Wrist trauma diagnosis, treatment and prognosis
Walenkamp, M.M.J.

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WRIST TRAUMA
DIAGNOSIS, TREATMENT AND PROGNOSIS

Monique M.J. Walenkamp
WRIST TRAUMA
DIAGNOSIS, TREATMENT AND PROGNOSIS

STELLINGEN
1. Physicians are afraid not to order radiography in patients with wrist trauma, even if they have a low clinical suspicion of a distal radius fracture • *dit proefschrift*

2. We urgently require a definition of what constitutes an unstable distal radius fracture • *dit proefschrift*

3. There is a considerable unwarranted variation in the treatment of patient with a distal radius fractures in the Netherlands • *dit proefschrift*

4. Open reduction and internal fixation with a volar locking plate is preferred over bridging external fixation for surgical treatment of distal radius fractures • *dit proefschrift*

5. Clinical decision models should be externally validated before implementation in clinical practise • *dit proefschrift*

6. Sample-size calculations should be based on the minimal clinically important difference of a patient-reported outcome measure • *dit proefschrift*

7. If you want something said, ask a man. If you want something done, ask a woman • *Margareth Thatcher*

8. Je kan beter spijt hebben van de dingen die je wel gedaan hebt dan van de dingen die je niet gedaan hebt • *Simona Walenkamp*

9. The world is a book, and those who do not travel read only one page • *Sint-Augustinus*

10. Zelfs een vlieg heeft een pols • *naar Desiderius Erasmus*
Nullius in Verba

PROMOTIECOMMISSIE

Promotor: prof. dr. J.C. Goslings
Co-promotores: dr. N.W.L. Schep
dr. S.D. Strackee

Overige leden: prof. dr. M.Maas
prof. dr. C.M.A.M. van der Horst
prof. dr. G.M.M.J. Kerkhoffs
prof. dr. E.W. Steyerberg
prof. dr. P.R.G. Brink
prof. dr. I.B. Schipper

Universiteit van Amsterdam
Maasstad Ziekenhuis
Universiteit van Amsterdam
Universiteit van Amsterdam
Erasmus Universiteit Rotterdam
Universiteit Maastricht
Universiteit Leiden

Faculteit der Geneeskunde

Voor mijn moeder
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GENERAL INTRODUCTION & OUTLINE OF THE THESIS

Wrist trauma is one of the most common Emergency Department attendances.\(^1\) Annually, 1 million patients are treated in one of the Dutch Emergency Departments,\(^2\) of which 29% constitute patients with hand and wrist injuries. This amounts to 287,000 patients each year. This thesis aims to improve diagnosis, treatment and prognosis of patients with wrist injury.

PART 1: DIAGNOSIS

Around 40% of the patients who attend the Emergency Department with wrist trauma have sustained a fracture.\(^3\) However, most patients are routinely referred for radiography.\(^4\) In a number of hospitals, patients receive radiographs even before clinical examination, challenging the traditional sequence of taking a history, performing a physical exam and (only) then ordering necessary diagnostic tests.

There are several possible explanations for this routine, including Emergency Department crowding and efficient management of time.\(^5\) Physicians working the Emergency Department may also be uncritical when it comes to referring patients for X-ray examinations to reassure the patient, or because of the possible medicolegal consequences of a missed fracture.\(^6\) The latter reason classifies as defensive medicine and is associated with high costs.\(^7\)

Selecting patients for wrist radiography could result in more efficient use of X-ray examinations in the Emergency Department.\(^8\) However, this requires physicians to be able to interpret clinical findings and accurately rule out a fracture of the wrist on the basis of their clinical findings alone.\(^9\) In Chapter 1 we examine physicians’ ability to rule out a distal radius fracture based on clinical findings.

Several studies have demonstrated differences among hospitals in referral ratio for X-rays of patients following wrist trauma.\(^10\) This variability between physicians in their perception of what constitutes clinical suspicion of fractures implies a lack of clear guidelines regarding the X-ray referral policy.\(^11\) A validated clinical decision rule could reinforce physicians’ clinical judgment and support them in their decision not to request radiography. Several clinical decision rules for musculoskeletal trauma already exist including for ankle,\(^12\) elbow,\(^13\) and knee trauma.\(^14\) The most famous clinical decision rule is probably the Ottawa Ankle Rules.\(^15\)

However, despite the high incidence of wrist trauma, there are no guidelines or criteria available that indicate which patients with wrist trauma require an X-ray. In Chapter 2 we derive and externally validate a clinical decision rule for the use of radiography in acute wrist trauma.

