If radiographic follow-up was incomplete during the first two treatment weeks, the patient was excluded. In case of severe cast complaints or insufficient casting, casting technicians were free to make cast alterations during follow-up to secure adequate fracture support.

Primary outcome

The primary outcome in this study is the redisplacement incidence of DRFs. For defining redisplacement, fracture alignment was measured on all radiographs (postero-anterior [PA] and lateral [LAT] view at trauma, post-reduction, 1 week and 2 week follow-up). Measurements were executed by two trained researchers (BB and SS) conform the measurement guidelines carried out by Medoff et al. (2005)[15]. Inter- and intra-observer reliability were calculated, using intraclass correlation coefficients (ICC, two-way mixed and absolute agreement). Intra-observer reliability for gap/step-off measurements on lateral radiographs was moderate (ICC 0.56). The ICC's for all other alignment measurements were excellent (ICC of 0.84 to 0.99). The endpoint for redisplacement was chosen at two weeks of treatment, since the primary applied cast is often replaced after two weeks. A longer follow-up could therefore introduce bias because of fracture redisplacement initiated by cast replacement or alignment changes influenced by a second attempt to closed reduction.

Redisplacement is described and analysed in two ways. Firstly, as the loss of acceptable alignment conform the Dutch guideline. Fractures that were correctly aligned on post-reduction radiographs, but had an unacceptable alignment after two weeks, were labelled as redisplaced. When correct alignment was maintained during two weeks, the fracture was labelled as non-displaced. Secondly, redisplacement is described in terms of fracture migration. DRFs most often loose threshold alignment because of progressive angulation or decreasing inclination over time [10]. Migration is defined as the absolute amount of displacement, in degrees of angulation and inclination. For example; one degree of dorsal angulation post-reduction could redisplace to 14 degrees of dorsal angulation after two weeks. The fracture remains stable conform the Dutch guideline, but could be considered as unstable because of the thirteen degrees of fracture migration.

Potential risk factors for redisplacement

Cast moulding quality was evaluated using three different cast indices, namely the TPI, CI and GI. These indices are based on specific spaces and distances in different cast regions that are considered important to optimally stabilise the fracture. Indices were measured on the PA and LAT radiographs taken after reduction and cast application. The measurements and indices formulas are shown in figure 1A and 2B, and measured as described in previous literature[5, 6, 12]. The TPI is calculated by adding three distances between the cast and the skin measured on the PA radiograph, divided by the contact length of the fracture. The same is done on the LAT radiograph. The sum of these two calculations constitutes the TPI. The CI is a measure of the inside diameter of the plaster on the LAT-radiograph as a ratio to the diameter on the PA-radiograph at the fracture site[12]. The GI is a measure of the space between the plaster and the skin, measured as a ratio to the inside diameter of the plaster. This is measured at the fracture site in both the PA and LAT radiographs[5]. The cut-off values for the indices are 0.8 for the TPI, 0.7 for the CI and 0.15 for the GI. A score up to the cut-off value represents a well-moulded cast whereas a score above the cut-off value represents a poorly moulded cast. Index measurements were performed by one trained researcher (MK) and a subset was measured by another trained researcher (KL) for a reproducibility analysis. The inter- and intra-observer reliability of the TPI, CI and GI were excellent, with ICC's ranging between 0.91 and 1.0.

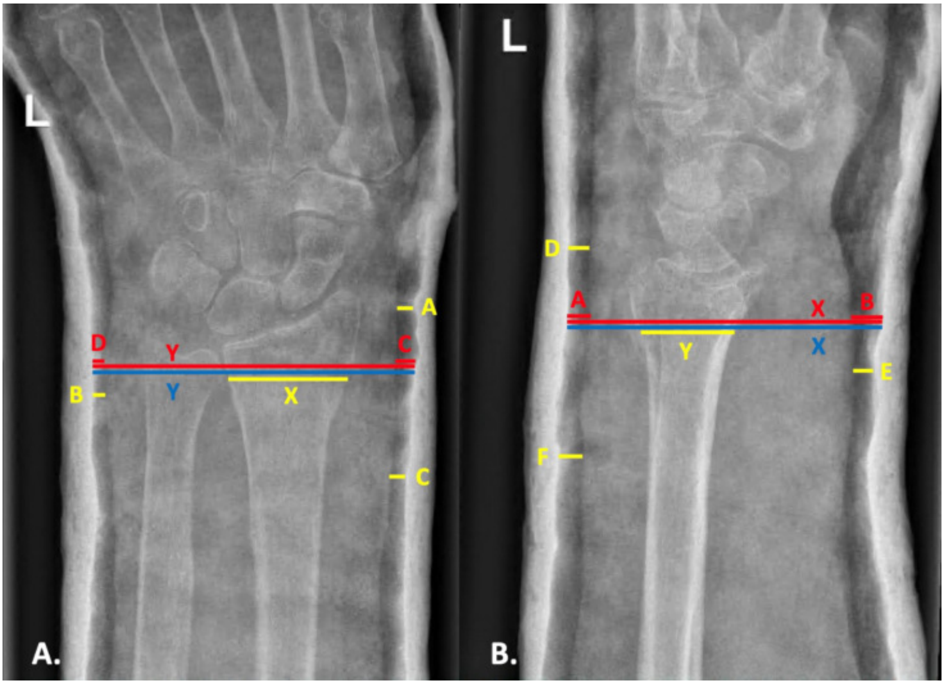

Figure 1A and B. Cast indices measurements shown on postero-anterior (A) and lateral (B) radiographs.

Yellow represents the Three-Point Index. A: The narrowest space around the radiocarpal or proximal carpal joint on the radial side; B: The narrowest space on the ulnar side, within 1cm of the fracture line; C: The narrowest space on the radial side, 3 to 7cm proximal of the fracture site; X: The contact length of the fracture; D: The narrowest gap on the dorsal side, around the radiocarpal or proximal carpal joint; E: The narrowest gap on the palmar side, within 1 cm of the fracture line; F: The narrowest gap on the dorsal side, within 3 to 7cm proximal to the fracture site; NB. In less common palmar angulated fractures, D and F are measured on the palmar side and E on the dorsal side. Y: The contact length of the fracture. TPI formula: $[(A+B+C)/X] + [(D+E+F)/Y]$.

Red represents the Gap Index. C: The gap between plaster and skin at the fracture zone on the radial side; D: The gap between plaster and skin at the fracture zone on the ulnar side; Y: The inside cast diameter at the fracture zone; A: The gap between plaster and skin at the fracture zone on the dorsal side; B: The gap between plaster and skin at the fracture zone on the palmar side; X: The inside cast diameter at the fracture line. GI formula: $(A+B)/X + (C+D)/Y$.

Blue represents the Cast Index. Y: The inside cast diameter at the fracture zone; X: The inside cast diameter at the fracture zone. CI formula: X/Y.

The occupation of healthcare provider applying the cast and the type of material used (plaster of Paris or synthetic casting) were denoted in a questionnaire filled out by the healthcare professional treating the patient at the time of inclusion. The CAST study was a pragmatic trial, and therefore the choice for cast applicant or material used was unconstrained.

Statistical analyses

Statistical analyses were performed using IBM SPSS version 28.0.1.0. P-values ≤ 0.05 are considered significant. Whether cast moulding quality (cast index above or beneath cut-off value), cast applicant or casting type are related to redisplacement (dependent variable) have been tested with multivariable logistic regression analyses. We corrected for potential confounding factors namely age and the following fracture characteristics at trauma: AO classification, intra-articular fracture involvement, the degree of radial inclination and radial shortening. Univariate logistic regression was used to select potential confounding patient- and fracture related factors. In case a relationship existed between the variable and redisplacement ($p < 0.2$), the variable was added in the multivariable logistic regression model. The sensitivity, specificity, positive predictive value, negative predictive value of the indices were calculated. To test whether casting type or type of cast applicant predicts migration outcome, we used multiple linear regression analysis. We corrected for the same potential confounders as mentioned for the logistic regression analyses. One-way ANOVA was used to compare cast indices outcomes amongst the cast applicants.

RESULTS

The inclusion criteria were met by 186 patients of which 172 were used in the final analyses (Figure 2). Eight patients were excluded from the final analyses because the cast was not completely visible on radiographs and 6 patients did not receive the allocated circumferential cast but were treated with a splint. Patient and fracture characteristics of the final study population are shown in Table 1.

Influence of cast moulding quality on the redisplacement risk

Fracture redisplacement as defined by the guideline occurred in 40% of DRFs (n = 76) within the first two weeks of immobilization. Cast indices outcomes are shown in Table 2. All three indices scored a mean index outcome above the threshold score, referring to poor cast moulding. There was no association found between casting indices and whether a fracture would redisplace or not conform the guideline (Table 3). Sensitivity, specificity, negative predictive value and positive predicting values of all indices are reported in the supplementary appendix, Table S1. During the first two weeks of cast immobilization, fractures showed a mean change in palmar tilt (migration in angulation) of 7.0 degrees (SD 6.4),and a mean loss of inclination (inclination migration) of 3.1 degrees (SD 3.6). These changes in palmar tilt and loss of inclination were not related to cast indices outcomes (details in Supplementary Appendix, Table S2). In 25 cases (13%), a cast replacement took place within two weeks. The redisplacement incidence, as well as mean cast indices outcomes were not different from the total study cohort (details in Supplementary Appendix, Table S3).

Influence of cast applicant on the redisplacement risk

In this cohort, casts were applied by five types of healthcare providers, namely emergency room (ER) nurses (n = 83), nurse practitioners (n = 50), casting technicians (n = 36), an ER specialist (n = 1) and a resident in orthopaedic surgery (n = 1). As shown in Table 3, the redisplacement risk was lowest in casts applied by nurse practitioners and casting technicians. The odds of a fracture to redisplace was significantly lower for fractures that were casted by nurse practitioners compared to ER nurses (odds ratio [OR] 0.2, 95% CI 0.09 to 0.54). However, the cast applicant was not significantly associated with migration outcomes (Table 4). Cast indices did not significantly differ between cast applicants. All mean index scores reached above the cut-off values (details in Supplementary Appendix, Table S4).

Influence of cast material on the redisplacement risk

Two types of cast material were used in this cohort to immobilize the fracture, namely plaster of Paris (n = 113 [66%]) and synthetic casting (n = 59 [34%]). DRFs immobilized with synthetic casting redisplaced less often compared to plaster of Paris (31% vs. 45%) but this association was not significant (OR 0.56, 95% CI 0.27 to 1.15, Table 3). Concerning migration outcomes, mean degrees of migration were lower in synthetic casts compared to plaster of Paris. The linear regression analysis however concludes that the material used for casting does not explain the variation in migration (Table 4).

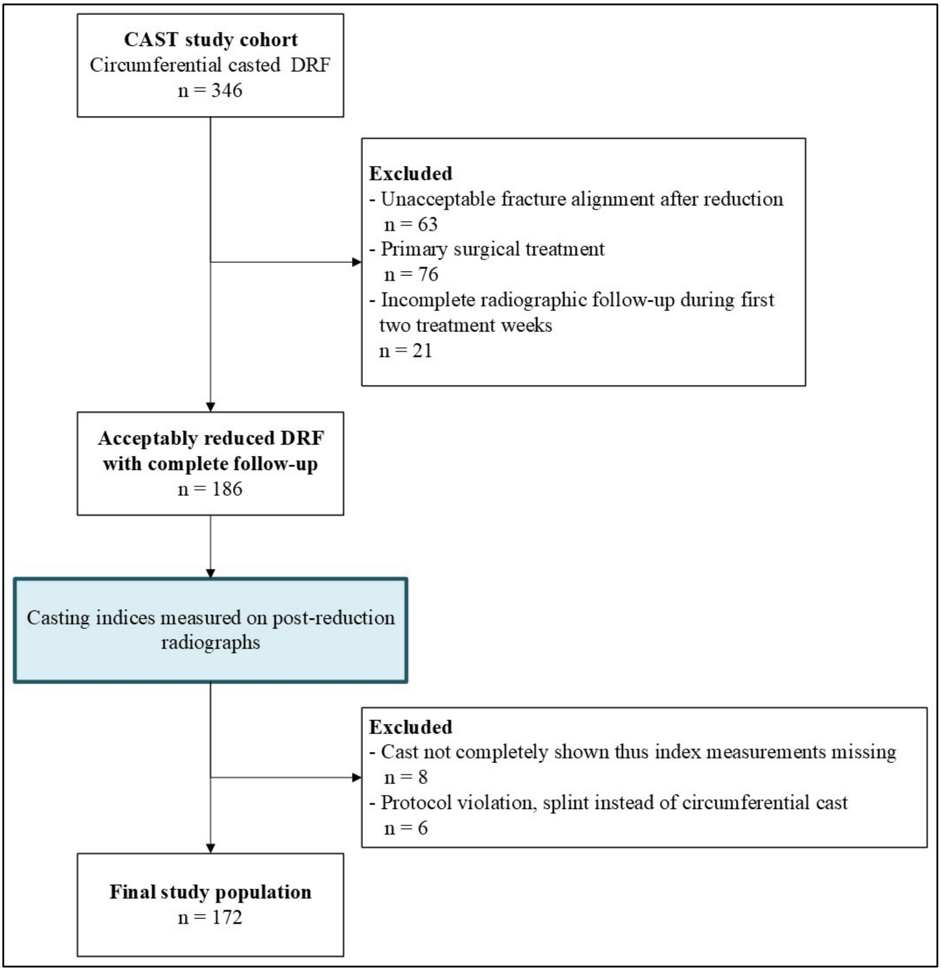

Figure 2. Flowchart of study population

Table 1. Patient and fracture characteristics of the study population

	Study population n = 172		
Patient characteristics			
Female, n (%)	142 (83)		
Age, years (SD, min-max)	62 (16.4, 18-91)		
BMI, kg/m^2 (SD, min-max)	24 (3.8, 16-40)		
Fracture characteristics			
Dominant wrist affected, n (%)	87 (51)		
Styloid ulnae fracture, n (%)	97 (56)		
Intra-articular, n (%)	80 (47)		
AO classification, n (%) A type B type C type	 92 (53) 13 (8) 67 (39)		
	Before reduction	Post reduction	At two weeks (n= 142*)
Dorsal angulation, n (%)	160 (93)	93 (54)	58 (70)
Angulation, ° (SD, min-max)	21 (10.4, 0-59)	5 (4.1, 0-19)	8 (6.5, 0-37)
Radial inclination, ° (SD, min-max)	17 (6.4, -5-28)	22 (3.6, 16-34)	19 (4.8, 7-30)
Radial shortening (yes)	85 (49)	27 (16)	55 (32)
- if yes: Severity of radial shortening in mm (SD, min-max)	3.0 (2.4, 0-14)	1.3 (1.2, 0-6)	1.1 (1.2, 0-5)

If not noted differently, information is presented as mean with standard deviation and range between parentheses. N: number of cases, BMI: body mass index.

*in 30 cases patients were treated surgically after redisplacement occurred at 1 week. Therefore no control-radiograph at two weeks is available.

Table 2. Index outcome distribution

			Poor cast moulding conform index	
	Index threshold[a]	Mean (SD)	Non-displaced n = 103 n (%)	Displaced n = 69 n (%)
Three point index	0.8	0.94 (0.36)	58 (56)	41 (59)
Casting index	0.7	0.85 (0.06)	99 (96)	67 (97)
Gap index	0.15	0.22 (0.07)	82 (80)	55 (80)

[a]An index score above the threshold value refers to poor cast moulding quality.

Table 3. Association of casting indices, type of cast applicant and type of casting material on the occurrence of fracture redisplacement

	Redisplacement incidence (%)	Odds ratio (95% CI)
Three Point Index > 0.8	59	1.2 (0.61 to 2.55)
Cast index > 0.7	97	2.4 (0.38 to 15.75)
Gap index > 0.15	80	1.6 (0.68 to 4.01)
Cast applicant		
Emergency room nurse	52	Reference
Nurse practitioner	22	0.2 (0.09 to 0.54)*
Casting technician	39	0.5 (0.20 to 1.19)
Casting material		
Plaster of Paris	45	Reference
Synthetic fiber	31	0.56 (0.27 to 1.14)

Multivariable logistic regression analyses was used, corrected for patient age, AO classification, fracture inclination, radial shortening, intra-articular fracture involvement. *P <0.01

Table 4. Association of casting material and cast applicant on fracture migration

	Angulation migration	Coefficient ß	Standard Error	p-value
Casting material				
Plaster of Paris	7.5 (6.9, 0-34)			Reference
Synthetic fiber	6.8 (5.7, 0-33)	-0.98	1.04	0.35
Cast applicant				
Emergency room nurse	7.3 (5.8, 0-21)			Reference
Nurse practitioner	7.3 (7.8, 0-34)	-0.74	1.17	0.53
Casting technician	7.0 (6.7 0-33)	-1.13	1.29	0.38
	Inclination migration	Coefficient ß	Standard Error	p-value
Casting material				
Plaster of Paris	3.3 (3.7, -15-17)			Reference
Synthetic fiber	2.6 (3.1, -4-10)	-0.44	0.52	0.40
Cast applicant				
Emergency room nurse	3.7 (4.0, -5-17)			Reference
Nurse practitioner	2.8 (2.9, -3-10)	-0.57	0.58	0.33
Casting technician	2.3 (3.0, -4-9))	-1.26	0.64	0.05

Migration outcomes are given as mean degrees with standard deviation and range between brackets. Multivariable linear regression analyses was used, corrected for patient age, AO classification, fracture inclination, radial shortening and intra-articular fracture involvement.

DISCUSSION

This retrospective study, utilizing prospective collected data, did not demonstrate any association between the cast moulding quality and the incidence of fracture redisplacement in adult DRFs. The predictive performances of the three tested indices (TPI, CI and GI) were poor. The cast indices scores were not related to the extent of migration in angulation or inclination during follow-up. This indicates that a poor cast moulding is not a risk factor for redisplacement. As for secondary outcomes, we found that casts applied by nurse practitioners resulted in less migration and redisplacement than casts applied by ER nurses. We did not identify any correlation between various cast materials and the occurrence of fracture redisplacement.

The rationale for this study was the absence of conclusive evidence regarding the influence of casting moulding quality on the redisplacement risk in adults. Only three studies have been published reporting on casting indices in adults[9-11]. Remarkably, Alemdaroğlu et al. found very high predictive performances of the TPI, implicating that insufficient cast moulding is the most important risk factor for redisplacement. However, we were unable to replicate these results. For example, we calculated a specificity of 44% compared to 96% in their study. A difference in redisplacement criteria could play a role in this. They defined a fracture as redisplaced when there was an increase of 10 degrees of dorsal or palmar angulation. However, the results of our analyses on angulation migration did not reveal any significant association either. We consequently doubt the value of cast indices in the adult population. When casting indices would adequately describe cast moulding quality, we would expect cast indices to be at least beneath threshold values when applied by casting technicians. Since the predictive performances of all three indices were poor in our cohort, we propose that casting indices are not useful as a tool to measure cast moulding quality in adult DRFs. Two studies support this opinion. Siddiqui et al. performed a retrospective study examining the TPI in 54 adults and they concluded that the TPI could not predict redisplacement[9]. Mimura et al. recently concluded that the gap index is also not associated with redisplacement.[10] Unfortunately, this research question was a small sub question in their study and therefore the used methodology has not been described in detail. Our study shows conclusively that cast moulding quality as measured by casting indices, is not associated to redisplacement.

The overall incidence of fracture redisplacement was 40% in this cohort. This incidence is comparable with reported incidences in previous prospective trials [4, 16-19]. We deliberately chose not to elaborate on the treatment of these fractures beyond two weeks, as the focus of this manuscript is solely on the impact of casting techniques on radiographic alignment. A detailed flowchart of follow-up decisions is provided in the main outcome paper of the CAST study, [4]. Despite adequate initial reduction, a high rate of redisplacement is well documented and continues to be a subject of ongoing discussion. Nevertheless, patient-reported outcomes and clinical results following non-operative management are generally favorable, even when radiographic alignment is not restored or maintained[4, 16, 20]. Consequently, achieving restored radiographic alignment may not be essential for a satisfactory outcome. Particularly in individuals with lower functional demands, non-operative treatment should therefore be considered as a treatment option.

As for the secondary outcomes, this current study is, to the best of our knowledge, the first to analyse whether redisplacement risks and casting indices differ between different specializations of cast applicants and between casts of different materials. Abson et al. studied if casting quality in paediatric fractures varied amongst surgeons with different levels of experience[21]. No significant difference was found. In our cohort, the redisplacement risk was lower in casts applied by nurse practitioners and casting technicians, compared to casts applied by ER nurses. The current results might imply that the experience of the cast applicant is of value for the redisplacement risk. It should be considered that post-reduction alignment might be a confounding factor. In the Netherlands, closed reductions are predominantly carried out by young and relatively inexperienced junior doctors. Specialized ER nurse practitioners and casting technicians typically possess greater experience with reducing fractures. Consequently, it may be plausible that their reductions more often result in a stable and (close to) anatomical fracture alignment. With regard to the influence of casting material, although not statistically significant, synthetically casted DRFs redisplaced less often in comparison to fractures treated with plaster of Paris. The redisplacement incidence was 14% lower. It could be argued that choice for a certain casting type might be influenced by patient- and fracture characteristics. An explorative analyses on this matter, shown in the supplementary appendix, Table S5 revealed that groups were comparable.

This study has certain limitations. First, while our overall group size is larger than that of related previous studies, the subgroup sizes were relatively small and therefore the results of subgroup analyses should be interpreted with caution. In our analyses, we adjusted for known factors that influence the redisplacement risk to minimize the risk of bias. Despite thorough checks with univariate logistic regression, other confounders may exist. For example, we did not study fracture comminution as it is not included in the national guideline and because it is difficult to measure the extend objectively on radiographs[22]. Lastly, in 21 cases (12.2%), C and/or F regions of the TPI were not completely visible on radiographs. In theory the TPI could therefore be underestimated in these cases. The analysis was repeated with the exclusion of these cases which did not alter the outcome. Therefore, all cases were retained and included in the analyses.

The strength of the present study lies in the detailed nature of the prospectively gathered data and its multicentre design. Hereby, a good reflection of the diversity in fractures and casts in daily practice is provided. Second, to the best of our knowledge this is the first study to compare the predictive performances of different casting indices in adults and to investigate the association between different cast applicants and cast materials used. Third, we decided to measure redisplacement by measuring fracture migration, in addition to adhering to established redisplacement criteria. Given the potential variations in redisplacement guidelines across regions and with changing standards over time, utilizing absolute measures of migration provides a more robust approach.

This study concludes that cast moulding quality as measured using the TPI, CI and GI does not significantly influence the risk of redisplacement in reduced adult DRFs. The utility of cast indices in describing cast moulding quality is doubted. However, an association was found between cast applicants and the redisplacement risk, in which DRFs casted by nurse practitioners had the smallest redisplacement risk. This suggests that experience in cast application decreases the redisplacement risk.

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SUPPLEMENTARY APPENDIX

Table S1. Sensitivity, specificity, negative predictive value and positive predictive value of all three indices.

	Three point index	Casting index	Gap index
Sensitivity	59.4%	97.1%	79.7%
Specificity	43.7%	3.9%	20.4%
Positive predictive value	41.4%	40.4%	40.1%
Negative predictive value	61.6%	66.7%	60.0%

Predictive performances of index outcome above threshold scores for predicting redisplacement.

Table S2. Association of casting indices with fracture migration.

	Three point index			Cast index			Gap index		
	'good' (≤ 0.8)	'poor' (> 0.8)	P-value	'good' (≤ 0.7)	'poor' (> 0.7)	P-value	'good' (≤ 0.15)	'poor' (> 0.15)	P-value
Migration in angulation, °	6.7 (5.5)	7.4 (7.0)	0.98	3.8 (2.7)	7.1 (6.5)	0.22	7.6 (5.1)	7.0 (6.7)	0.18
Migration in inclination, °	3.4 (3.1)	2.9 (3.9)	0.33	2.1 (1.2)	3.1 (3.6)	0.40	3.6 (3.7)	3.0 (3.5)	0.22

Results are presented as means with standard deviation between brackets.

EXPLORATIVE ANALYSIS EARLY CAST REPLACEMENTS

In 25 cases (13%), the circumferential cast was replaced by a new circumferential cast within two weeks. In 4 cases, the cast replacement took place within one week because of cast complaints. In the other cases, the cast was replaced at the scheduled follow-up visit at the casting room one week after injury. The reasons for these cast replacements was not further specified.

In this cohort, fracture redisplacement occurred in 10 cases (40%). This is consistent with the complete cohort. Cast index outcomes are shown in table 2. Mean index scores and their relation to cast redisplacement are not different from the complete study cohort.

Table S3. Index outcome distribution.

			Poor cast moulding conform index	
	Index threshold[a]	Mean (SD)	Non-displaced n = 15 n (%)	Displaced n = 10 n (%)
Three point index	0.8	1.13 (0.33)	9 (75)	6 (67)
Casting index	0.7	0.85 (0.04)	12 (100)	9 (100)
Gap index	0.15	0.25 (0.07)	11 (92)	7 (78)

[a]An index score above the threshold value refers to poor cast moulding quality.

Table S4. Association of healthcare provider with fracture migration.

	n	Three point index	Cast index	Gap index
ER nurse	83	0.97 (0.36)	0.85 (0.05)	0.22 (0.08)
Nurse practitioner	50	0.85 (0.33)	0.86 (0.06)	0.20 (0.06)
Casting technician	36	0.99 (0.36)	0.85 (0.08)	0.23 (0.08)
P value		0.12	0.38	0.12

Results are presented as means with standard deviation between brackets. ER: Emergency Room, n: number of patients

EXPLORATIVE ANALYSES CASTING TYPE

No significant differences were seen concerning patient- and fracture characteristics between both casting types (see S4). Synthetic casting is most often applied by casting technicians and nurse practitioners. ED nurses use synthetic casting in 7% of cases, whilst casting technicians and nurse practitioners use synthetic casting more frequently, with 69% and 54% respectively.

Table S5. Patient- and fracture characteristics for both casting types.

	Synthetic fiber n=59	Plaster of Paris n=113	P value
Patient characteristics			
Female, n (%)	50 (85)	93 (82)	0.30
Age, years	64 (14)	62 (17)	0.18
BMI, kg/m^2	24 (4)	24 (4)	0.38
Fracture characteristics			
Dominant side affected, n (%)	32 (54)	55 (49)	0.48
Angulation, °	21 (10)	21 (11)	0.64
Inclination, °	18 (5)	16 (7)	0.09
Styloid Ulnae fracture, n (%)	36 (61)	61 (54)	0.38
Radial shortening, n (%)	34 (58)	51 (45)	0.16
Intra-articular, n (%)	26 (44)	54 (48)	0.64

If not noted differently, information is presented as mean with standard deviation between parentheses. N: number of patients, BMI: body mass index.

PART III

Non-operative, operative and delayed operative treatment

Chapter 8

Is Delayed Surgical Treatment of Distal Radius Fractures inferior to Direct Surgical Treatment? A Comparative Study of Prospective Gathered Data

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ABSTRACT

Background: Distal radius fractures (DRFs) are the most common fractures among adults, with increasing incidence over time. Treatment options of reduced DRFs include either cast immobilization or immediate surgical stabilization. More than half of well aligned fractures heal properly after reduction with non-operative treatment [2,3]. The rate of unnecessary surgical intervention will be reduced if surgical treatment is reserved for patients with re-displaced distal radius fractures. Therefore, this study aims to evaluate whether surgical treatment within or after 7 days affects patient reported outcome in reduced distal radius fractures.

Methods: This retrospective analysis utilized prospectively collected data from the CAST study, a multicenter cluster-randomized controlled trial conducted in the Netherlands. Adult patients (age >18) with displaced DRFs requiring closed reduction were included. We selected those patients who underwent early (<8 days post-injury) or late surgical treatment (8-42 days post-injury) of their DRF. A linear mixed model was used to estimate differences in mean Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH) and Patient Rated Wrist/Hand Evaluation (PRWHE) scores during follow-up at 6 weeks, 3, 6 and 12 months.

Results: Out of 275 patients analyzed, 92 underwent early surgery (mean 4.9 days post-injury, SD 1.6) and 183 underwent late surgery (mean 13.2 days post-injury, SD 3.7). Early surgery resulted in significantly better PRWHE scores at 6 weeks with a between group difference of -6.3 (95% CI -12.2 to -0.5) and at 3 months with a between group difference of -5.7 (95% CI -11.2 to -0.1), but no significant differences were observed at 6 and 12 months. QuickDASH scores did not differ significantly between-groups at any time point.

Conclusion: Early surgical treatment offers short-term functional benefits at 6 weeks and 3 months post-injury compared to late surgery, but these differences did not reach clinically significant differences. Long-term functional outcomes at 6 and 12 months were not affected by the timing of surgery. Both early and late surgical treatments are associated with similar complication rates. These findings suggest that it is safe to only perform surgery on re-displaced distal radius fractures without compromising the long-term patient outcomes. This approach could substantially reduce the number of surgical procedures for distal radius fractures.

INTRODUCTION

Distal radius fractures (DRFs) are the most common fractures in the adult population and the incidence continues to increase over time [1]. Following a distal radius fracture, the choice between non-operative treatment with cast immobilization or surgical intervention is made based on the stability and alignment of the fracture. Non-operative treatment is often preferred in stable and well-aligned fractures, whereas surgical treatment is offered in case there is no acceptable alignment obtained or remained after reduction. The goal of treatment is to achieve optimal functional recovery and patient-reported outcomes, rather than perfect radiographic alignment.

To reach this goal many clinicians are increasingly opting for immediate operative treatment, believing it leads to quicker recovery and lowers the risk of potential problems in cast related to non-operative treatment. Surgical intervention is indicated for unstable fracture patterns, as these are unlikely to maintain alignment after closed reduction. However, more than half of stable and well aligned distal radius fractures heal satisfactorily after closed reduction and with non-operative treatment [2, 3]. So, an alternative option would be to observe the stable and well aligned fractures in cast and when the fracture re-displaces over time to choose for the operative treatment in second instance.

It is unclear whether this delay in operative treatment affects patients' outcome. Results from a retrospective single center study suggest that a delay in surgery negatively affects short-term functional outcomes at 4 and 12 weeks, but not on the long-term [4]. Surgical treatment within two weeks after injury is most often preferred and also advised in several guidelines [5]. The British Society for Surgery of the Hand (BSSH) and the National Institute for Clinical Excellence (NICE) guidelines are stricter and recommend surgical intervention within 72 hours of injury for intra-articular fractures and within one week for extra-articular fractures [6,7]. However, clear evidence is lacking that supports the benefit of immediate operative treatment above late surgery after alignment worsened.

In clinical practice, patients with a displaced but successfully reduced DRF are typically reviewed after one week to assess maintenance of reduction. If redisplacement occurs surgery is then performed during the following days. Whether these patients, operated later because the fracture initially appeared stable, experience worse or comparable outcomes remains uncertain. Determining this is crucial, as equivalent outcomes would support more selective surgical approach and help reduce the number of operations performed for DRFs.

Therefore, the aim of this study is to evaluate whether surgical treatment within versus after 7 days affects patient reported outcome in reduced distal radius fractures. We hypothesized that the timing of surgical treatment (within ≤7 days versus 8-42 days post-injury) would not significantly affect patient-reported functional outcomes in adults with reduced distal radius fractures.

METHODS

Study design and setting

This is a retrospective study based on prospectively collected data from a subset of patients that participated in the CAST study, a multicenter cluster-randomised controlled trial. The trial protocol and primary outcomes are published previously [3,8]. The aim of the CAST study was to determine whether circumferential casting resulted in a lower incidence of fracture redisplacement in reduced DRFs in adults, when compared to plaster splinting. The CAST study prospectively enrolled adult patients (aged >18) with displaced distal radius fractures requiring closed reduction. The present analysis includes only those patients who subsequently underwent surgical treatment. The study included patients in ten hospitals in the Netherlands from May 2020 to November 2021.

Patient population

From all patients included in the CAST trial, we selected those patients who underwent early or late surgical treatment of their DRF. Patients who received surgical intervention within 7 days following injury were categorized into the early surgical treatment group, whereas those who underwent surgery between 8- and 42-days post-injury were classified as the late surgical treatment group. Patients were excluded from the study if they failed to complete any of the follow-up questionnaires or underwent surgery beyond a post-injury duration of 42 days. The latter exclusion criterion was based on the understanding that a DRF typically heals within approximately six weeks (or 42 days) when treated conservatively.

Radiographic assessment

Radiographic parameters, including dorsal or volar angulation, radial inclination, radial shortening and translation, were evaluated on standard posteroanterior and lateral radiographs obtained at presentation and after reduction. Redisplacement was defined by the Dutch guidelines when one or more of the following criteria were met: ≥10° of dorsal angulation, ≥20° of volar angulation, ≤15° of radial inclination, ≥3 mm of radial shortening or ≥2 mm of intra-articular step-off [5]. All measurements were performed by two investigators (BB and SS). The inter- and intraobserver reliabilitiy of these measurements has been reported previously and was almost perfect for all parameters, with intraclass correlation coefficients (ICCs) between 0.84 and 0.99. Only step off measurements on lateral radiographs showed moderate intraobserver reliability, with an ICC of 0.56.

Outcome measures

The primary outcome was the between-group-differences in patient reported functional recovery, measured using the Patient Rated Wrist/Hand Evaluation (PRWHE) and the Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH) questionnaires, at four time points: 6 weeks, 3, 6, and 12 months after trauma. Both these questionnaires yield numerical scores ranging from 0 to 100, with higher scores indicative of elevated levels of disability, pain and functional impairment. Both questionnaires possess established validation for the evaluation of functional outcomes in patients with a DRF [9,10,11]. The minimal clinically important difference (MCID) for the PRWHE score was set to 11.5 points and for the QuickDASH score to 16 points [12,13].