Radiographic imaging following acute wrist trauma is often performed routinely in children as well.\(^16\) This unnecessarily exposes children to possible stressful examinations and radiation. Although radiation exposure of plain radiography of the wrist is low, it is important to prevent unnecessary radiation exposure.\(^17\)

With the potential benefits of selective radiography in children in mind, Webster et al. attempted to develop a clinical decision rule for paediatric patients with acute wrist trauma.\(^18\) However, their decision rule was never externally validated. External validation is the process of assessing the generalizability of a clinical prediction model or rule.\(^19\) This is attained by testing the rule a different patient population and comparing the observed outcomes to the predicted outcomes. Evaluating the performance of a prediction model or a clinical decision rule in a new patient population is essential before its implementation. In Chapter 3, we derive and externally validate a clinical decision rule for the use of radiography in acute wrist trauma for paediatric patients.

PART 2: TREATMENT

The most common fracture of the wrist is the distal radius fracture, followed by a scaphoid fracture.\(^20\) The annual incidence of distal radius fracture in the Netherlands is around 200 to 400 per 100,000 persons.\(^21\) The incidence increases after the age of fifty, especially in women due to osteoporosis.\(^22\) With the current ageing of the population, it is likely that the incidence of distal radius fracture will further rise in the near future.

Despite the high incidence of distal radius fractures, no evidence regarding the best treatment method exists. And as such, management of distal fractures continues to stimulate debate. Non-dislocated fractures generally tend to be stable and can be treated conservatively. However, two-thirds of the distal radius fractures are displaced and require reduction.\(^23\) The optimal treatment of these types of fractures hinges on alleged fracture instability.

Treatment of unstable distal radius fractures is the subject of numerous studies. Nevertheless, a prerequisite for implementing the findings of these studies is the generalizability of the results. Generalizability refers to the degree to which the findings in the study population can be applied to another, future population of patients.\(^24\) Studies that focus on the treatment of unstable distal radius fractures should therefore clearly describe what they regarded as an unstable fracture. However, instability is in the eye of the beholder and therefore a situation that is difficult to capture in a definition. In Chapter 4 we describe the most common definitions of an unstable distal radius fracture in literature to examine if there is one preferred evidence-based definition for future authors.

The absence or variability in definitions of an unstable distal radius fracture in literature hampers apparent comparison of studies. As such, there is still no optimum treatment for distal radius fractures.\(^25\) While the evidence remains inconclusive, the choice of treatment is frequently based on surgeon’s preference. These preferences vary according to surgeon’s age and background and likely result in variations in practice across hospitals.\(^26\) Variation based on these non patient-related factors is unwarranted and suggests potential to improve cost-effectiveness. The first step in addressing potentially unwarranted variation is insight into the extent in which variation across practices exists. In Chapter 5 we examine
the variation in surgical treatment rates across all Dutch hospitals.

When two types of treatment generally achieve acceptable results and literature does not substantiate the choice for one over the other, cost-effectiveness comes into play. Annually, hand and wrist injuries account for 740 million U.S. dollars and are the most expensive type of injury, outranking lower limb and knee fractures. Around 56% of the costs are related to loss of productivity. Internal fixation allows early mobilisation of the injured wrist possibly resulting in less absence from work. However, the direct costs of operative management are two to three times higher than conservative treatment. Conversely, secondary fracture dislocation following closed reduction occurs in up to 59% of the patients, after which surgical fixation is the treatment of choice. In Chapter 6 we compare functional outcome of volar locking plate versus external fixation in patients with unstable distal radius fractures. In Chapter 7 we describe the design of a multicentre randomised controlled trial to compare the functional outcome following surgical reduction and fixation with a volar locking plate with the functional outcome following closed reduction and plaster immobilisation in patients with displaced extra-articular distal radius fractures. Simultaneously, we describe the parallel economic evaluation study of these two treatment modalities.

If secondary fracture dislocation is left untreated, patients can develop a symptomatic malunion of the distal radius. A corrective osteotomy for patients with a malunited radius fracture can improve wrist function and reduce stiffness and pain. However, malunions of the radius commonly involve complex three dimensional deformations in different planes, and therefore represent a therapeutic challenge to surgeons. Conscientious preoperative planning of the procedure and accurate surgical repositioning is required to achieve accurate anatomical reconstruction. Computer-assisted preoperative and intra-operative planning may optimise the results of corrective osteotomies of the radius. In Chapter 8 we analyse the radiological results of computer-assisted 3-D planned corrective osteotomy in a series of patients with a malunited radius fracture.