The secondary outcome was to evaluate potential differences in complications following surgical intervention between the early and the late surgical treatment group. Complications were monitored over a twelve-month period post-injury.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 28.0.1.0. P-values ≤ 0.05 are considered significant. To estimate differences in mean QuickDASH and PRWHE scores during follow-up between the two treatment groups, we used linear mixed-effects models. This model takes into account that observations within a subject are correlated. The QuickDASH and PRWHE scores at 6 weeks, 3, 6 and 12 months follow up were used as a dependent variable. The group (early and the late surgical treatment), follow-up period and interaction between the group and the follow-up period (multiplication of group and follow-up period as interaction term) were added to the model as fixed factors. Hospital, age, sex and fracture characteristics as shortening, intra articular, angulation and inclination were included in the models as independent variables to correct for potential confounding. The covariance structure was modelled as unstructured. The model residuals were checked for linearity, homoscedasticity and normality. Complications were reported as relative frequencies.

RESULTS

Patients

During the study period, a total of 293 patients met the predetermined inclusion criteria, out of which 275 were used in the final analysis. Fourteen patients were excluded because they did not complete any of the follow up questionnaires and four patients because they underwent surgery after 42 days. A flowchart of patient enrollment is shown in Figure 1. Of the total cohort, 92 patients underwent surgical intervention within 7 days post-injury and were classified as the early surgery group (mean interval of 4.9 days (SD 1.6)). While

183 patients underwent surgery between 8- and 42-days post-injury and formed the late surgery group (mean interval of 13.3 days (SD 3.8)).

The baseline characteristics of the enrolled patients are presented in Table 1. There was a significant difference in dorsal angulation and intra-articular fractures between the early and late group pre-reduction. Additionally, there was a significant difference in the degree of angulation, presence of radial shortening, and the ulnar variance post reduction.

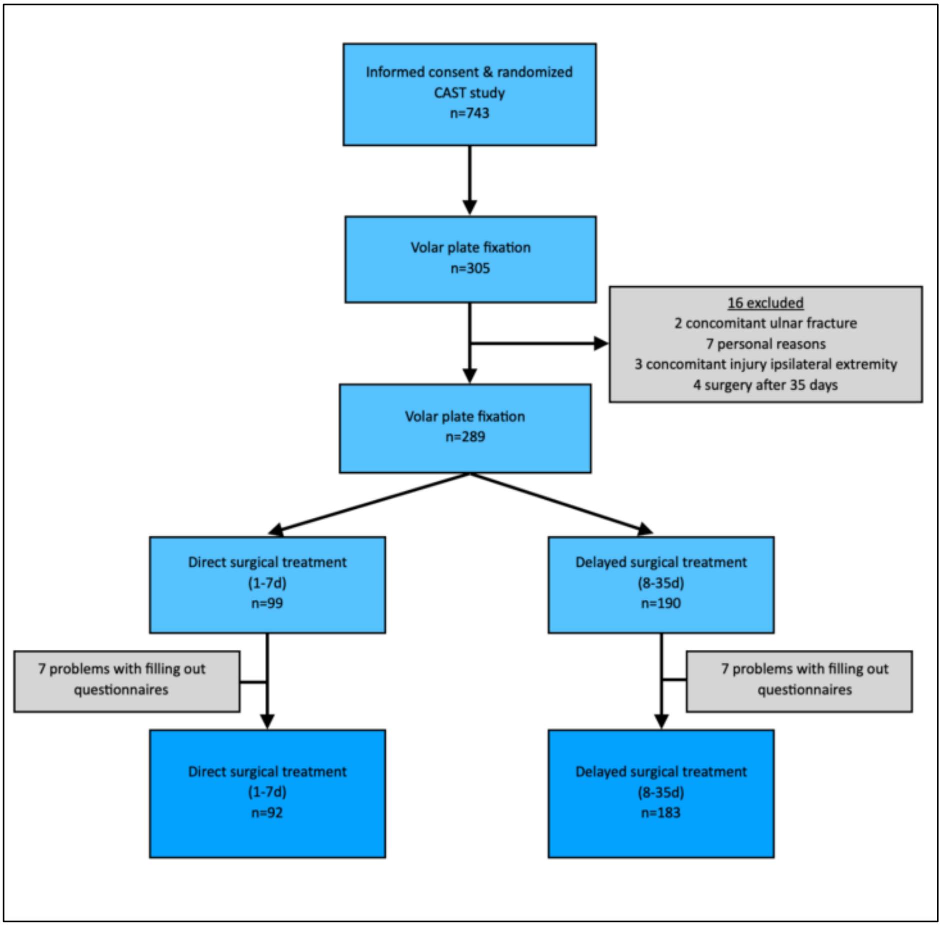

Figure 1. Flowchart of study population

Table 1. Baseline characteristics

	Direct surgical treatment (1-7 days) n = 92	**Delayed surgical treatment** (8-35 days) n = 183	***p-value***
Days until surgery	4.9 (1.6)	13.3 (3.8)	*<0.001*
Patient characteristics			
Female, n (%)	76 (83)	150 (82)	*NS*
Age in years	59.6 (12.3)	61.3 (13.4)	*NS*
BMI, kg/m^2	25.6 (4.3)	25.2 (4.2)	*NS*
Osteoporosis, n (%)	7 (7)	14 (8)	*NS*
Diabetes, n (%)	0 (0)	8 (4)	*NS*
Smoking, n (%)	11 (12)	17 (9)	*NS*
Fracture characteristics			
Dominant side affected, n (%)	44 (48)	78 (43)	*NS*
Styloid ulnae fracture, n (%)	52 (55)	94 (51)	*NS*
Dorsal angulation, n (%)	73 (79)	170 (93)	*0.014*
Angulation, °	28.2 (11.3)	26.3 (12.7)	*NS*
Radial inclination, °	12.9 (7.4)	12.9 (7.5)	*NS*
Radial shortening, n (%)	67 (73)	121 (66)	*NS*
If yes, ulnar variance, mm	4.1 (2.3)	3.6 (2.4)	*NS*
Intra-articular, n (%)	74 (80)	121 (66)	*0.011*
Translation on lateral radiograph, n (%)	51 (55)	106 (58)	*NS*
Translation on PA radiograph, n (%)	15 (16)	24 (13)	*NS*
Post reduction fracture alignment			
Dorsal angulation, n (%)	68 (74)	126 (69)	*NS*
Angulation, °	11.9 (7.9)	8.9 (6.8)	*0.001*
Radial inclination, °	18.2 (4.7)	19.4 (4.8)	*NS*
Radial shortening, n (%)	39 (42)	43 (23)	*0.001*
If yes, ulnar variance, mm	3.1 (1.6)	2.3 (0.8)	*0.007*
Translation on lateral radiograph, n (%)	36 (39)	65 (36)	*NS*
Translation on PA radiograph, n (%)	23 (25)	29 (16)	*NS*

Data are reported as mean with standard deviation between parentheses, or reported otherwise

Patient reported outcomes

Results are shown in Table 2. There was a significant difference in PRWHE score at six weeks and three-months follow-up between the two groups. At six weeks, the early surgery group had a PRWHE score of 47, while the late surgery group had a PRWHE score of 53 (between-group difference: -6.3, 95% CI -12.2 to -0.5, p-value = 0.033). At three months, the PRWHE score was 25 in the early surgery group and 31 in the late surgery group (between-group difference: -5.7, 95% CI -11.2 to -0.1, p-value = 0.046). No significant differences were noted at other time points. For the QDASH no statistically significant differences were observed at any of the follow up time points. Both QDASH and PRWHE scores exhibited improvement over the follow up period for both groups.

Complications

The complications are listed in Table 3. In the late surgery group, 4 patients experienced carpal tunnel syndrome (CTS) symptoms after surgery, for which they did not receive a release. In the early surgery group, no patients reported CTS symptoms. The overall number of complications was comparable between the two groups, but no statistical analysis was performed due to the small sample size.

Table 2. Estimated mean QDASH and PRWHE scores during follow-up

	6 weeks	**3 months**	**6 months**	**12 months**
Response rate				
Direct	97%	97%	88%	92%
Delayed	92%	90%	87%	90%
QDASH				
Direct	40 (30 to 49)	21 (7 to 36)	13 (-4 to 29)	10 (-2 to 21)
Delayed	43 (30 to 56)	24 (-9 to 58)	15 (-15 to 46)	11 (-10 to 32)
Between-group difference	-3.5 (-8.8 to 1.9)	-3.0 (-7.4 to 1.5)	-2.6 (-6.5 to 1.3)	-1.5 (-4.7 to 1.7)
	NS	*NS*	*NS*	*NS*
PRWHE				
Direct	47 (27 to 67)	25 (5 to 45)	13 (-6 to 33)	12 (0 to 24)
Delayed	53 (29 to 78)	31 (7 to 55)	18 (-5 to 40)	14 (-8 to 36)
Between-group difference	-6.3 (-12.2 to -0.5)	-5.7 (-11.2 to -0.1)	-4.3 (-9.1 to 0.5)	-1.9 (-6.2 to 2.4)
	p=0.033	*p=0.046*	*NS*	*NS*

Estimated QDASH and PRWHE scores, with associated 95% confidence intervals. The scores range from 0 to 100, with higher scores indicating a greater level of disability, pain and functional disability.
NS = not significant

DISCUSSION

This study aimed to compare the timing of surgical treatment, either within 7 days or between 8- and 42-days following injury, regarding patient-reported outcomes in reduced DRFs. We found that early surgical treatment provided a statistically significant, but not clinically relevant difference in PRWHE scores at the six-week and three-month follow-up compared to late surgery. No significant differences were observed in the time-frame between 6 and 12 months post-trauma. Additionally, there were no significant differences in QuickDASH scores at any follow-up time points between the two groups.

The significant differences in PRWHE scores at early follow-up suggests that patients receiving early surgical treatment experience better short-term functional recovery and less pain. It is noteworthy that, while a significant difference in PRWHE scores was observed at both time points, the magnitude of this difference did not reach the MCID of 11.5 points for the PRWHE score [12]. This suggests that there is no clinical relevance of this difference. Our results align with the study of Yamashita et al. (2015), a retrospective study comparing patients who underwent internal fixation within 0-1 days post-injury (n=76) with those who had surgery after 7 days (n=30), that shows a significant better outcome in range of motion, grip strength and DASH score at early postoperative follow up for patients who underwent surgical treatment within 7 days [4]. Early surgical stabilization of the fracture likely contributes to more immediate biomechanical stability, reducing the period of immobilization and allowing for earlier mobilization, which accelerate functional recovery in the initial weeks post-injury.

The absence of significant differences in PRWHE and QDASH scores at six and twelve months indicates that the timing of surgery does not impact overall functional outcomes in the long term. These findings align with existing literature. Yamashita et al. (2015) found no significant difference in DASH scores at 48 weeks [4]. Similarly, Howard et al. (2021) utilized BSSH and NICE guidelines to classify patients. They compared 71 patients with intra-articular DRFs who underwent fixation within 3 days post-injury with 65 patients who had surgery after 3 days. For extra-articular DRFs, they compared 78 patients who had surgery within 7 days with 16 patients who had surgery after 7 days. Both closed reduction with K-wire fixation and open reduction with plate fixation were included. No significant differences in PRWHE scores were observed at the 12-month follow-up for both groups [14]. Asdown et al. (2021) also conducted a retrospective cohort study, including 158 patients who underwent plate fixation for intra-articular or displaced DRFs. They found no association between the timing of surgery and PRWHE scores at an average follow-up of 36 months (range 24-56 months) [15]. Additionally, Weil et al. (2015), in a retrospective matched case-control study, initially found a significant difference in QDASH scores at 12 months follow-up between surgeries performed within 21 days and those after 21 days. However, after controlling for outliers, this difference was no longer significant [16]. These studies collectively demonstrate that there is flexibility in the timing of surgical management for well-aligned distal radius fractures. They suggest that when surgery is performed later, due to logistical or clinical factors, it does not compromise long-term functional outcomes. Our findings are consistent with this evidence but add to the current body of knowledge through a substantially larger, multicenter cohort derived from prospectively collected data. In contrast to most prior studies, which were single-center and retrospective, our analysis benefits from standardized inclusion criteria, validated outcome measures and adjustment for potential confounders, thereby strengthening the external validity of our conclusions.

The incidence of complications was similar between the groups. This suggests that both early and late surgical interventions are relatively safe and do not significantly differ in their risk profiles concerning these complications. The comparable complication rates support the safety of observing initially well-aligned fractures and reserving surgical intervention for cases where alignment deteriorates. This finding is supported by the study of, Howard et al. (2021), where no significant differences in reoperation rate for complications was found between the direct and late fixation cohorts. In contrast to our findings, Campbell et al. (2017) found a higher rate of reoperations in the late surgical group (>12 days) (7.7% vs 20.0%, OR 2.98; 95% CI: [1.21, 7.03]), including implant removal, surgery for aseptic loss of fixation, infection, tendon rupture and carpal tunnel syndrome [17].

The findings of this study have several clinical implications. Firstly, the short-term benefits of early surgical intervention concerning functional recovery and pain relief are not clinically relevant compared to late surgery. Furthermore, a delay in operative fixation has no negative impact on long-term outcomes. Therefore, there is no need to rush into surgery, providing both patients and doctors with more time to make a joint decision about whether to pursue surgical or conservative treatment. This is particularly relevant as stable and well-aligned DRFs often have good outcomes with conservative management, making it a viable option to consider. Taking the time to make well-considered choices leads to better-informed decisions. Additionally, many well-aligned fractures remain stable in a cast, as previously demonstrated in the CAST study, highlighting the importance of monitoring fracture stability before proceeding to surgery [3]. This study supports that waiting to ensure stability does not negatively impact outcomes. Consequently, many patients could avoid surgery, leading to less surgical complications, cost savings in healthcare and reducing the burden on already full surgical schedules.

This study has some limitations. Although our data was prospectively gathered, the retrospective nature of the analysis may introduce selection bias. The groups in our study were not randomly assigned to treatment conditions and the decision to perform early versus late surgery may have been influenced by factors that are not fully accounted for in our analysis. Notably, there was a difference in the degrees of angulation, presence of radial shortening and the ulnar variance between the two groups in post-reduction fracture alignment, probably because patients with unacceptable alignment after reduction were more likely to undergo early surgery. However, we adjusted for these baseline differences by including fracture characteristics, age, sex and hospital as covariates in our linear mixed-effects model to minimize potential confounding. Additionally, the study did not account for other factors such as patient comorbidities, which might influence recovery and outcomes. Future prospective studies with larger sample sizes are needed to confirm these findings and further explore the impact of surgical timing on various subgroups of patients with distal radius fractures.

CONCLUSION

Early surgery within 7 days post-injury offers statistically significant but not clinically relevant short-term improvements in functional outcomes for patients with reduced distal radius fractures. The timing of surgical intervention does not appear to affect long-term functional outcomes up to one-year post-injury. Both early and late surgical treatments are associated with similar complication rates. This study demonstrates that it is reasonable to monitor the stability of well-aligned fractures and to reserve surgical intervention for cases of secondary displacement, which may help reduce unnecessary surgical procedures. This reduction is particularly beneficial given the decreasing hospital capacity.

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9

Chapter 9

Costs and health-related quality of life of non-operative and surgical treatment modalities for displaced distal radius fractures: A comprehensive overview based on the CAST study

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ABSTRACT

Objectives: The aim of this study was to provide a comprehensive overview of costs and health-related quality of life associated with three treatment modalities for common displaced distal radius fractures (DRFs): 1) non-operative treatment, 2) direct plate fixation and 3) delayed plate fixation, when fracture redisplacement occurs during follow-up.

Methods: A cost analysis was performed based on data collected during the CAST study, a multicenter cluster-randomized controlled trial including adult patients with a displaced DRF, randomized between immobilization with a plaster splint or circumferential cast. Included patients were prospectively followed for one year. Operatively treated patients also continued questionnaire follow-up. Healthcare costs, patient and family costs, and indirect (i.e. productivity) costs were collected. Patients completed questionnaires on health-related quality of life (EQ-5D-5L), healthcare consumption and work absence.

Results: In total, 693 patients were included in this cost analysis (non-operative: 402, direct plate fixation: 165, delayed plate fixation: 126). The mean total costs per patient were €2172 for non-operative treatment, €4321 for direct plate fixation and €4601 for delayed plate fixation. Health-related quality of life improved in all groups up to one year after fracture sustainment. No clinically relevant differences in quality of life were observed between groups.

Conclusions: A comprehensive overview of costs of displaced DRF treatment is provided in this study. Non-operative treatment is least costly. The cost differences between direct and delayed plate fixation are minimal and health-related quality of life improved to the same level in all groups. Delayed plate fixation should be considered as a standalone treatment strategy, next to non-operative and direct surgical treatment.

INTRODUCTION

With an incidence ranging from 20 to 32 per 10.000 persons per year, distal radius fractures (DRFs) are among the most common injuries seen in emergency departments in the Netherlands.[1] The financial burden of DRFs is considerable, particularly as operative treatment has increased in popularity. During the first months, operative treatment with plate fixation results in improved fracture alignment and better functional outcome compared to non-operative treatment. However, after three months no clinically relevant differences in functional outcome are observed.[2-4]

One argument for choosing surgery is the considerable redisplacement risk during cast immobilization. However, more than half of non-operatively treated displaced DRFs remain correctly aligned and do not require surgery.[5-7] It should therefore be considered to start non-operative treatment with cast immobilization and monitor fracture alignment changes during the first treatment weeks. If redisplacement occurs, plate fixation can then be offered. The choice of treatment should be tailored to the individual patient. Plate fixation may be recommended to patients with high functional demand while non-operative treatment might be preferred for those with less demanding needs.

Healthcare and societal costs are important factors to consider, especially when functional outcomes are similar. Several studies have investigated cost-effectiveness of operative versus non-operative treatment.[8-11] Results suggest that plate fixation is most cost-effective in patients with paid employment due to the accelerated recovery. However, in these studies, delayed plate fixation resulting from redisplacement is categorized as a complication. Alternatively, it could be viewed as a distinct treatment strategy, where the decision to proceed with surgery depends on the occurrence of redisplacement.

The aim of this study was to provide a comprehensive overview of the costs of three treatment modalities for displaced DRFs; 1) non-operative treatment, 2) direct plate fixation and 3) delayed plate fixation. Health-related quality of life was assessed alongside to provide clinical perspective on how the three treatment modalities impact patients' quality of life.

MATERIALS AND METHODS

Settings and participants

For this study, data of a prospective cohort including patients with a displaced DRF requiring closed reduction was used. The cohort initiated from the CAST study, a multicenter cluster-randomized trial which aimed to determine whether circumferential casting reduces the incidence of redisplacement in reduced DRFs and improve one-year functional outcomes compared to plaster splinting. The trial was approved by the medical ethical board of the Erasmus University Medical Center (MEC-2019-0528) and registered at ClinicalTrials.gov (NL8311). All patients gave written informed consent. Ten Dutch hospitals (nine general hospitals, one academic) included eligible patients (age ≥ 18 years) with a displaced DRF requiring closed reduction from May 30, 2020 until November 11, 2021. Exclusion criteria included both-bone fractures (solitary ulnar styloid process fractures were accepted), ipsilateral injuries affecting DRF treatment, polytrauma (Injury Severity Score ≥ 16), or inability to complete questionnaires due to cognitive impairment or insufficient understanding of the Dutch language. The trial design and results of the CAST study are published earlier.[7, 12]

Patients were included in the CAST study prior to closed reduction of the DRF and were randomized between two non-operative treatments: circumferential casting versus plaster splinting. The CAST study was a pragmatic trial. In case post-reduction alignment was considered non-acceptable, the treating physician had the authority to opt for direct surgical treatment. In other patients, where fracture alignment worsened during the immobilization period, the decision was made to proceed with delayed operative treatment. Patients treated with surgery were asked to complete one-year questionnaire follow-up but were excluded from the primary outcome analysis of the CAST study.

The CAST study concluded that type of casting is not of influence on the redisplacement risk. Also, functional results, health-related quality of life and costs were comparable. We subsequently decided to conduct a cost analysis on non-operative and operative treatment. All CAST study inclusions were subdivided over three groups as shown in Figure 1, irrespective of their initial allocation: 1) Non-operative treatment with cast immobilization (non-operative treatment), 2) Immediate operative treatment planned after closed reduction (direct plate fixation), 3) Initial non-operative treatment but operative treatment performed in second instance (delayed plate fixation).

We deliberately chose not to conduct a cost-effectiveness analyses, as patients were not randomized for this purpose. Baseline differences between groups are expected, making direct comparisons unreliable. Instead, to gain a broader understanding of the patient population and potential differences in patient demand between groups, we analyzed health-related quality of life alongside.

Assessments and follow-up

All patients were followed for one year after fracture sustainment. At baseline, sociodemographic and clinical data were collected. *Sociodemographic data* consisted of age, sex, BMI, hand dominance, level of education and working status. The following *clinical data* were registered: fracture mechanism and fracture treatment (type of reduction, type of casting applied). Patients completed multiple questionnaires at 1,2 and 6 weeks, and 3, 6, and 12 months follow-up. The questionnaires conducted at 1 and 2 weeks focused on complaints and analgesic use. The questionnaires at 6 weeks and 3, 6 and 12 months were similar and focused on functional outcomes, health-related quality of life and healthcare consumption and productivity loss.

The primary outcome for this analysis was total costs, consisting of direct (healthcare consumption) and indirect (productivity loss) costs. The secondary outcome was health-related quality of life.

Cost measurement

Emergency department visits, outpatient medical specialist and casting technician visits, operative procedures, non-operative treatment (i.e. casting), hospital admissions, fracture-related adverse events and medical imaging during follow-up (i.e. radiographs, CT, MRI and ultrasound imaging) were derived from electronic patient files of the included hospitals during one year follow-up. Extramural healthcare consumption was measured using the validated iMTA Medical Consumption Questionnaire (iMCQ) and included the number of visits to the general practitioner, physical therapist and occupational physician, use of domestic care and analgesic use. Patient-reported analgesic use was extracted from the 1-, 2- and 6-week questionnaires and was divided in three subtypes: 1) use of paracetamol/acetaminophen, 2) use of non-steroid anti-inflammatory drugs (NSAIDs) and 3) opioid use. Since the quality of patient-reported daily dosage was moderate, we used the average dosage per analgesics subtype per day per time measurement as the standard daily dose for all patients in the cohort. The validated iMTA Production Consumption Questionnaire (iPCQ) was used to gather information about work productivity by questioning work absenteeism and resumption.

The total healthcare and societal costs of the three treatment modalities were assessed from respectively a healthcare and a societal perspective during the first year after fracture sustainment. With the time horizon of one year, discounting was not applied. Healthcare costs comprised both in- and out of hospital medical care costs, categorized into costs for the emergency department, operative procedure costs, medical follow-up costs, analgesic costs and extramural healthcare costs. Patient and family costs comprised travel costs related to healthcare visits. Costs outside of the healthcare sector consisted of costs related to productivity loss at work (i.e. absenteeism).

Costs were calculated by multiplying healthcare consumption (i.e. volumes) by the corresponding cost prices per consumption unit and were converted to 2021 Euros (€) using the Dutch Consumer Price Index, because the CAST study was conducted in 2021.[13] Cost prices for healthcare resources were primarily derived from the Dutch manual for costing research.[14] The cost prices for closed reduction of the DRF, direct and delayed plate fixation, and secondary operative procedures (such as carpal tunnel release, plate removal and correction osteotomy) and casting material were based on the financial registrations of the participating hospitals in which we distinguished cost prices for general versus academic hospitals. Analgesic costs were derived from the Dutch Medication and Aid Information Project database (i.e. www.medicijnkosten.nl). Indirect costs due to productivity loss were based on the hours of work absence, calculated as recommended in the Dutch guidelines, using the friction cost method with a friction period of 85 days.[14] A detailed overview of data sources and prizes is shown in Table 1.

Health-related quality of life

Health-related quality of life was examined using the EuroQol-5 Dimension 5 level questionnaire (EQ-5D-5L) and the accompanying EQ VAS.[15] The EQ-5D-5L has 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, on which patients score their perceived general health. With the scores on the 5 dimensions, an index value was calculated using the Dutch tariff. This value ranges from -0.446 to 1, indicating the poorest and full health respectively.[15] EQ VAS records the patient's self-rated health on a visual analogue scale from 0 ('The worst health you can image') to 100 ('The best health you can image').

Statistical analysis

This cost analysis is descriptive and not comparative since the study groups were not randomized for this purpose in the CAST study. Therefore, no statistical comparisons were made for the outcomes. Missing data were imputed in SPSS version 26.0 using multiple imputation with fully conditional specification using predictive mean matching to draw imputed values. The number of imputations was set to ten. For each treatment modality, costs and EQ-5D-5L outcomes are presented as mean (standard deviation [SD]) and median (inter quartile range [IQR]). Nonparametric bootstrap analysis with 1,000 replication was performed in R version 4.3.2 to generate 95% confidence intervals around differences in mean (sub)total costs for all groups.

RESULTS

In total, 743 patients were included in the CAST study. Fifty patients were excluded shortly after inclusion and were thus not further followed for study purposes. In the current study, 693 patients were included (Figure 2). From this cohort, 402 patients (58%) received non-operative treatment, 165 (24%) were treated directly with plate fixation and 126 (18%) started non-operative treatment but were later operated. Baseline patient and fracture characteristics are presented in Table 2. Patients in the direct plate fixation group were relatively younger and more likely to be employed compared to those in the other groups. The number of intra-articular fractures was considerably higher and the post-reduction fracture alignment was slightly worse in the direct plate fixation group compared to non-operative and the delayed plate fixation group.

Costs

Costs per category and total healthcare and societal costs per treatment group are presented in Table 3. The mean total societal costs per patient were €2,172 (95% confidence interval [95% CI] 2,112-2,227) for non-operative treatment, €4,321 (95% CI 4,231-4,404) for direct plate fixation and €4,601 (95% CI 4,494-4,703) for delayed plate fixation.

For each treatment modality, total societal costs are mainly driven by healthcare costs. Non-operative treatment is incurring the lowest costs since no costly surgical procedure is performed to fixate the DRF, saving on average €2,000. The mean total societal costs difference between direct and delayed plate fixation is €280. The extra expenses in the delayed plate fixation group are mainly driven by additional medical imaging, casting technician consultations and secondary surgical procedures.

Heathcare utilization

The emergency department visits were least costly in direct plate fixation group. In the non-operative group, 6 patients underwent a correction osteotomy. Plate removal was performed five and three times in the direct- and delayed plate fixation group, respectively. With respect to extramural healthcare, no large cost differences are noted. Also, patient and family costs are similar between groups. Productivity loss costs incurred only 4.6% to 5.8% from total societal costs and were lowest in the delayed plate fixation group.

Health-related quality of life

In Table 4, health-related quality of life pre-injury and three- and twelve months after fracture sustainment are presented. Pre-injury health-related quality of life, presented by EQ-5D-5L utility index score was above 0.91 for all groups. One year after fracture sustainment, all groups report mean values ≥0.85, with the direct plate fixation group reporting a mean (SD) utility score of 0.91 (0.11). Patients in all three groups did not reach pre-injury EQ-5D utility index outcomes. Patient's mean self-rated health-related quality of life (EQ-VAS) was lowest in the non-operative group at all time points.

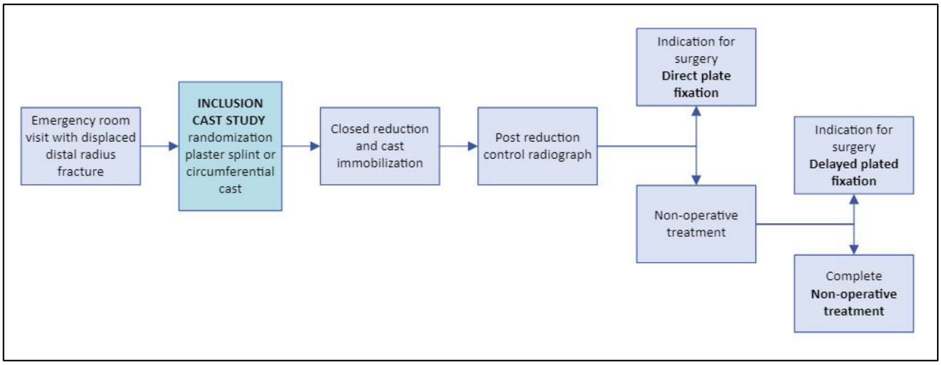

Figure 1. Study group formation after inclusion of patients in the CAST study

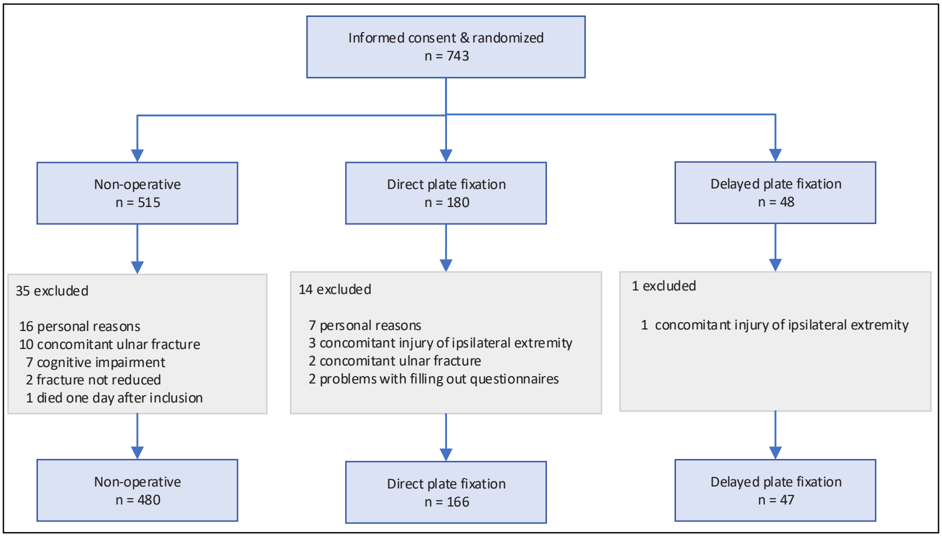

Figure 2. Flowchart of study population

DISCUSSION

This cost analysis provides a comprehensive overview of the healthcare and societal costs associated with the treatment of displaced DRFs in adults. In the Netherlands, the mean costs of non-operative DRF treatment, direct plate fixation and delayed plate fixation are €2,172, €4,321 and €4,601 respectively. One year after the fracture, health-related quality of life was ≥0.85 in all groups.

This cost analysis demonstrates that operative treatment of DRFs is almost twice as expensive as non-operative treatment, primarily due to the costs of the surgical procedure. The cost difference between direct plate fixation and delayed plate fixation is small, amounting to €280 in favor of direct plate fixation. The costs of the surgical procedure used in this study is comparable to previous Dutch studies.[8, 9] However, compared to other countries, surgical costs in the Netherlands are relatively low.[16]

As mentioned throughout the manuscript, this study has a descriptive rather than comparative purpose because of baseline differences. The differences in baseline characteristics between the non-operative and delayed plate fixation group are rather small. However, patients in the direct plate fixation group are relatively younger and more frequently employed compared to those in the non-operative and delayed plate fixation group. Additionally, post-reduction fracture alignment is poorest in this group, which explains the choice for operative fixation. However, we noticed similarities and differences we think are noteworthy to point out. Firstly, emergency room visits were least costly in the direct plate fixation group. This is explained by the higher number of patients who had an additional emergency room visit in the non-operative and delayed plate fixation group. Most often, these additional visits were due to pain complaints. Secondly, cost differences for secondary surgical procedures were small between groups. While disabling malunions in the non-operative group may lead to costly correction osteotomies, these costs do not exceed the secondary surgery costs in the other treatment groups. Thirdly, costs for outpatient clinic visits were considerably higher for patients who underwent direct or delayed surgery. This is primarily due to the fact that a cast technician consultation is less expensive than consultation of a medical orthopedic trauma specialist. Fourthly, contrary to previous literature, we observed that medical imaging follow-up costs are lower after direct operative treatment compared with the non-operative group as well as the delayed plate fixation group.[8, 9, 11] This difference is probably due to the additional radiographs taken during non-operative treatment (and prior to delayed plate fixation) to monitor fracture alignment. Lastly, productivity costs are higher in the plate fixation and the delayed plate fixation group compared to the non-operative group. This difference most probably exists due to baseline differences between the groups. Half of both the non-operative and delayed plate fixation group were retired whilst this was only 30% in the direct plate fixation group. It is hypothesized that operative treatment facilitates rapid return to work due to shorter immobilization duration, thereby reducing productivity costs. Given the baseline differences in our cohort, we cannot draw definitive conclusions on this. Further investigation in a younger patient population is warranted.

Pre-injury health-related quality of life was not achieved within any group one year after fracture sustainment, possibly due to persistent complaints. It may also be explained by recall bias as the pre-injury EQ-5D-5L was measured retrospectively (one week after fracture sustainment) which could have led patients to overestimate their pre-injury state. The direct plate fixation scored highest at all time points. These patients are younger and therefore baseline differences in physical functioning are expected which could influence the higher quality of life rating. However, the differences between groups are small (<0.10) and all groups score above the Dutch population reference value of 0.84 for those over 60 years of age.[15]

A strength of this study is the extensive prospectively gathered data. In-hospital healthcare costs have most impact on the total costs and these costs are directly and reliably collected from patient files. In addition to total healthcare and societal costs, this study provides insight into the type of care utilized by patients with a DRF.

A limitation of this study, as mentioned throughout this manuscript, are the baseline differences between the groups. We did not aim to demonstrate superiority or cost-effectiveness of either treatment, instead, our goal was to provide a comprehensive overview of costs based on detailed prospectively collected data. The baseline differences, with younger patients and more severe fractures in the direct plate fixation group, were expected. The treatment choice in these patients aligns with recent literature, underlining that the younger and more demanding patients benefit from plate fixation.[2] Furthermore, 49% of the direct plate fixation group is employed whilst the other two groups have higher rates of retired patients. The non-operative group and the delayed surgery group were however comparable concerning patient characteristics and post-reduction fracture alignment. One other limitation to note is that participants might have undergone a corrective osteotomy after the designated endpoint of one year, potentially increasing total healthcare and, therefore, societal costs in the non-operative group. Ultimately, a limitation of this study is the presence of missing data (34-41%) across all groups, primarily due to participants not completing all iMCQ and iPCQ questionnaires throughout the year. Although we imputed the missing data, this introduces some level of uncertainty, particularly affecting estimates of extramural healthcare and productivity loss costs.