PART 3: PROGNOSIS

Ideally, patients with a significant risk of secondary fracture displacement are identified at the time of presentation and selected for pre-emptive surgical treatment. This would enable timely definitive management, avoid unnecessary painful manipulation and possibly reduce the incidence of malunions. Unfortunately, patients with potentially unstable distal radius fractures are difficult to identify. In Chapter 9 we describe the results of a meta-analysis of predictors of secondary displacement in distal radius fractures. Another method to identify a patient with an unstable distal radius fracture is by using a clinical prediction model. The largest study to develop a clinical decision rule was Mackenney et al., who performed a study in over 4,000 patients. However, although the model is available as an online calculator and can thus be used in clinical practice, it has never been externally validated. In Chapter 10 we describe the results of the external validation of this model in a different patient population with displaced distal radius fractures.

Although the goal of treatment of distal radius fractures is to achieve and maintain anatomic alignment, radiologic parameters are not always predictive for functional outcome. Especially in elderly patients, for whom subjective functional results generally tend to be less susceptible to distal radius fracture alignment. This is one of the reasons why patient-reported outcomes have started to gain importance in orthopaedic research. Concretely, a numeric change in score that is less than the MCID, even if statistically significant, does not represent a true clinically relevant change. Because the MCID defines a difference that is considered important to patients, it also serves as the basis for estimating the necessary sample size in designing future studies.

One of the most frequently used outcome measures in distal radius fracture studies is the Patient-rated Wrist Evaluation score, a 15-item questionnaire designed to measure patient wrist pain and disability. To recognize a treatment effect expressed as a change in PRWE score, it is important to be aware of the minimum clinically important difference (MCID) of the PRWE score. The MCID represents the smallest change in score that would be perceived by the patient as beneficial. Consequently, a numeric change in score that is less than the MCID, even if statistically significant, does not represent a true clinically relevant change. Because the MCID defines a difference that is considered important to patients, it also serves as the basis for estimating the necessary sample size in designing future studies.
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PART 1 GENERAL INTRODUCTION AND OUTLINE OF THE THESIS


PART 1

DIAGNOSIS
CHAPTER 1

A MULTICENTRE CROSS SECTIONAL STUDY TO EXAMINE PHYSICIANS’ ABILITY TO RULE OUT A DISTAL RADIUS FRACTURE BASED ON CLINICAL FINDINGS

M.M.J. Walenkamp
M.P. Rosenwasser
J.C. Goslings
N.W.L. Schep

Eur J Trauma Emerg Surg. 2015
INTRODUCTION
Radiography for patients with wrist trauma is routine in most hospitals. However, only 40% of these patients have sustained a fracture of the wrist. This conservative approach entails unnecessary exposure to radiation, waiting time for the patient and additional healthcare expenditure.

Selecting patients for radiography could result in more efficient use of X-ray examinations in the Emergency Department. However, others advocate that the high prevalence of fractures in patients with wrist trauma mandates radiography in all patients. Regardless, since there are no recognized guidelines or criteria available to rely on, physicians will have an overly cautious attitude and continue to request X-rays on a routine basis.

A validated clinical decision rule could reinforce physicians’ clinical accuracy and reduce the use of radiography in the Emergency Department. However, this requires physicians to be able to interpret clinical findings and accurately rule out a fracture of the wrist on the basis of their clinical findings alone.

The aim of this study was to study the efficiency of current use of radiography in patients with wrist trauma and examine physicians’ ability to accurately rule out a distal radius fracture based on their physical examination.

METHODS
Study design and setting
We performed a multicentre cross-sectional observational study in five Emergency Departments between November 2010 and June 2014 and included all consecutive adult patients with wrist trauma. Physicians were asked to perform a standardized examination of the wrist and to subsequently indicate the probability of a distal radius fracture.

Results
The majority of the 924 included patients were referred for radiography (99.6%). Of the 920 patients that were imaged, 402 (44%) had sustained a distal radius fracture, 82 (9%) an isolated carpal fracture and 12 (1%) an isolated ulna fracture. Overall, physicians were able to accurately discriminate between patients with and without a distal radius fracture (area under the receiver operating characteristics curve: 0.87, 95% CI: 0.85 - 0.89). Physicians were absolutely certain of their clinical diagnosis in 180 patients (19%), for whom they indicated either a 0% or a 100% probability. In these patients, physicians showed a 99% sensitivity (95% CI: 98% - 100%) and 67% specificity (95% CI: 53% - 80%) for predicting a distal radius fracture.

Conclusions
Although physicians in the ED are able to accurately discriminate between patients with and without a distal radius fracture based on their physical findings, they were only completely certain of their diagnosis in 19% of the patients. A validated clinical decision rule could reinforce physician’s clinical judgment and support them in their decision not to routinely request radiography.

ABSTRACT
Purpose
To study current use of radiography in patients with wrist trauma and examine physicians’ ability to rule out a distal radius fracture based on their physical findings.

Methods
We performed a multicentre cross-sectional observational study in five Emergency Departments (ED) between November 2010 and June 2014 and included all consecutive adult patients with wrist trauma. Physicians were asked to perform a standardized examination of the wrist and to subsequently indicate the probability of a distal radius fracture.

Results
The majority of the 924 included patients were referred for radiography (99.6%). Of the 920 patients that were imaged, 402 (44%) had sustained a distal radius fracture, 82 (9%) an isolated carpal fracture and 12 (1%) an isolated ulna fracture. Overall, physicians were able to accurately discriminate between patients with and without a distal radius fracture (area under the receiver operating characteristics curve: 0.87, 95% CI: 0.85 - 0.89). Physicians were absolutely certain of their clinical diagnosis in 180 patients (19%), for whom they indicated either a 0% or a 100% probability. In these patients, physicians showed a 99% sensitivity (95% CI: 98% - 100%) and 67% specificity (95% CI: 53% - 80%) for predicting a distal radius fracture.

Conclusions
Although physicians in the ED are able to accurately discriminate between patients with and without a distal radius fracture based on their physical findings, they were only completely certain of their diagnosis in 19% of the patients. A validated clinical decision rule could reinforce physician’s clinical judgment and support them in their decision not to routinely request radiography.
present or not). This was ensured, by cross-checking the medical records of all patients 6 months after inclusion and verifying that radiographs had been requested by a provider from the same hospital (and not the General Practitioner). Additionally, the discharge letters were reviewed for any sign that patients had been referred to the Emergency Department with X-rays obtained elsewhere.

For all patients without radiographs taken on the initial visit, we assessed the radiology report during a 6 month period after the ED visit to check for missed fractures. Additionally, we contacted the patients by telephone and inquired if they had visited any other hospital since their ED visit or suffered from prolonged (>2 weeks) wrist pain.

Methods and measurements
Data was collected prospectively using standardized Case Record Forms (CRF). The assessors were asked to perform a standardized examination of each patient with pain or tenderness secondary to wrist trauma. Items included mechanism of injury, physical examination of the wrist and functional tests (Table 1). Additionally, they were asked to indicate the probability of the presence of a distal radius fracture on a 10-cm Visual Analogue Scale (VAS) from 0 to 100. Referral for radiography and type of treatment was at the discretion of the treating physician.

### Table 1. Elements of standardized physical examination

<table>
<thead>
<tr>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Hand dominance</td>
</tr>
<tr>
<td>Mechanism of injury:</td>
</tr>
<tr>
<td>FOOSH</td>
</tr>
<tr>
<td>Traumatic hyperflexion</td>
</tr>
<tr>
<td>Traffic accident</td>
</tr>
<tr>
<td>Direct blow or compression</td>
</tr>
<tr>
<td>Punch</td>
</tr>
<tr>
<td>Other or unknown</td>
</tr>
<tr>
<td>Swelling of the wrist</td>
</tr>
<tr>
<td>Visible deformation</td>
</tr>
<tr>
<td>Distal radius tender to palpation</td>
</tr>
<tr>
<td>Distal ulna tender to palpation</td>
</tr>
<tr>
<td>Active mobility painful at:</td>
</tr>
<tr>
<td>Dorsiflexion</td>
</tr>
<tr>
<td>Palmar flexion</td>
</tr>
<tr>
<td>Supination</td>
</tr>
<tr>
<td>Ulnar deviation</td>
</tr>
<tr>
<td>Radial deviation</td>
</tr>
<tr>
<td>Functional tests painful</td>
</tr>
<tr>
<td>Radioulnar ballottement test</td>
</tr>
<tr>
<td>Axial compression of forearm</td>
</tr>
</tbody>
</table>

FOOSH, fall on outstretched hand

a. A direct blow to the wrist or compression between two surfaces

b. Test is positive if pain occurs when the ulna is translated from volar to dorsal while the radius manually fixated

Assessors
In the Netherlands, most Emergency Departments are run by emergency physicians. Providers include emergency physicians; emergency medicine registrars; surgical registrars; orthopaedic registrars; junior doctors not in training and 2nd year general practice registrars. Registrars are either supervised by emergency physicians or by their attending (surgeon or orthopaedic surgeon).

The assessors included interns under supervision of a registrar; junior doctors not in training; emergency medicine physicians; emergency medicine registrars; surgical registrars; orthopaedic registrars and 2nd year general practice registrars. All physicians (interns, emergency medicine physicians; emergency medicine registrars; surgical registrars; orthopaedic registrars and general practice registrars) received regular instructions and training on how to assess the clinical variables in a standardized manner. Additionally, we provided informative pocket cards and posters. Medical students and nurses operated under supervision and
were instructed by one of the physicians.