This study provides an comprehensive overview of the costs and health-related quality of life in DRF treatment. This study is the first to reflect on delayed plate fixation as a standalone treatment strategy. We found only a small difference in costs when opting for operative treatment in second instance while health-related quality of life remains comparable to that of direct plate fixation. Starting with non-operative treatment and later deciding whether to proceed with operative treatment based on alignment changes during follow-up, could be considered as a viable treatment option.

Table. 1 Data sources and unit prices of all healthcare cost categories

Cost category	Unit	Number of fixed units for NO/P/DP[a]	Source of data	Source of valuation	Unit price (€)
Emergency department					
Emergency department visit	Visit	1/1/1	Electronic patient files	Cost manual	€287,66
Radiographs	Radiograph	Variable	Electronic patient files	Hospital financial registry	€45,10[b] / €51,10[c]
Wrist reduction					
Wrist reduction, *performed by:*	Procedure	1/1/1	Questionnaire/Electronic patient files	Hospital financial registry	€72,32[c] / €211,10[b]
- Resident	Minute	30 min	Questionnaire/Electronic patient files	Dutch CLA	€0,44[c] / €0,48[b]
- Emergency department nurse	Minute	30 min	Questionnaire/Electronic patient files	Dutch CLA	€0,37[b] / €0,45[c]
- Nurse practitioner	Minute	30 min	Questionnaire/Electronic patient files	Dutch CLA	€0,48[c] / €0,53[b]
- Casting technician	Minute	30 min	Questionnaire/Electronic patient files	Dutch CLA	€ 0,47
Application of immobilization					
Casting type: Circumferential cast	Procedure	Variable	Questionnaire	Hospital financial registry	€63,23[c] / €75,78[b]
Plaster splint	Procedure	Variable	Questionnaire	Hospital financial registry	€56,14[c] / €68,33[b]
Casting material: Plaster of Paris, *applied by*	Plaster	Variable	Questionnaire	Hospital financial registry	€2,09
Synthethic casting, *applied by*	Plaster	Variable	Questionnaire	Hospital financial registry	€4,84
- Resident	Minute	15 min	Questionnaire/Electronic patient files	Dutch CLA	€0,44[c] / €0,48[b]

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Cost category	Unit	Number of fixed units for NO/P/DP[a]	Source of data	Source of valuation	Unit price (€)
- Emergency department nurse	Minute	15 min	Questionnaire/Electronic patient files	Dutch CLA	€0,37[b] / €0,45[c]
- Nurse practitioner	Minute	15 min	Questionnaire/Electronic patient files	Dutch CLA	€0,48[c] / €0,53[b]
- Casting technician	Minute	15 min	Questionnaire/Electronic patient files	Dutch CLA	€0,47
Surgical procedures					
Plate fixation	Procedure	0/1/variable	Electronic patient files	Hospital financial registry	€1.954,87[b] / €3.312,33[c]
Correction osteotomy	Procedure	0/0/variable	Electronic patient files	Hospital financial registry	€1.656,22[b] / €3.888,00[c]
Plate removal	Procedure	Variable	Electronic patient files	Hospital financial registry	€1.188,09[b] / €1.255,00[c]
Carpal tunnel release	Procedure	Variable	Electronic patient files	Hospital financial registry	€223,96[b] / €788,86[c]
Medical follow-up					
Consultation casting technician	Visit	Variable	Electronic patient files	Cost manual	€17,54
- Cast adjustment	Procedure	Variable	Questionnaire	Hospital financial registry	€3,53
- Cast removal	Procedure	Variable	Questionnaire	Hospital financial registry	€10,69
- Cast replacement	Procedure	Variable	Questionnaire	Hospital financial registry	€73,92[c] / €86,47[b]
Outpatient clinic medical specialist	Visit	Variable	Electronic patient files	Cost manual	€88,85[b] / €181,04[c]
Medical imaging					
- Radiographs	Radiograph	Variable	Electronic patient files	Hospital financial registry	€45,10[b] / €51,10[c]
- CT scan	CT scan	Variable	Electronic patient files	Cost manual	€161,05
- MRI scan	MRI scan	Variable	Electronic patient files	Cost manual	€254,34
- Ultrasound	Ultrasound	Variable	Electronic patient files	Cost manual	€96,63
Hospitalization	Day	Variable	Patient questionnaire	Cost manual	€492,03[b] / €713,05[c]

Cost category	Unit	Number of fixed units for NO/P/DP[a]	Source of data	Source of valuation	Unit price (€)
Analgesic use					
- Paracetamol	Standard daily dose[g]	Variable	Patient questionnaire	Medicijnkosten.nl	€0.02
- NSAID[e]	Standard daily dose[h]	Variable	Patient questionnaire	Medicijnkosten.nl	€0.10
- Opioids[f]	Standard daily dose[i]	Variable	Patient questionnaire	Medicijnkosten.nl	€0.04
Extramural healthcare costs					
Consultation general practitioner	Visit	Variable	Patient questionnaire	Cost manual	€36,65
Consultation physiotherapist	Visit	Variable	Patient questionnaire	Cost manual	€36,65
Consultation occupational physician	Visit	Variable	Patient questionnaire	Cost manual	€54,10
Domestic care: domestic help	Hour	Variable	Patient questionnaire	Cost manual	€23,88
Domestic care: nursing	Hour	Variable	Patient questionnaire	Cost manual	€55,53

All costs are expressed in 2021 Euros. CLA: collective labour agreement

[a] Number of units for fixed costs are displayed for non-operative (NO), direct plate fixation (P), delayed plate fixation (DP).

[b] General hospital cost prices

[c] Academic hospital cost prices

[d] Due to limited data quality, analgesic use is subdivided in three medication categories namely paracetamol, non-steroid anti-inflammatory drugs (NSAID) and opioids. Per category, the cost price of the most frequently reported analgesic is used. Daily dosage is based on mean daily dosages used.

[e] Cost price based on Ibuprofen

[f] Cost price based on Oxycodon

[g] Week 1: 6 p/d, week 2 5 p/d, week 4-6 5 p/d

[h] Week 1: 3 p/d, week 2 2 p/d, week 4-6 2 p/d

[i] Week 1: 3 p/d, week 2 3 p/d, week 4-6 3 p/d

Table 2. Patient and fracture characteristics of trial participants per treatment group

	Non-operative n = 402	Direct plate fixation n = 165	Delayed plate fixation n = 126
Patient characteristics			
Age, year	65 (16)	59 (13)	63 (13)
BMI, kg/m^2	26 (5)	26 (4)	25 (4)
Female, n (%)	341 (85)	134 (81)	103 (82)
Work status, n (%)			
Paid work	134 (33)	80 (49)	47 (37)
Retired	199 (50)	49 (30)	63 (50)
No paid work[a]	48 (12)	17 (10)	12 (10)
Unknown	21 (5)	19 (11)	4 (3)
Fracture characteristics			
Dominant side affected, n (%)	206 (51)	74 (45)	57 (45)
Fracture mechanism, n (%)			
Sports	74 (18)	43 (26)	30 (24)
Traffic	55 (14)	22 (13)	20 (16)
Fall, minor impact	228 (57)	82 (50)	62 (49)
Fall, major impact	29 (7)	16 (10)	14 (11)
Other	16 (4)	1 (1)	0
Styloid ulnae fracture, n (%)	207 (52)	90 (55)	61 (48)
Fracture dorsally angulated, n (%)	377 (94)	139 (84)	119 (94)
Dorsal angulation, degrees	21 (12)	29 (13)	24 (11)
Inclination, degrees	16 (6)	13 (8)	13 (7)
Radial shortening, yes n (%)	199 (50)	120 (73)	79 (63)
If yes, shortening in mm	2.7 (1.9)	3.9 (2.4)	3.7 (2.3)
Intra-articular, n (%)	155 (39)	133 (81)	71 (56)
Post reduction alignment			
Dorsal angulation, yes n (%)	213 (53)	124 (75)	81 (64)
Degrees of dorsal angulation	6 (5)	12 (8)	7 (6)
Inclination, degrees	21 (4)	18 (5)	20 (5)
Radial shortening, yes n (%)	69 (17)	57 (35)	33 (26)
If yes, shortening in mm	1.9 (1.2)	2.8 (1.2)	2.2 (1.0)

If not mentioned differently, data is presented as mean with SD between brackets.

[a.] Student, unemployed and unfit for work were clustered.

Table 3. Mean (sub)total costs (in 2021 Euros) per patient during 12 months follow-up based on multiple imputation (10 sets)

	Non-operative treatment		Direct plate fixation		Delayed plate fixation	
n	402 (58%)		165 (24%)		126 (18%)	
Deceased during follow-up	8		0		1	
Healthcare costs	**mean (SD)**	**median (IQR)**	**mean (SD)**	**median (IQR)**	**mean (SD)**	**median (IQR)**
Emergency department						
- Emergency department visit[a]	670 (463)	468 (468-756)	590 (288)	468 (468-756)	635 (324)	468 (468-756)
- Closed wrist reduction[b]	224 (37)	225 (225-227)	219 (35)	225 (225-226)	224 (26)	225 (225-227)
- Initial cast application[c]	79 (6)	76 (73-84)	78 (6)	75 (73-83)	80 (6)	83 (73-84)
Surgical procedures						
- Plate fixation[d]	0 (0)	0 (0-0)	2045 (340)	1955 (1955-1955)	1998 (239)	1955 (1955-1955)
- Secondary surgical procedures[e]	27 (202)	0 (0-0)	36 (204)	0 (0-0)	28 (181)	0 (0-0)
Follow-up						
- Casting technician consultations[f]	129 (47)	140 (123-140)	15 (28)	0 (0-18)	46 (46)	18 (18-57)
- Outpatient visits	97 (148)	0 (0-178)	370 (307)	267 (267-444)	320 (165)	267 (267-355)
- Medical imaging during follow-up[g]	284 (112)	271 (271-271)	143 (132)	90 (90-192)	194 (115)	180 (90-271)
- Hospitalizations	11 (220)	0 (0-0)	62 (216)	0 (0-0)	53 (157)	0 (0-0)
Analgesic use[h]	2 (2)	2 (1-4)	3 (3)	3 (1-4)	3 (3)	2 (1-4)
Extramural healthcare						
- General practitioner	13 (30)	0 (0-0)	12 (28)	0 (0-7)	16 (42)	0 (0-22)
- Physiotherapist	363 (472)	218 (0-497)	376 (430)	263 (70-513)	411 (515)	218 (57-559)
- Occupational physician	13 (39)	0 (0-0)	23 (45)	0 (0-22)	24 (51)	0 (0-5)
- Domestic care[i]	117 (598)	0 (0-0)	110 (653)	0 (0-0)	122 (559)	0 (0-0)

	Non-operative treatment		Direct plate fixation		Delayed plate fixation	
n	402 (58%)		165 (24%)		126 (18%)	
Deceased during follow-up	8		0		1	
Healthcare costs	**mean (SD)**	**median (IQR)**	**mean (SD)**	**median (IQR)**	**mean (SD)**	**median (IQR)**
Total healthcare costs	**2049 (1180)**	**1689 (1340-2351)**	**4037 (1061)**	**3837 (3346-4338)**	**4315 (1077)**	**4006 (3514-4891)**
Bootstrapped mean (95% CI)	**2048 (1999-2094)**		**4037 (3959-4106)**		**4314 (4229-4395)**	
Patient & family costs	**24 (15)**	**20 (14-30)**	**28 (14)**	**26 (19-35)**	**31 (16)**	**27 (21-35)**
Bootstrapped mean (95% CI)	**25 (24-25)**		**28 (27-29)**		**31 (30-32)**	
Productivity costs	**127 (433)**	**0 (0-0)**	**222 (477)**	**0 (0-218)**	**210 (555)**	**0 (0-61)**
Bootstrapped mean (95% CI)	**128 (108-144)**		**222 (185-255)**		**212 (159-260)**	
Total societal costs	**2143 (1316)**	**1755 (1390-2467)**	**4322 (1247)**	**4042 (3456-4798)**	**4605 (1303)**	**4199 (3662-5130)**
Bootstrapped mean (95% CI)	**2172 (2112-2227)**		**4321 (4231-4404)**		**4601 (4494-4703)**	
% missing societal costs	34%		41%		41%	

[a] Emergency department (ED) visit: ED visit, diagnostic radiographs
[b] Wrist reduction: wrist reduction procedure and occupant performing the reduction
[c] Application of immobilization: casting type, casting material and occupant applying the plaster
[d] Plate fixation: operative correction of fracture alignment including plate fixation
[e] Other surgical procedures: carpal tunnel release, plate removal, corrective osteotomy
[f] Casting room consultations: consultation cast technician, cast adjustment, cast removal, cast replacement
[g] Medical imaging during follow-up: radiograph, CT scan, MRI scan, ultrasound
[h] Analgesic use: use of paracetamol, non-steroid anti-inflammatory drugs, opioids during the first 6 treatment weeks
[I] Domestic care: domestic help and nursing

Table 4. Health-related quality of life and patient reported outcomes per patient at 3 and 12 months follow-up.

	Non-operative (n=402)		Direct plate fixation (n=165)		Delayed plate fixation (n=126)	
EQ-5D-5L utility	**mean (SD)**	**median (IQR)**	**mean (SD)**	**median (IQR)**	**mean (SD)**	**median (IQR)**
Baseline (pre-injury)	0.91 (0.14)	1.00 (0.86-1.00)	0.95 (0.09)	1.00 (0.90-1.00)	0.93 (0.15)	1.00 (0.89-1.00)
3 months	0.78 (0.18)	0.82 (0.74-0.89)	0.83 (0.13)	0.85 (0.79-0.89)	0.84 (0.11)	0.85 (0.78-0.89)
12 months	0.85 (0.18)	0.89 (0.81-1.00)	0.91 (0.11)	0.90 (0.85-1.00)	0.89 (0.15)	0.89 (0.84-1.00)
EQ-5D-5L VAS						
Baseline (pre-injury)	85 (15)	89 (77-96)	90 (11)	91 (82-100)	87 (12)	90 (80-97)
3 months	77 (17)	80 (70-90)	83 (12)	84 (76-90)	80 (18)	80 (70-90)
12 months	81 (17)	82 (74-93)	85 (14)	87 (80-95)	85 (14)	87 (75-95)
12 months follow-up rate	86%		84%		90%	

EQ-5D-5L: EuroQol-5 Dimension 5 level questionnaire, SD: Standard deviation, IQR: Interquartile range

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Chapter 10

General discussion

GENERAL DISCUSSION

Since the early nineties, there has been an exponential increase in the number of publications on distal radius fractures (DRFs) in adults, peaking between 2018 and 2020, when over 400 manuscripts were published annually. Even though knowledge about different treatment strategies for DRFs has increased rapidly, important questions remain unanswered. The general aim of this thesis is to address unresolved questions related to the prediction of (re)displacement, the influence of casting techniques on redisplacement, and whether we should treat these fractures surgically and if so, whether immediately.

Part I

Predicting (re)displacement

Part I of this thesis focuses on displacement in DRFs. Specifically, we examined the role of additional CT imaging in objectively assessing fracture alignment and evaluated the potential of artificial intelligence to predict fracture redisplacement.

Displacement of DRFs

The current Dutch guideline for DRFs, published August 2021 states that a DRF is considered unacceptably aligned (displaced) if one or more of the following criteria are met: ≥ 10° dorsal angulation, ≥ 20° volar angulation, ≤ 15° radial inclination, ≥ 3 mm radial shortening and ≥ 2 mm intra-articular step-off.[1] For most studies included this thesis, we adhered to the previous Dutch guideline which differs in two criteria. Firstly, the previous guideline considered dorsal angulation up to 15° acceptable. Secondly, an intra-articular gap over 2 mm was considered unacceptable, whereas the most recent guideline does not take intra-articular gaps into consideration.

International guidelines for DRF treatment generally agree on the criteria defining acceptable fracture alignment, although high quality evidence supporting these thresholds is lacking. This is reflected in small differences between (inter)national guidelines and the diverse range of definitions used in the literature.[1-4] Although treatment guidelines are largely comparable, their differences underscore the ongoing uncertainty among experts regarding the impact of minor alignment variations on functional outcomes. For example, while both the Dutch and American (AAOS) guidelines were updated in 2021 to incorporate the most recent evidence, they differ in several aspects. Compared to the AAOS guideline, the Dutch guideline provides more detailed thresholds, particularly for volar angulation (> 20°), radial inclination (> 15°) and translation (< 2 mm). Guidelines from the Nordic Orthopaedic Federation countries also lack uniformity. For example, Sweden and Norway do not incorporate threshold values for inclination and volar angulation in in their guidelines.

The alignment thresholds used in the aforementioned guidelines are mostly based on the systematic review and meta-analysis by Mulders et al. (2018).[5] In this study, the relationship between radiographic alignment and patient-reported outcomes was investigated.