**Outcomes**
The reference standard was the presence of a distal radius fracture on the conventional X-ray at presentation, as described in the radiologist report. A fracture was defined as the presence or disruption of one or more of the cortices of the bone. A fissure and an avulsion were recorded as a fracture. The reporting radiologist was blinded to the contents of the Case Record Forms. Patients without any bony fractures of the wrist were diagnosed with a wrist sprain or contusion. Radiographic series comprised at least one posterior-anterior (PA) and one lateral view with approximately 90 degrees of elbow flexion; and any further conventional imaging available (for example scaphoid series). Findings on additional Computed Tomography scans or Magnetic Resonance Image scans were not taken into account. Patients who were not imaged did not return or went elsewhere because persisting complaints were classified as not having sustained a distal radius fracture.

**Analysis**
Data entry and analysis were performed with the Statistical Package for Social Sciences (SPSS) version 21.0 for Windows. We calculated test characteristics (sensitivity, specificity, predictive values and likelihood ratios) with 95% confidence intervals for patients in the no risk group (0% probability) and the definite fracture group (100% probability). To estimate the ability of the assessors to discriminate between patients with and without a distal radius fracture, we calculated the area under the receiver operating characteristics curve (AUC) of the predicted probability. The AUC ranges from 0.5 to 1, with higher scores indicating better prediction.

**RESULTS**
During the study period, 1018 patients visited the ED for wrist trauma and were enrolled in our study. Ninety-two patients (9%) were excluded from the analysis for various reasons (Fig. 1). A total of 924 patients were analyzed (Table 2). The majority of patients were referred for radiography (99.6%). Of the 920 patients that were imaged, 402 (44%) had sustained a distal radius fracture, 82 (9%) an isolated carpal fracture, 12 (1%) an isolated ulna fracture, and 11 (1%) a fracture of the distal radius and a concomitant carpal fracture. There were 48 scaphoid fractures, 32 triquetrum fractures and 2 other carpal fractures.
The mean predicted probability of a distal radius fracture was 58% (SD: 33) and the median was 65% (IQR: 25 - 90). Overall, the physicians’ predicted probability showed a good discrimination between patients with and without a distal radius fracture: the area under the receiver operating characteristics curve (AUC) was 0.87 (95% CI: 0.85 - 0.89, Fig. 2). The AUC was similar for all types of physicians.

Most patients (N = 292, 32%) were considered to have a medium to high risk of a distal radius fracture. Of those, 123 (42%) had sustained a distal radius fracture (Fig. 3). Physicians were absolutely certain of their clinical diagnosis in 180 patients (19%), for whom they indicated either a 0% or a 100% risk of a distal radius fracture. In 31 patients, the assessors indicated no risk (0%) of a distal radius fracture. They correctly ruled out a distal radius fracture in 30 patients, and missed one minor nondisplaced fracture. In 149 patients, physicians predicted a definite distal radius fracture (100%). They were correct in 134 (90%) patients and incorrect in fifteen (10%) patients. Three of those fifteen patients had sustained a scaphoid fracture and not a distal radius fracture. This resulted in a sensitivity of 99% and a specificity of 67% for predicting a distal radius fracture (Table 4).

There were eight different types of assessors (Table 3). Surgical registrars and emergency physicians completed most Case Record Forms (Table 3). Four patients were not imaged. The physicians indicated a probability of a distal radius fracture of 0% for two patients and 20% for the other two patients. None of these four patients returned because of persisting complaints, nor did they indicate to have gone elsewhere for a diagnostic workup.

| Table 2. Demographic characteristics of study population (N = 924) |
|-----------------|-----------------|-----------------|-----------------|
| Age, median (IQR) | 49 (31-63)       | Female, no. (%)  | 558 (60)        |
| | Traumatic hyperflexion: 26 (3) | Punch: 18 (3) | Other or unknown: 133 (14) |
| Patients with distal radius fracture, no. (%) | 402 (44) | Patients with isolated distal ulna fracture, no. (%) | 12 (1) |
| Patients with carpal fracture, no. (%) | 82 (9) | Patients with multiple wrist fractures, no. (%) & | 11 (1) |
| Treatment | Expectant: 184 (20) | Compression bandage: 447 (48) | Reductio and plaster immobilisation: 184 (20) |
| | Not recorded in patients records: 7 (1) | |

IQR, interquartile range; FOOSH, fall on outstretched hand.  
a. Patients with a distal radius fracture and a concomitant fracture of one or more of the carpal bones.

Table 3. Characteristics of assessors and their diagnostic accuracy

<table>
<thead>
<tr>
<th>Background assessor (N = 924)</th>
<th>Number of assessors</th>
<th>Number of patients assessed (%)</th>
<th>AUC (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical registrar</td>
<td>60</td>
<td>284 (31)</td>
<td>0.85 (0.80 - 0.89)</td>
</tr>
<tr>
<td>Emergency physician</td>
<td>16</td>
<td>214 (23)</td>
<td>0.90 (0.86 - 0.94)</td>
</tr>
<tr>
<td>Junior doctor</td>
<td>16</td>
<td>171 (19)</td>
<td>0.92 (0.87 - 0.96)</td>
</tr>
<tr>
<td>2nd year GP registrar</td>
<td>43</td>
<td>122 (13)</td>
<td>0.82 (0.74 - 0.90)</td>
</tr>
<tr>
<td>Intern under supervision</td>
<td>42</td>
<td>66 (7)</td>
<td>0.78 (0.67 - 0.90)</td>
</tr>
<tr>
<td>Emergency registrar</td>
<td>10</td>
<td>59 (6)</td>
<td>0.92 (0.85 - 0.99)</td>
</tr>
<tr>
<td>Orthopaedic registrar</td>
<td>4</td>
<td>5 (0.5)</td>
<td>Not calculated</td>
</tr>
<tr>
<td>Not recorded in patients files</td>
<td>-</td>
<td>3 (0.5)</td>
<td>Not calculated</td>
</tr>
</tbody>
</table>

AUC, area under the receiver operating characteristics curve; CI, confidence interval; GP, general practitioner;  
* Area under the receiver operating characteristics curve for physicians’ predicted probability of a distal radius fracture.
PART 1

30 31

44% shows that physicians tend to overestimate the probability of a distal radius fracture. This study also shows that most patients were classified in the “grey area” with a probability of 41% - 80% of a distal radius fracture. Physicians were only completely sure about their diagnosis in 19% of the patients. Nevertheless, once they were certain, they were able to predict a distal radius fracture with high sensitivity. The low negative likelihood ratio of 0.01 confirms that physicians’ judgement is a powerful tool to rule out a distal radius fracture in adults.

Although our study did not mandate radiography for all patients, physicians requested X-rays for 99.6%. This high referral ratio implies a lack of support of physicians in their decision-making and a potential for more efficient use of radiography for wrist trauma. A similar situation existed for ankle injury in the early nineties. Still et al. [6] found that physicians requested X-rays for most patients with ankle injury, even though they were able to accurately discriminate between patients with and without a fracture. Their findings suggested a great potential for more efficient use of radiography and lead to the development of the renowned Ottawa Ankle Rules.

This study has several limitations. We did not ask physicians to indicate the probability of a carpal or ulnar fracture. Wrist X-rays are not only requested to rule out a distal radius fracture, but also carpal bone and ulnar fractures. Physicians were not asked to corroborate their decision to request an X-ray of the wrist. It is therefore possible that patients were imaged because of a suspected scaphoid fracture, while a low probability of a distal radius fracture was indicated. Furthermore, physicians might have felt obligated to request an X-ray of the wrist because of the introduction of this study. Although they were otherwise instructed, this could have resulted in an overestimation of the true ratio of patients referred for radiography.

The findings of this study might not be generalizable to other Emergency Departments. In Dutch hospitals, patients are generally examined by emergency physicians, junior doctors not in training or registrars (surgical, emergency, GP and orthopaedic). These include physicians with various levels of training and experience who might put less trust in their clinical judgement. Nevertheless, our results showed a similar diagnostics accuracy among physicians from different backgrounds (Table 3). We acknowledge that clinical judgement is not the only factor that affects the decision to refer a patient for radiography. Patient’s expectations, crowded EDs and possible medicolegal consequences of a missed fracture also play a substantial role. However, these factors do not completely account for different referral ratios found among hospitals. The significant variability in clinical practice among similar institutions suggests a lack of clinical guidelines.

DISCUSSION

This study confirms our expectation that physicians in the Emergency Department are able to accurately rule out the presence of a distal radius fracture based on physical findings alone. For a randomly selected pair of patients, one with and one without a distal radius fracture, the probability that a physician working in the ED will correctly identify the patient with a distal radius fracture is 87%.

The mean predicted probability of 58% versus the observed distal radius fracture rate of

![Graph showing the distribution of patients with and without distal radius fracture by physicians' predicted probability.](image)

**Fig. 3** Distribution of patients (N = 922) with and without fracture by physicians’ predicted probability of a distal radius fracture. The percentages are the proportions of patients with a distal radius fracture in each probability group.