Radiographic outcome was classified as either acceptable or unacceptable, based on radial inclination (≥15°), dorsal angulation (<15°), volar angulation (>20°) and radial shortening (< 5mm). Interestingly, the 16 studies included in the systematic review reported conflicting results. Ten studies found that unacceptable alignment negatively affects patient-reported outcomes, whereas six studies found no such association. Furthermore, two studies reported that the negative impact was observed only in patients younger than 65 or 60 years. The meta-analysis included six studies, comprising a total of 582 patients. A significant difference in PROMs was found in favor of an acceptable reduction; however, this difference was considered clinically irrelevant. Based on these studies, we assume that the effect of redisplacement (ie. fracture malalignment) on clinical outcome is difficult to quantify.

In **Chapter 2** we demonstrated that additional CT imaging provides improved assessment of fracture alignment compared to conventional radiographs, particularly with regard to intra-articular fracture incongruency. In half of the cases, the DRF appeared acceptably aligned on plain radiographs, but was reclassified as unacceptably aligned on CT imaging. Intra-articular step-off variations were the primary cause of this reclassification. Since intra-articular incongruity is associated with an increased risk of redisplacement, obtaining a CT scan can be a valuable tool for early identification of this risk factor.[6, 7] Furthermore, an intra-articular fracture malunion is associated with increased complaints because joint surface incongruence contributes to the development of radiocarpal osteoarthritis.[8] We found that, apart from intra-articular alignment, other fracture characteristics can be accurately measured on plain radiographs, consistent with previous literature.[9] Due to the retrospective nature of the dataset used in **Chapter 2**, we were unable to assess whether the additional CT scan can lead to changes to the initial treatment plan. Arora et al. (2010) showed that CT changed the plan in 23% of cases.[10] However, the literature remains inconclusive regarding whether inter- and intra-observer agreement on treatment decisions improves with CT compared to plain radiographs.[10, 11] In summary, accurate assessment of fracture alignment can be achieved using radiographs alone. However, when intra-articular incongruity is suspected, additional CT scanning should be considered in vital patients to determine whether operative treatment is warranted to restore the intra-articular surface.

Redisplacement of DRFs

Redisplacement occurs when a well-aligned fracture (without reduction or after reduction) displaces beyond the threshold for acceptable fracture alignment. Unfortunately, the incidence of redisplacement in acceptably reduced DRFs is notably high. According to recently performed randomized controlled trials including our own, between one-third and two-thirds of reduced DRFs redisplace (lose threshold alignment as defined by guideline criteria) during cast immobilization.[12-15]

The surgeon's assessment of the redisplacement risk is a key factor influencing the decision to proceed with immediate surgical intervention. However, accurately predicting fracture stability at the start of treatment remains challenging. Treatment decisions are often based on personal experience and local preferences, which can vary significantly.[16] We should aim to move from an experience-based opinion towards a scientific and truly patient-specific redisplacement prediction. If we are able to predict fracture redisplacement more accurately, we can better identify cases that will genuinely benefit from direct operative treatment. The ultimate goal is to find the optimal balance between over- and under treatment. Overtreatment occurs when surgery is chosen based on subjective assessment of presumed fracture instability, leading to surgical interventions in cases that would have healed satisfactorily with non-operative treatment. Undertreatment occurs when non-operative management is chosen in unstable fractures, resulting in untreated redisplacement and subsequent malunion. This may lead to debilitating wrist symptoms and, in some cases, necessitate a corrective osteotomy.

When discussing the pros and cons of non-operative versus operative treatment with a patient, it is often difficult to accurately estimate the risk of redisplacement for their specific DRF. Not only post-reduction fracture alignment, but also specific patient- and fracture related characteristics are associated with an increased risk of redisplacement such as female sex, age over 60 years, intra-articular incongruity, and the presence of dorsal comminution.[17] The multifactorial nature of this redisplacement risk makes accurate estimation challenging. Oude Nijhuis et al. observed that it is surprisingly difficult to predict DRF instability based on trauma and post-reduction radiographs.[unpublished data] The accuracy of clinicians was only 54% and the inter-observer agreement was just fair. It is essential that predictive accuracy exceeds random chance, as this estimation ultimately forms the basis for the advice given to the patient. Given the significant potential for improvement, we hypothesize that the application of big data and artificial intelligence (AI) could aid in identifying fracture instability.

In **Chapter 3**, we described the development of a convolutional neural network (CNN), which may represent a significant step forward in predicting redisplacement. Based on radiographs, combined with patients' age and sex, it provides a fracture- and patient-specific estimation of the redisplacement risk. With an accuracy of 76% and an area under the curve of 82%, this algorithm could substantially assist physicians and patients in the decision-making process regarding whether to start non-operative treatment or to opt for surgery. When the redisplacement risk is estimated to be high, surgical intervention should be offered in vital patients (active elderly with limited comorbidities). Conversely, non-operative management with cast immobilization and radiographic monitoring may be appropriate for patients with a lower probability of redisplacement. This convolutional neural network (CNN) is the first in orthopaedic trauma to predict a disease pattern encouraging the application of this technique to other challenges. External validation and implementation of this tool in current practice remains challenging.[18] For external validation, a conservatively treated cohort with complete radiographic follow-up needs to be identified. Such cohorts are scarce because radiographic alignment is often not assessed beyond two weeks of treatment when non-operative treatment is chosen. It is therefore essential to reach out to prospective cohorts to collaborate in this effort. Secondly, implementing an AI-driven prediction-tool into patient-care means that it must adhere to the medical device regulation (MDR). The MDR is a European regulation that ensures a robust, transparent and sustainable regulatory framework to maintain a high level of safety. It is costly and time-consuming to finalize this step. While the deployment of AI is a hot topic, many algorithms stall after initial development and never progress to reach the patient.[19] This highlights the need for an 'open access mentality' to create reliable algorithms through collaborative effort, rather than fragmented individual initiatives.[20]

Part II

Can we prevent redisplacement with casting techniques?

In the second part of this thesis, we studied whether casting influences redisplacement of DRFs. In **Chapter 4** we found that circumferential casting significantly reduced the risk of redisplacement. Because of this promising finding, along with the lack of consensus on casting type in the Netherlands[21], we decided to further explore this possible association through a randomized controlled trial. However, in the CAST study, described in **Chapter 5 and 6**, no relationship was found between casting type and the incidence of redisplacement. We consider this finding to be robust as the risk of bias from patient- or fracture-related characteristics is minimal, known confounding parameters were accounted for in our analysis. Additionally, the multicentre and pragmatic design of the CAST study, along with the large number of participants ensures that the study group is representative of both the population and diversity of this fracture type. The discrepancies observed between the findings in **Chapter 4** and **Chapter 6** might be attributable to confounding in **Chapter 4**. In this retrospective cohort, casting type preferences varied between the participating hospitals, meaning that circumferential casting was not used in all participating centres. Consequently, the lower incidence of redisplacement in circumferential casted fractures may be explained by differences in fracture characteristics between the hospital populations, or, alternatively, by variation in skill level of the personnel performing the reductions.

The influence of casting on the risk of redisplacement in reduced DRFs has been scarcely investigated in adults. Camur et al. (2021)[22] compared reversed sugar tong splinting with below-elbow casting and found no differences in radiological outcome. Espejo-Reina et al. (2021)[23] conducted a biomechanical study to test flexion forces in forearm casts and found that circumferential casts demonstrated greater rigidity compared to dorsal splints. However, the impact on redisplacement in clinical cases has never been tested.

In addition to the comparable risk of redisplacement between circumferential casts and splints, **Chapter 6** demonstrates that clinical and patient-reported outcomes were also similar in our CAST study cohort. This further underlines that casting type is not associated with DRF outcomes. Based on the CAST study results, circumferential casting does not appear to be contraindicated as initial treatment. The common belief that circumferential casting increases pain and discomfort is not supported - and is even refuted - by our findings. Patients with circumferential casting reported significantly fewer complaints of swelling and experienced less pain during the first week of treatment. Also, no cases of compartment syndrome were observed in our cohort. Remarkably, one in five patients required an extra hospital visit, regardless of the casting type. These extra visits were primarily due to cast-related complaints, such as severe finger swelling or cast tightness. This incidence is consistent with previous literature, reporting additional visits in 22-31% of cases.[24, 25] These high rates of additional hospital visits raise questions about the quality of our current immobilization methods, which will be discussed later.

In **Chapter 7** we further explored the influence of other casting-related factors on the incidence of redisplacement. In paediatric DRFs, multiple studies have suggested that cast moulding affects the risk of redisplacement.[26-30] We anticipated similar findings in adult fractures, as suggested by previous retrospective research.[31] However, in our cohort, no association was found between cast moulding quality and the redisplacement risk. In fact, the overall cast quality in our study was assessed as poor, based on three different casting indices. Interestingly, cast index scores were poor in both stable and displaced fractures, suggesting limited utility of cast indices. This perspective is further supported by the finding that cast moulding quality was not significantly better in casts applied by professional casting technicians. Previous literature similarly reported that experience does not significantly improve cast indices.[32] Combining the findings from **Chapter 6 and 7**, we conclude that casting type, cast moulding quality and the individual applying the cast do not influence fracture redisplacement.

As mentioned earlier, severe cast-related complaints occurred in a significant number of patients, leading to additional hospital visits in one out of every five patients. We have not examined whether cast replacement or cast alterations affect the redisplacement risk. The literature on this topic is scarce. In their retrospective study, Drager et al. (2014) found no association between cast alterations and loss of alignment.[24] To study a possible interaction, detailed information is needed on how cast replacements are performed. For example, whether finger traction was used or re-manipulation took place during cast replacement. These data are often inadequately documented making them unreliable for retrospective collection from patient files. To determine whether cast replacements or alterations affect the risk of redisplacement, a prospective study should be conducted including radiographs obtained before and after cast replacement. Additionally, patient complaints and observations by casting technicians should be carefully documented.

Although we concluded that casting cannot prevent fracture redisplacement, we believe that adequate immobilization is essential in the treatment of reduced distal radius fractures. Christersson et al. (2016)[33] studied the duration of immobilization for reduced distal radius fractures. They concluded that casting for 10 days compared to one month increased the number of fracture displacements. This underscores the need for effective immobilization for a duration exceeding 10 days in the management of reduced DRFs. Since the type of immobilization does not appear to be associated with the risk of redisplacement, greater emphasis should be placed on reduction of pain and improving patient comfort. Personalized 3D-printed forearm braces may offer a promising alternative. Multiple recent studies have reported improved patient satisfaction and comfort with these personalized 3D-printed forearm braces compared to traditional casts.[34-40]

However, disadvantages of 3D-printed braces include higher costs and additional time required for preparation and assembly. Moreover, it is challenging to immediately prepare and assemble a custom brace in the emergency room. An alternative to 3D-printed bracing could be the use of thermoplastic braces, which are commonly used for carpal, metacarpal, and phalangeal fractures. The benefits of thermoplastic bracing include its ease of application, which is comparable to that of plaster splinting. When heated, the plastic becomes easily mouldable and thermoplastics are available in various degrees of rigidity. High-quality comparative studies are needed to further evaluate the advantages of custom braces or the use of thermoplastic casts. Currently, several companies are developing cast alternatives, with a focus on fracture stability and patient comfort. These companies are experimenting with materials designed to provide a constant pressure on the reduced fracture, regardless of the amount of swelling. Their efforts appears promising. A recent randomized controlled trial compared 3D-printed splints with traditional casting and found significantly lower pain levels with the 3D-printed splints, while no differences were observed in radiographic outcome parameters.[41]

Along with improving our immobilization methods, future research should focus on identifying modifiable factors associated with redisplacement. For example, it is assumed that the quality of the initial closed reduction may be related to the risk of redisplacement. The majority of DRFs are reduced by relatively inexperienced junior doctors. As with many medical procedures, experience often results in higher success rates[42], and simulation-based learning is increasingly prevalent in many surgical training programs and significantly enhances practical skills.[43] However, simulation training to gain experience with reducing fractures is rarely offered, despite the high incidence of this injury. Several fracture reduction simulators have been shown to improve clinical reduction skills resulting in enhanced post-reduction alignment.[44-46] In our cohort, fracture redisplacement occurred less frequently when reduction and cast application were performed by dedicated nurse practitioners. These nurse practitioners work in the emergency department and have a special focus on treating musculoskeletal injuries. Their experience with fracture reductions may have contributed to this finding, supporting the need for further studies on this topic. We intend to retrospectively analyse this possible relationship within our CAST study cohort in the near future.

Part III

Non-operative versus operative treatment of displaced DRFs

Fracture malalignment after non-operative treatment is frequently observed and is associated with an increased risk of impaired function and pain. However, there is significant uncertainty regarding the extent of this risk. Earlier performed randomized controlled trials report that approximately one-third of redisplaced fractures result in a symptomatic malunion that may require corrective osteotomy.[12, 13] In contrast, other large randomized controlled trials have not demonstrated clinically relevant differences in long-term outcome between non-operatively and operatively treated fractures. This may suggest that redisplacement has minimal impact on the final functional outcomes, particularly in elderly patients.[47, 48]

In displaced DRFs, there remains ongoing controversy about which specific cases would benefit most from operative treatment. **Chapter 8 and 9** focus on comparing three treatment modalities for displaced DRFs: 1) non-operative treatment with cast immobilization, 2) immediate plate fixation and 3) delayed plate fixation following redisplacement during non-operative treatment. In **Chapter 8,** we found that patient-reported functional outcomes, measured using the PRWHE and Q-DASH questionnaires, were comparable for the three treatment options six months post-trauma. Functional outcomes within the first three months were significantly better in patients who underwent immediate plate fixation within one week of injury. However, these differences did not reach the minimal clinically important difference (MCID). Based on these findings, we suggest that following successful closed reduction, it is appropriate to start with non-operative treatment and monitor for fracture redisplacement during the first two treatment weeks. If redisplacement occurs, surgical intervention can then be considered, taking the patient's preferences into account.

If a fracture redisplaces, continued non-operative treatment may still be considered in consultation with the patient. In our CAST study cohort, 48% of fractures redisplaced beyond guideline thresholds by the end of five weeks of cast immobilisation. However, patient-reported outcomes remained within the Patient Acceptable Symptom State (PASS). These findings are supported by the meta-analysis from Mulder et al. (2018).[5] Given that delays in surgery may negatively impact productivity, it would be valuable to further investigate whether patient-reported outcomes differ across age groups or preferably, across groups of patients with varying functional demands. For example, in elderly patients (aged over 65 years), non-operative treatment appears to be non-inferior to plate fixation.[48, 49] However, age alone does not always accurately reflect a patients' physiological fitness or functional demands. It is plausible that a delay in surgical treatment may be less burdensome for patients with lower demands.

In **Chapter 9**, we provided a comprehensive cost analysis of the CAST study. The CAST cohort was subdivided into three treatment modalities: complete non-operative treatment, direct plate fixation, and delayed plate fixation. Non-operative treatment is the least costly option, and delayed plate fixation results in a minimal increase in total costs compared to direct plate fixation. Patients should be informed that operative reduction and fixation may not be necessary if a fracture remains stable, which occurs in approximately half of acceptably reduced DRFs. Since fracture stability is difficult to predict, monitoring fracture alignment during the first weeks of cast immobilization is recommended. Allowing a period of observation to assess fracture stability may help avoid unnecessary surgeries and reduce healthcare costs.

We observed that the decision to proceed with surgery was often relatively arbitrary. Many patients with acceptable post-reduction alignment nevertheless underwent immediate surgical intervention. In contrast, over 20% of our cohort who began non-operative treatment had unacceptable post-reduction alignment, which would typically warrant surgery according to the national protocol. This indicates that the decision to proceed with surgical reduction and fixation is not based solely on alignment measurements.

Some randomized controlled trials reported a significant benefit of operative treatment over cast immobilization.[12, 13] Other studies have demonstrated that differences in long-term outcomes between non-operative and operative treatment are not clinically significant.[48, 50] Our results confirm that surgical treatment benefits individuals with higher functional demands by accelerating recovery. In contemporary medicine, where emphasis is often placed on demonstrating the superiority of surgical interventions, **Chapter 8 and 9** provide evidence to support shared-decision making discussions. This evidence underscores that non-operative treatment can be a viable and non-inferior option.

Future perspectives

Improving our ability to predict fracture redisplacement

Redisplacement is influenced by factors beyond fracture characteristics alone, including patient-specific and treatment-related variables. Identifying and systematically evaluating modifiable risk factors for redisplacement in future research is essential. Not only radiographic alignment, but also patient-specific characteristics affect both the redisplacement risk and patient-reported outcome. To accurately predict both redisplacement and final functional outcome, a multifactorial approach is warranted. The deployment of big data is a promising approach to integrate multiple factors, and develop a patient- and fracture-specific prediction tool. To further develop predictive models, national and international collaborations are essential to expand datasets and integrate valuable expertise. A key challenge lies in integrating AI models into our healthcare pathways to ensure they are easily accessible and support in the individualized assessment of the redisplacement risk.

Preventing redisplacement

Although this thesis provides evidence that cast immobilisation does not influence the risk of redisplacement, we believe certain extrinsic factors may still affect fracture stability. Our findings suggest that reductions performed by dedicated nurse practitioners were associated with a lower risk of redisplacement, potentially due to their experience in performing closed reductions. Further studies should investigate whether (simulation-based) training or greater involvement of skilled personnel can reduce the risk of fracture redisplacement. Secondly, the benefits of cast alternatives -such as 3D printed braces and pressure adaptive materials- deserve further investigation.