**Table 4** Diagnostic accuracy of physicians when certain of a presence of distal radius fracture (95% CI)

<table>
<thead>
<tr>
<th>Probability of Fracture</th>
<th>Patients with Distal Radius Fracture</th>
<th>Patients without Distal Radius Fracture</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk (0%)</td>
<td>31</td>
<td>30</td>
<td>61</td>
</tr>
<tr>
<td>Definite fracture (100%)</td>
<td>149</td>
<td>15</td>
<td>164</td>
</tr>
<tr>
<td>Total</td>
<td>180</td>
<td>45</td>
<td>225</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>99.3 (97.8 - 100.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>67.7 (52.9 - 80.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>3.0 (2.0 - 4.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.01 (0.0 - 0.08)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval
CONCLUSION
Although physicians in the ED are able to accurately discriminate between patients with and without a distal radius fracture based on their physical findings, they were only completely certain of their diagnosis in 19% of the patients. These findings confirm the potential for more efficient use of radiography for wrist trauma in the Emergency Department. A validated clinical decision rule could reinforce physicians’ clinical judgment and support them in their decision not to request radiography. We are currently developing such a clinical decision rule.39
REFERENCES


CHAPTER 2

THE AMSTERDAM WRIST RULES: THE MULTICENTRE PROSPECTIVE DERIVATION AND EXTERNAL VALIDATION OF A CLINICAL DECISION RULE FOR THE USE OF RADIOGRAPHY IN ACUTE WRIST INJURY

M.M.J. Walenkamp
A. Bentohami
A. Slaar
M.S.H. Beerekamp
M. Maas
L.C. Jager
N.L. Sosef
R. van Velde
J.M. Ultee
E.W. Steyerberg
J.C. Goslings
N.W.L. Schep
BACKGROUND
Wrist trauma is one of the most common Emergency Department (ED) attendances and accounts for approximately 20% of all injuries.\(^1^,\)\(^2\) Only 39% of patients with wrist trauma have a fracture; however, most patients are routinely referred for radiography.\(^3^,\)\(^4\) Unlike ankle\(^7\), elbow\(^8\) and knee\(^9\) injury, there are no guidelines or criteria available that indicate which patients with wrist trauma require an X-ray. A clinical decision rule that selects patients for radiography could avoid unnecessary wrist X-rays and therefore decrease radiation exposure; ED waiting times and reduce health care expenditure.\(^6^,\)\(^10^,\)\(^11\) Two previous studies investigated the diagnostic value of physical findings in patients with acute wrist trauma.\(^13^,\)\(^14\) However, these studies were limited by small study populations and did not present a clinical decision rule.

The purpose of this study was to derive and externally validate a clinical decision rule that selects patients with acute wrist trauma in the Emergency Department (ED) for radiography.

METHODS
Study design and setting
This multicenter prospective study consisted of three components: (1) derivation of a clinical prediction model for detecting wrist fractures in patients following wrist trauma; (2) external validation of this model; and (3) design of a clinical decision rule. The study was conducted in the EDs of five Dutch hospitals: one academic hospital (derivation cohort) and four regional hospitals (external validation cohort). We included all adult patients with acute wrist trauma. The main outcome was fracture of the wrist (distal radius, distal ulna or carpal bones) diagnosed on conventional X-rays.

Results
A total of 882 patients were analysed; 487 in the derivation cohort and 395 in the validation cohort. We derived a clinical prediction model with eight variables: age; sex; swelling of the wrist; swelling of the anatomical snuffbox; visible deformation; distal radius tender to palpation; pain on radial deviation and painful axial compression of the thumb. The Area Under the Curve at external validation of this model was 0.81 (95% CI: 0.77 - 0.85). The sensitivity and specificity of the Amsterdam Wrist Rules (AWR) in the external validation cohort were 98% (95% CI: 95% - 99%) and 21% (95% CI: 15% - 28). The negative predictive value was 90% (95% CI: 81% - 99%).

Conclusions
The Amsterdam Wrist Rules is a clinical prediction rule with a high sensitivity and negative predictive value for fractures of the wrist. Although external validation showed low specificity and 100% sensitivity could not be achieved, the Amsterdam Wrist Rules can provide physicians in the Emergency Department with a useful screening tool to select patients with acute wrist trauma for radiography. The upcoming implementation study will further reveal the impact of the Amsterdam Wrist Rules on the anticipated reduction of X-rays requested, missed fractures, Emergency Department waiting times and health care costs.
Data collection and variables
Eligible patients were included upon presentation in the Emergency Department. Data were collected prospectively by the treating physicians on standardized Case Record Forms (CRF).