Improving patients comfort in non-operative treatment

A significant proportion of patients with reduced DRFs report severe cast-related complaints. Given that casting type and cast moulding quality are not associated with fracture redisplacement, future studies should prioritise improving patient comfort and pain management during non-operative treatment. Personalised 3D-printed forearm braces and thermoplastic bracing are both promising immobilisation methods that deserve consideration. High-quality comparative studies are needed to evaluate their effectiveness in terms of fracture stability, patient experience, and costs.

Understanding the relationship between radiographic malalignment and functional outcome

Recent literature, including our own work, may have placed disproportionate emphasis on radiographic outcomes. Future research should shift focus toward functional and patient-reported satisfaction as primary endpoints. In the CAST study, nearly half of all fractures redisplaced beyond guideline thresholds; however, this did not appear to directly correlate with patient satisfaction.

Towards patient-centred care (at lower costs)

Future research should focus on identifying patient subgroups that might benefit most from early surgical intervention. Stratifying outcomes by age, activity level, and occupational demands in future studies could help guide more tailored treatment recommendations. Our findings suggest that delaying surgery does not adversely affect long-term outcomes; however, its potential impact on short-term productivity remains unclear. Particularly in working-age populations, it is important to assess whether delayed surgery affects return-to-work times and overall patient well-being. Understanding these factors could enhance shared decision-making by balancing clinical benefits with socioeconomic considerations. Given rising healthcare costs, our cost analysis underscores the financial advantages of non-operative treatment when appropriate.

By focusing on these areas, future research can contribute to optimising the management of DRFs, improving patient-centered care.

CONCLUSION

With the completion of this thesis, we have gained deeper insight into the management of displaced distal radius fractures. Particular focus was placed on predicting (re)displacement, assessing the influence of casting techniques on redisplacement risk, and the decision-making process regarding early surgical intervention.

Our findings indicate that the redisplacement risk is influenced by factors beyond radiographic alignment, and that accurately predicting redisplacement remains a significant challenge. Emerging technologies, such as big data and artificial intelligence, hold promise for enhancing predictive accuracy.

Importantly, our research demonstrates that casting techniques do not impact the redisplacement rate. We found no differences in radiographic, functional or patient-reported outcomes between plaster splinting and circumferential casting. This implies that both techniques are safe and effective. However, patients frequently experience significant pain post-trauma and casts are often reported as uncomfortable. This emphasizes the need to improve our immobilization methods.

Lastly, radiographic alignment alone does not appear to be a strong predictor of functional, and patient-reported outcomes. When acceptable reduction is achieved, non-operative treatment should be considered a valid initial approach, as approximately half of these fractures maintain proper alignment during follow-up. For those fractures that redisplace within the first two weeks, delayed plate fixation remains a viable option, with careful consideration of the patient's preferences and functional demands. Six months after trauma, patient-reported outcomes are comparable for non-operative treatment, delayed plate fixation, and immediate plate fixation.

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SUMMARY

The general aim of this thesis was to elucidate the complexities surrounding the management of displaced distal radius fractures (DRFs). This thesis covers three themes. **Part one** focuses on quantifying fracture displacement and predicting redisplacement. **Part two** examines the influence of cast types and casting techniques on the redisplacement risk. **Part three** compares non-operative treatment, immediate operative treatment, and delayed surgical intervention. **Chapter 1** provides a general introduction to DRF management and covers the three topics of this thesis in light of the current literature.

Part I

Predicting (re)displacement

Assessing whether a fracture is unacceptably aligned on plain radiographs can be challenging. In **Chapter 2**, we concentrated on assessing whether CT imaging is of additional value to conventional radiographs to assess DRF displacement. We found that intra-articular incongruency is best observed on CT. Intra-articular incongruency significantly increases the redisplacement risk during non-operative treatment with cast immobilisation and, subsequently the risk of developing a symptomatic malunion. Additional CT imaging is therefore particularly valuable in intra-articular fractures to assess the extent of articular incongruency when operative treatment is considered.

When non-operative treatment is chosen, the risk that the fracture will redisplace while in a cast is considerable. The decision to opt for operative treatment is, in part, based on the estimation of whether the fracture will redisplace or remain stable during immobilisation. With an accuracy of 54%, it seems challenging for surgeons to predict whether a DRF will remain correctly aligned. Given the significant potential for improvement, we aimed to deploy artificial intelligence to identify fracture instability on trauma radiographs. In **Chapter 3**, a convolutional neural network algorithm is presented capable of predicting clinically relevant loss of alignment. The overall accuracy of predicting fracture instability increased to 74%, based on injury and post-reduction radiographs and patients' age and sex. This prediction model could substantially assist physicians and patients in making truly patient- and fracture-specific decisions whether operative treatment is warranted. A challenge lies in further improving our algorithm with additional datasets and externally validating it before it can be implemented in the clinical setting.

Part II

Influence of casting techniques on redisplacement

The second part of this thesis explores the influence of casting types and casting techniques on the redisplacement risk of adequately reduced distal radius fractures. Approximately 40-60% of reduced DRFs will redisplace during cast immobilisation. The number of symptomatic malunions and costly surgical interventions will diminish when redisplacement could be prevented. No modifiable factors have yet been identified that reduce the risk of redisplacement. Therefore, we investigated whether the casting type –plaster splints versus circumferential casts– and other cast related factors might influence the redisplacement risk.

We hypothesized that a circumferential cast would provide a better fixation and therefore lower the redisplacement risk. In **Chapter 4**, we retrospectively observed that circumferential casting appeared promising in reducing the redisplacement risk in DRFs. In **Chapter 5,** we further studied this relationship in the CAST study a pragmatic, multicentre, cluster-randomised controlled trial. The study sample comprised 420 patients, included in 10 participating hospitals. In this large cohort, nearly half of the fractures redisplaced (circumferential cast: 49%, plaster splint 47%). Although redisplacement rates were high, patient reported outcome was above Patient Acceptable Symptom State, suggesting that radiographic redisplacement does not necessarily lead to clinically relevant symptoms or functional impairment. Circumferential casting did not result in a significantly different rate of redisplacement compared to the use of a plaster splint. Clinical outcomes were comparable between the two groups after three months. Patient-reported outcomes measured with the QuickDASH and PRWHE questionnaires also did not differ significantly at one-year follow-up. Lastly, this study was the first to elaborate on cast related complaints. Patients treated with plaster splinting reported significantly higher pain scores during the first week. However, this difference is small and most probably not clinically relevant. Overall, one in five patients scheduled an additional hospital visit because of cast related complaints. Although the rates of complaints were similar between the groups, the discomfort highlights the need for alternative, more comfortable immobilization options.

In **Chapter 6**, we further explored the influence of cast-related factors on the redisplacement risk. We hypothesized that a well-moulded cast would provide adequate stabilization. The quality of cast moulding was objectified by measuring three different casting indices. Casting indices are mostly used and documented in paediatric fractures. No association was found between cast moulding quality and redisplacement. Interestingly, mean index scores were poor within all three indices. Since the predictive performances of all three indices were poor, we propose that casting indices are not helpful for measuring cast moulding quality in adult DRFs. In this chapter, we further explored the association between redisplacement, the casting material used and the professional background of those applying the cast. There was no difference in redisplacement incidence between DRFs treated with plaster of Paris versus synthetic fiber casts. Interestingly, the redisplacement risk was lower in casts applied by nurse practitioners and casting technicians, compared to casts applied by ER nurses. The current results might imply that the experience in cast application decreases the redisplacement risk. In the near future we hope to study whether the experience in closed reduction plays a part as well.

Part III

Non-operative, operative and delayed operative treatment

In the last part of this thesis, comparisons between different treatment modalities for displaced DRFs were made. The three treatment modalities compared concern 1) non-operative treatment with cast immobilisation, 2) direct operative treatment and 3) delayed operative treatment when redisplacement occurred during cast immobilisation. Since more than half of acceptably reduced DRFs remain well aligned during five weeks of cast immobilisation, a wait-and-see approach might be considered. Monitoring fracture alignment during cast immobilization and opting for plate fixation in a second instance when a fracture redisplaces, can be considered as a treatment strategy. The aim of **Chapter 7** was to assess whether delayed plate fixation affects patient-reported outcomes during one treatment year. We found that patient-reported functional outcomes, measured with the PRWHE and QuickDASH questionnaires, are comparable from six months post-trauma onwards. Outcomes up to three months were significantly better in patients that were treated surgically within one week. However, these differences did not reach the thresholds for minimal clinically important difference (MCID) of both questionnaires. At six months and one year after trauma, no significant differences in patient-reported outcomes were observed.

Delayed operative intervention should be considered as a distinct treatment strategy, in which the occurrence of redisplacement determines whether surgery is beneficial to the patient. In **Chapter 8**, we aimed to provide an extensive overview of the costs of 1) non-operative treatment, 2) direct plate fixation and 3) delayed plate fixation. The findings of this cost analysis support the approach mentioned above. Non-operative treatment is least costly, as expected. The cost differences between direct and delayed plate fixation are minimal, and patient-reported quality of life are small. These studies underline the importance of tailoring treatment based on patient needs and functional demands. It would be valuable to further investigate whether patient-reported outcomes differ across age groups or preferably, across groups of patients with varying functional demands.

Overall, this thesis advances our understanding of displaced DRFs. By employing artificial intelligence, we introduced an innovative approach to predict redisplacement in an early phase. Our results highlight the high incidence of fracture redisplacement in adequately reduced DRFs in which neither the type of immobilisation, nor the quality of cast moulding influences the risk. In current practice, where operative treatment is readily proposed, this thesis emphasizes that, despite the high incidence of redisplacement, patients are generally satisfied with the final outcome of nonsurgical treatment. Finally, by comparing non-operative and operative treatment strategies, supplemented by a comprehensive cost analysis, we attempted to provide a thorough overview of all treatment options. This thesis underscores the importance of patient-specific care in managing displaced distal radius fractures and identifies key areas for further research to optimise treatment outcomes and enhance patient experience.

NEDERLANDSE SAMENVATTING

De algemene doelstelling van dit proefschrift was om de complexiteit van de behandeling van polsfracturen met een niet acceptabele stand –gedisloceerde distale radiusfracturen (DRF's)– te bestuderen en te verduidelijken. Dit proefschrift heeft drie hoofdthema's. Deel één richt zich op het kwantificeren van fractuurdislocatie en het voorspellen van secundaire dislocatie. Deel twee onderzoekt de invloed van gipssoorten en gipstechnieken op het risico op secundaire dislocatie. Deel drie vergelijkt conservatieve behandeling, directe operatieve behandeling en uitgestelde operatieve behandeling. In **Hoofdstuk 1** wordt een algemene inleiding op de behandeling van DRF's gegeven en worden de drie hoofdonderwerpen van dit proefschrift in het licht van de huidige literatuur besproken.

Deel I

Voorspellen van (re)dislocatie

Het beoordelen of een fractuur een acceptabele stand heeft op basis van conventionele röntgenfoto's kan heel lastig zijn. In **Hoofdstuk 2** onderzochten we of beeldvorming met een CT-scan aanvullende waarde heeft bij het beoordelen van DRF dislocatie, ten opzichte van standaard röntgenfoto's. We kwamen tot de conclusie dat vooral onregelmatigheid in het gewrichtsoppervlak, ofwel intra-articulaire incongruentie, beter zichtbaar is op een CT scan. Intra-articulaire incongruentie verhoogt significant het risico op secundaire dislocatie tijdens conservatieve behandeling met gips. Daarmee is er ook een verhoogd risico op een symptomatische malunion. Dit betekend een blijvend pijnlijke of functioneel beperkte pols doordat de fractuurdelen niet in de goede stand aan elkaar zijn vastgegroeid. Aanvullende CT-beeldvorming is daarom vooral van waarde bij intra-articulair verlopende fracturen om de mate van gewrichtsincongruentie in kaart te brengen.

Het risico op secundaire dislocatie na gesloten repositie van een gedisloceerde DRF is aanzienlijk wanneer gekozen wordt voor conservatieve behandeling middels gipsimmobilisatie. Het besluit om al dan niet operatief te behandelen is deels gebaseerd op de inschatting of de fractuur stabiel blijft of opnieuw disloceert. Met een voorspellende accuratesse van 54% blijkt het voor chirurgen lastig om te voorspellen of een DRF weer verplaatst of niet in het gips. Gezien de ruimte voor verbetering bij deze voorspelling, onderzochten we of kunstmatige intelligentie kan helpen bij het identificeren van instabiele fracturen die secundair zullen gaan disloceren. In **Hoofdstuk 3** presenteren we een algoritme op basis van een convolutioneel neuraal netwerk (CNN) dat in staat is om secundaire dislocatie te voorspellen. Deze voorspelling wordt gemaakt op basis van de eerste röntgenfoto's na het ongeval in combinatie met het invoeren van de leeftijd en het geslacht van de patiënt. De accuratesse van de voorspelling van het algoritme is met 74%

sterk verbeterd ten opzichte van de voorspelling door de chirurg. Dit voorspellingsmodel kan artsen en patiënten helpen bij het maken van patiënt- en fractuur-specifieke behandelkeuzes. Een uitdaging ligt in het controleren van de accuratesse op andere datasets (externe validatie) alvorens implementatie in de klinische praktijk mogelijk is.

Deel II

Invloed van gipssoorten en gipstechnieken op secundaire dislocatie

Het tweede deel van dit proefschrift onderzoekt de invloed van gipssoorten en gipstechnieken op het risico op secundaire dislocatie van adequaat gereponeerde DRF's. Ongeveer 40–60% van de adequaat gereponeerde DRF's disloceert opnieuw tijdens de gipsbehandeling. Het voorkomen van die secundaire dislocatie zou het aantal symptomatische malunions en kostbare chirurgische ingrepen aanzienlijk kunnen verminderen. Tot op heden zijn er geen beïnvloedbare factoren geïdentificeerd die het secundaire dislocatierisico verlagen. Daarom onderzochten we of het type gips – een gipsspalk versus een circulair gips – en andere gips gerelateerde factoren hierop van invloed zijn.

We veronderstelden dat een circulair gips meer stabiliteit zou geven en daarmee het risico op secundaire dislocatie zou verlagen. In **Hoofdstuk 4** zagen we in een retrospectief opgezette dataset dat een circulaire gips veelbelovend leek ten aanzien van fractuurstabiliteit. In **Hoofdstuk 5** onderzochten we dit verder in de CAST-studie, een pragmatische, multicenter, cluster-gerandomiseerde trial. De onderzoeksgroep bestond uit 420 patiënten, geïncludeerd in tien deelnemende ziekenhuizen. In deze grote onderzoekspopulatie trad bij bijna de helft van de patiënten secundaire dislocatie op (circulair gips: 49%, spalk: 47%). Hoewel de secundaire dislocatiepercentages hoog waren, lag de uitkomst boven de Patient Acceptable Symptom State (PASS). Een uitkomst boven de PASS suggereert dat secundaire dislocatie niet leidt tot klinisch relevante klachten of functieverlies. Er werd geen significant verschil gevonden in de incidentie van secundaire dislocatie tussen beide gipsvormen. Ook de klinische uitkomsten na drie maanden en de patiënt-gerapporteerde uitkomsten na één jaar (gemeten met de QuickDASH en PRWHE-vragenlijsten) verschilden niet significant. Ons onderzoek beschreef ook voor het eerst gips gerelateerde klachten. Patiënten met een spalk rapporteerden in de eerste week significant meer pijn, maar dit verschil was klein en waarschijnlijk niet klinisch relevant. Eén op de vijf patiënten zocht extra medische hulp vanwege gips gerelateerde klachten. Hoewel de frequentie van klachten gelijk was tussen de groepen, onderstreept het ongemak de noodzaak om te kijken naar comfortabelere immobilisatiemethoden.

In **Hoofdstuk 6** onderzochten we verder of andere gips gerelateerde factoren het secundaire dislocatierisico beïnvloeden. We formuleerden de hypothese dat een goed gemodeleerd gips de fractuur beter zou stabiliseren. De kwaliteit van het modeleren werd objectief gemeten met drie verschillende gipsindices. Deze indices zijn voornamelijk onderzocht bij kinderfracturen. Er werd in onze studie geen verband gevonden tussen de gemeten gipsindices en het optreden van secundaire dislocatie. Dit betekend dat zelfs een goed gevormd en goed aanliggend gips geen positief effect heeft op secundaire dislocatie van de fractuur. Opvallend was dat de gemiddelde scores op alle drie de indices laag waren, wat zou betekenen dat de gipsen gemiddeld gezien niet goed aangelegd zouden zijn in onze onderzoekspopulatie. Omdat de voorspellende waarde van deze indices laag bleek, concluderen we dat gipsindices geen betrouwbare maat zijn voor het weergeven van de gipskwaliteit bij volwassen. We onderzochten ook het gebruikte gipsmateriaal en de professionele achtergrond van degene die het gips aanbracht. Er werd geen verschil gevonden in secundaire dislocatie tussen kalkgips en kunststof gips. Interessant genoeg was het secundaire dislocatierisico lager wanneer het gips werd aangelegd door verpleegkundig specialisten of gipsverbandmeesters, in vergelijking met verpleegkundigen van de spoedeisende hulp. Dit suggereert dat ervaring in gipsapplicatie mogelijk wel bijdraagt aan een lager secundaire dislocatierisico. In de toekomst willen we onderzoeken of ervaring in gesloten repositie eveneens een rol speelt.

Deel III.

Conservatief, operatief en uitgesteld operatief beleid

In het laatste deel van dit proefschrift worden verschillende behandelstrategieën voor gedisloceerde DRF's vergeleken: 1) conservatieve behandeling middels gipsimmobilisatie, 2) directe operatie, en 3) uitgestelde operatie wanneer tijdens de gipsbehandeling secundaire dislocatie is opgetreden. Omdat meer dan de helft van de adequaat gereponeerde DRF's goed gepositioneerd bleef gedurende de gipsbehandeling, lijkt een afwachtende strategie verdedigbaar. In dat geval wordt de stand van de fractuur tijdens gipsbehandeling opgevolgd met röntgenfoto's, en wordt alsnog geopereerd wanneer secundaire dislocatie optreedt. Het doel van **Hoofdstuk 7** was om te onderzoeken of uitgestelde operatie invloed heeft op de patiënt-gerapporteerde uitkomsten in het eerste behandeljaar. Patiënten werd gevraagd om twee vragenlijsten in te vullen over hand-polsfunctie op 6 weken, 3, 6 en 12 maanden na het oplopen van de fractuur. We vonden dat de uitkomsten vanaf zes maanden na trauma vergelijkbaar waren tussen de groepen. In de eerste drie maanden waren de uitkomsten beter bij patiënten die direct chirurgisch behandeld werden, maar de verschillen overschreden niet de drempelwaarden voor minimale klinisch relevante verschillen (MCID) van beide vragenlijsten. Na zes maanden en ook één jaar na het ongeval waren er geen significante verschillen meer in patiënt-gerapporteerde uitkomsten.

Een uitgestelde operatie zou moeten worden beschouwd als een op zichzelf staande strategie, waarbij de uiteindelijke beslissing tot chirurgie afhangt van het optreden van secundaire dislocatie. In **Hoofdstuk 8** gaven we een uitgebreid overzicht van de kosten van de drie behandelstrategieën; 1) conservatieve behandeling, 2) directe operatie en 3) uitgestelde operatie. De resultaten van deze kostenanalyse ondersteunen de eerder genoemde strategie. Zoals verwacht is conservatieve behandeling het minst kostbaar. De kostenverschillen tussen directe en uitgestelde operatie zijn gering, terwijl de gerapporteerde kwaliteit van leven vergelijkbaar is. Deze studies benadrukken het belang van een gepersonaliseerde aanpak, gebaseerd op de behoeften en functionele eisen van de patiënt. Verder onderzoek is wenselijk om te bepalen of patiënt-gerapporteerde uitkomsten verschillen per leeftijdsgroep of – nog relevanter – per niveau van functionele belasting.

CONCLUSIE

Dit proefschrift vergroot ons begrip van de behandeling van gedisloceerde distale radiusfracturen. Door het inzetten van kunstmatige intelligentie introduceerden we een innovatieve methode om in een vroeg stadium het risico op secundaire dislocatie te voorspellen, zodat met meer zekerheid de juiste behandelstrategie gekozen kan worden. Onze bevindingen onderstrepen de hoge incidentie van secundaire dislocatie bij adequaat gereponeerde distale radiusfracturen, waarbij noch het type immobilisatie, noch de kwaliteit van het gipsonderdeel hierbij van invloed lijkt. In de huidige praktijk, waarin snel tot operatieve behandeling wordt overgegaan, laat dit proefschrift zien dat patiënten ondanks de hoge secundaire dislocatiepercentages over het algemeen tevreden zijn met het eindresultaat van conservatieve behandeling. Tot slot biedt dit proefschrift, door de vergelijking van conservatieve en operatieve behandelstrategieën én een uitgebreide kostenanalyse, een volledig overzicht van de beschikbare behandelmogelijkheden. Het onderstreept het belang van patiënt-specifieke zorg en benoemt belangrijke aandachtspunten voor toekomstig onderzoek gericht op het verbeteren van behandeluitkomsten en de patiëntervaring.

LIST OF PUBLICATIONS

Open-source convolutional neural network to classify distal radial fractures according to the AO/OTA classification on plain radiographs.
K.D. Oude Nijhuis, J. Prijs, **B. Barvelink**, H. van Luit, Y. Zhao, Z. Liao, R.L. Jaarsma, F.F.A. IJpma, M.M.E. Wijffels, J.N. Doornberg, J.W. Colaris; Machine Learning Consortium.
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Eur J Trauma Emerg Surg. 2024 Oct;50(5):2313-2321.

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K.D. Oude Nijhuis, L.H.M. Dankelman, J.P. Wiersma, **B. Barvelink**, F.F.A. IJpma, M.H.J. Verhofstad, J.N. Doornberg, J.W. Colaris, M.M.E. Wijffels, Machine learning Consortium
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Under review at Bone and Joint Journal

Is delayed surgical treatment of distal radius fractures inferior to direct surgical treatment? A comparative study of prospective gathered data.
S. Smidt, **B. Barvelink**, M. Reijman, J.W. Colaris, CAST study group
Under review after revisions at Injury

Costs and health related quality of life of non-operative and surgical treatment modalities for displaced distal radius fractures: A comprehensive overview based on the CAST study.
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Under review at European Journal of Trauma and Emergency Surgery

Can surgeons accurately estimate loss of threshold alignment (instability) of distal radius fractures? The influence of imaging: diagnostic accuracy of radiographs versus computed tomography.
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Accepted at Bone and Joint Open

PHD PORTFOLIO

Summary of PhD training and teaching

Name student: Britt Barvelink
Erasmus MC department: Department of Orthopaedics and Sports Medicine
PhD Period: January 2020 - June 2025
Promotor: Prof. Dr. J.A.N. Verhaar
Co-promotors: Dr. J.W. Colaris & Dr. M. Reijman

Courses: General	Year	ECTS
Endnote - *Erasmus MC, Rotterdam*	2020	0.2
Systematic literature retrieval in PubMed - *Erasmus MC, Rotterdam*	2020	0.2
Research integrity – *Erasmus MC, Rotterdam*	2020	0.3
BROK (Basiscursus Regelgeving Klinisch Onderzoek) - *NFU, Rotterdam*	2020	1.5
Gemstracker & Limesurvey - *Erasmus MC, Rotterdam*	2020	0.2
Presentation course – *Reprezens, Rotterdam*	2020	1.0
Biomedical writing for PhD candidates - *Erasmus MC, Rotterdam*	2021	1.5
Personal Leadership & Communication – *Erasmus MC, Rotterdam*	2022	1.0
Workshop coaching ‘Wederzijds waarderen’ – *Erasmus MC, Rotterdam*	2022	0.3
Diversity & Inclusivity – *Erasmus MC, Rotterdam*	2023	0.1
Workshop ‘Grensverkenning’ – *Erasmus MC, Rotterdam*	2023	0.3
	Total	6.7

Courses: Statistics	Year	ECTS
Biostatistical Methods I: Basic Principles – *Erasmus MC, Rotterdam*	2021	5.7
The Basic Course on R – *Erasmus MC, Rotterdam*	2021	1.8
Advanced Clinical Trials – *Erasmus MC, Rotterdam*	2022	1.9
Logistic regression – *Erasmus MC, Rotterdam*	2022	1.4
	Total	10.8

(Inter)national podium presentations	Year	ECTS
Oral presentation: An insight in life- and research struggles of a PhD candidate during the COVID pandemic *Science Day, Rotterdam, The Netherlands*	2021	1.0
Poster presentation: Automatische herkenning van instabiele distale radiusfracturen op trauma- en repositie röntgenfoto's. *NOV conference, Utrecht, The Netherlands*	2022	1.0
Oral presentation: Predicting redisplacement in distal radius fractures using machine learning *EFFORT conference, Lisboa, Portugal*	2022	1.0
Oral presentation: Artificial intelligence, exciting developments in orthopaedics *Science Day, Rotterdam, The Netherlands*	2022	1.0
Oral presentation: Predicting redisplacement in distal radius fractures using machine learning *OTA conference, Tampa, USA*	2022	1.0
Oral presentation: Kan machine learning helpen met het voorspellen van instabiliteit bij distale radiusfracturen? *ROGO dag, Delft, The Netherlands*	2022	1.0
Oral presentation: Predicting redisplacement in wrist fractures using machine learning *IMechE webinar*	2022	1.0
Oral presentation: Predicting redisplacement in distal radius fractures using machine learning *iOTA conference, Amsterdam, The Netherlands*	2022	1.0
Oral presentation: Uitkomsten van de CAST studie *ALV gipsverbandmeesters, Nieuwegein, The Netherlands*	2023	1.0
Oral presentation: Uitkomsten van de CAST studie *NOV conference, Utrecht, The Netherlands*	2023	1.0
Oral presentation: All you want to know about casting techniques and wrist fractures *Science Day, Rotterdam, The Netherlands*	2024	1.0
Oral presentation: The influence of casting on distal radius fracture redisplacement rates: a cluster randomized controlled trial *NOF conference, Rotterdam, The Netherlands*	2024	1.0
Oral presentation: The influence of casting type on distal radius fracture redisplacement rates: A cluster-randomized controlled trial Oral presentation: The influence of cast quality, cast applicant and type of casting on the redisplacement risk of reduced adult distal radius fractures *FESSH conference, Rotterdam, The Netherlands*	2024	1.0
Oral presentation: Uitkomsten van de CAST studie Poster presentation: Gipstechniek en materiaal heeft geen invloed op het secundaire dislocatie risico bij gereponeerde distale radiusfracturen (DRFs) *Traumadagen, Amsterdam, The Netherlands*	2024	1.0
Oral presentation: Is het tijd om 3-puntsfixatie in gips te verlaten? *Esser masterclass hand-wrist, Rotterdam, The Netherlands*	2025	1.0

	Total	15

Teaching activities and student supervision	Year	ECTS
Coaching medical bachelorstudents (7 students)	2020-2024	2.5
Teaching medical master students ‘Workshop presentatietechnieken’ and ‘Observationeel onderzoek an RCT’	2020-2024	0.5
Supervising medical master student Sanne Smidt – *Differences between circumferential casting and plaster splinting of displaced distal radius fractures: pain, comfort and number of revisions*	2021	3.0
Supervising medical master student Mirte Kok - *The effect of casting quality – measured using the three-point index – on fracture redisplacement in distal radius fractures*	2021	3.0
Supervising medical master student Kevin van Lakwijk – *Artificial intelligence as a tool in fracture treatment: Is an algorithm able to predict fracture instability in distal radius fractures*	2021	3.0
Supervising final assignment minor ‘Orthopaedics and Sports Medicine’	2022	
Supervising Healthcare management master student Lynn van der Weide – *Patient participation in medical research. How to share study results with study participants*	2023	3.0

	Total	15

Organizing activities	Year	ECTS
Organization Science Day 2022	2021-2022	1.0

	Total ECTS	**48.5**

Awards	Year
Beste poster Traumadagen	2021
Van Rens Prijs Award for best oral presentation	2023
Beste voordracht Traumadagen	2024

Other activities	Year
Co-author of the Researchflits	2020-2022
Taskforce Diversity and Inclusion – *Erasmus MC, Rotterdam*	2022-2024

CURRICULUM VITAE

Britt Barvelink werd op 15 mei 1992 geboren in Deventer. Zij woonde haar gehele jeugd met haar ouders en twee zussen in Holten. Na het behalen van haar VWO-diploma op De Waerdenborch te Holten, verhuisde zij in 2010 naar Groningen om Bewegingswetenschappen te studeren aan de Rijksuniversiteit Groningen. In 2011 behaalde zij haar propedeuse en begon nadien met de studie Geneeskunde.

Na de start van de studie Geneeskunde in 2011, behaalde zij in 2014 haar Bachelor Geneeskunde. Tijdens haar Bachelor was zij betrokken bij verschillende extra curriculaire activiteiten. In het eerste jaar was zij commissielid van ISCOMS, een internationaal studenten congres in Groningen. Zij werkte bij het Promtheus Nierteam, dat tijdens orgaandonatie- en transplantatie procedures gegevens voor wetenschappelijk onderzoek verzameld. Tevens werkte zij als NAW-assistent bij de Doktersdienst Groningen.

In 2014 startte zij met haar Master Geneeskunde. Haar wetenschappelijke stage verrichte zij bij de afdeling Orthopedie in het Universitair Medisch Centrum Groningen (UMCG). Onder supervisie van Dr. Hepping en Dr. Stevens assisteerde zij met de uitvoering van de GOPRO studie, een klinische observationele studie gericht op het functionele herstel van complexe onderarmfracturen bij kinderen. Ze startte nadien met haar coschappen en verhuisde in 2016 naar Deventer voor haar tweede jaar coschappen. Haar interesse in het bewegingsapparaat was gewekt waarbij keuzecoschappen gelopen werden bij oa. de orthopedische chirurgie, plastische chirurgie en revalidatiegeneeskunde. Haar oudste coschap vond plaats bij de algemene chirurgie in het Deventer Ziekenhuis en de traumachirurgie in het UMCG. Gedurende haar coschappen bleef zij actief betrokken bij de onderzoeksprojecten van de afdeling Orthopedie, wat heeft geresulteerd in meerdere publicaties.

In mei 2018 behaalde Britt haar artsendiploma en werkte zij aansluitend tot augustus 2019 als ANIOS Chirurgie in het Deventer Ziekenhuis. Vanaf september 2019 werkte zij als ANIOS Orthopedie in het Medisch Spectrum Twente te Enschede, totdat zij werd aangenomen voor een promotietraject in Rotterdam.

In januari 2020 startte zij met een promotietraject op de afdeling Orthopedie en Sportgeneeskunde in het Erasmus MC te Rotterdam onder begeleiding van co-promotoren dr. Max Reijman en dr. Joost Colaris en promotor prof. Dr. Jan Verhaar. Dit promotieonderzoek was gericht op de conservatieve behandeling van complexe distale radiusfracturen. Als hoofdproject voltooide zij de multicenter gerandomiseerde trial ‘De CAST studie’.

De band met Universiteit Groningen bleef bestaan door een samenwerkingsproject gericht op het voorspellen van fractuurinstabiliteit middels kunstmatige intelligentie, onder leiding van prof. dr. Joost Doornberg.

In 2024 werd Britt aangenomen voor de opleiding tot orthopedisch chirurg waarvoor zij in mei 2024 is gestart met de vooropleiding algemene chirurgie in het Franciscus Gasthuis en Vlietland te Rotterdam (opleider dr. Poelman). Haar opleiding tot orthopedisch chirurg zal vanaf april 2026 worden voortgezet in het Erasmus MC te Rotterdam (opleider dr. Bos) en nadien in het Elizabeth Tweesteden Ziekenhuis te Tilburg (opleider dr. van der Jagt).

DANKWOORD

Aan het einde van mijn studie Geneeskunde zei ik dat ik nooit zou gaan promoveren. Het liep anders! Ik raakte betrokken bij inspirerende wetenschappelijke projecten en ontmoette enthousiaste mensen die de wetenschapper in mij hebben weten aan te wakkeren. Een proefschrift schrijven doe je niet alleen. Afgelopen jaren heb ik dankzij vele samenwerkingen en hulp van anderen met veel plezier aan mijn wetenschappelijke carrière gewerkt. Het is bijna onmogelijk om iedereen persoonlijk te bedanken die een bijdrage heeft geleverd.

Mijn dank gaat allereerst uit naar mijn co-promotor **dr. Joost Colaris**. Beste Joost, de meeste van jouw publicaties had ik al gelezen toen ik je ontmoette. Wat een enorme eer dat jij mij vroeg om een promotietraject bij jou in Rotterdam te overwegen. Ik heb geen seconde spijt gehad van dit grote besluit. Je bent inspirerend en enthousiasmerend. Vanaf het begin heb je mij veel vrijheid gegeven om projecten op mijn eigen manier invulling te geven, waarbij je mij bijstuurde en coachte waar nodig.

Dan volgt co-promotor **dr. Max Reijman**. Beste Max, wat is het toch prettig om jou als co-promotor te hebben. Ik kon letterlijk altijd bij je binnenlopen of inbellen, voor vragen, een praatje of een fanatiek potje tafelvoetbal. Je bent tijdens alle fasen van mijn promotie heel betrokken geweest en wist altijd feilloos hoe het met mij ging, zowel betreft de projecten als privé.

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Hartelijke dank aan alle bedrijven en organisaties die financieel hebben bijgedragen aan de totstandkoming van dit boekje, namelijk **de afdeling Orthopedie en Sportgeneeskunde van het Erasmus MC, de Erasmus Universiteit Rotterdam, de Nederlandse Orthopaedische Vereniging (NOV), de Nederlandse Vereniging van Handchirurgie (NVVH), EXO360, Oudshoorn, Materialise, Bauerfeind, ABN AMRO, ChipSoft,** en **VREST.**

Alle patiënten die deel hebben genomen aan de CAST studie, dit proefschrift was niet tot stand gekomen zonder jullie. Bedankt.

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