Box 1. Potential predictors considered in the full model

<table>
<thead>
<tr>
<th>Predictor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (if male)</td>
</tr>
<tr>
<td>Age (continuous)</td>
</tr>
<tr>
<td>Swelling of wrist</td>
</tr>
<tr>
<td>Swelling of the anatomical snuffbox</td>
</tr>
<tr>
<td>Visible deformation</td>
</tr>
<tr>
<td>Distal radius tender to palpation</td>
</tr>
<tr>
<td>Distal ulna tender to palpation</td>
</tr>
<tr>
<td>Anatomical snuffbox tender to palpation</td>
</tr>
<tr>
<td>Scaphoid tubercle tender to palpation</td>
</tr>
<tr>
<td>Active mobility painful</td>
</tr>
<tr>
<td>dorsiflexion</td>
</tr>
<tr>
<td>palmar flexion</td>
</tr>
<tr>
<td>supination</td>
</tr>
<tr>
<td>pronation</td>
</tr>
<tr>
<td>ulnar deviation</td>
</tr>
<tr>
<td>radial deviation</td>
</tr>
<tr>
<td>Functional tests painful</td>
</tr>
<tr>
<td>radioulnar ballottement test*</td>
</tr>
<tr>
<td>axial compression of forearm</td>
</tr>
<tr>
<td>axial compression thumb</td>
</tr>
<tr>
<td>pinch grip test</td>
</tr>
</tbody>
</table>

* Test is positive if pain occurs when the ulna is translated from volar to dorsal while the radius manually fixed.

Except for age, all predictors were ordinal and coded yes (if present) or no (of not present).

 Patients were evaluated for 19 clinical variables including patient characteristics, physical examination and functional testing (Box 1). We based the selection of variables on clinical experience and previous studies. The questions on the Case Record Form (CRF) were presented in a dichotomous nature (yes/no). Eligibility and data collection forms were verified by two authors by cross-checking the medical records of all patients six months after inclusion.

The assessors were all physicians and included consultant emergency medicine physicians; emergency medicine residents; surgical residents; orthopaedic residents and general practice residents. All physicians received regular instructions and training on how to assess the clinical variables in a standardized manner. Additionally, we provided informative pocket cards and posters. In order not to disrupt common practice, referral for radiography and type of treatment were at the discretion of the treating physician. Although the study did not mandate radiographs on all wrist-injured patients, only 5 out of 1019 patients (0.5%) did not receive an X-ray of the wrist.

Outcomes
The reference standard was the presence of a fracture of the distal radius, ulna or one of the carpal bones, as assessed by the attending radiologist on the X-ray at presentation. A fracture was defined as a disruption of one or more of the cortices. A fissure and an avulsion were recorded as a fracture. The radiologist was blinded to the contents of the Case Record Forms. Radiographic series comprised at least one posterior-anterior (PA) and one lateral view with 90 degrees of elbow flexion; and any further conventional imaging available (for example scaphoid series). We did not take findings on additional Computed Tomography scans or Magnetic Resonance Image scans into account.

Sample size
A common rule of thumb to determine the sample size of the development of a prediction model is at least ten events (fractures) per variable. Patients were evaluated for 19 variables. Therefore the inclusion of minimum of 190 patients who sustained a fracture was required in the derivation cohort. According to a similar rule of thumb, external validation requires at least 100 patients with an event (fracture) and 100 patients without an event (no fracture). We continued enrolling patients after the required sample size was achieved to maintain the study infrastructure required for the subsequent implementation study.

Analysis
For efficient statistical analysis, we used imputation techniques to impute the missing values (aregImpute function from the Hmisc library, R, version 3.0.1.) For each variable containing missings, the aregImpute package draws values from a random sample from the non-missing values with replacement. Using this data, aregImpute fits a flexible model that predicts the missing target variable while finding its optimum transformation. Each missing variable is then imputed with the observed value whose predicted transformed value is closest to the predicted transformed value of the missing variable. We considered an imputation model that included all dichotomous variables; prehensile grip strength and the outcome. The set of first imputations was used for the analyses.

Model development and internal validation
We derived two clinical prediction models: one for all wrist fractures (distal ulna, distal radius and carpal bone) and one for distal radius fractures only. Using data on patients enrolled in the academic hospital, multivariate logistic regression models with all 19 potential predictors were fit. These full modes were reduced using a stepwise backward elimination process based on a liberal p-value of 0.2. To estimate the internal validation of performance we used bootstrapping (500 replications). Bootstrapping provided the shrinkage factor that was
used for the regression coefficients.\textsuperscript{21}

\textbf{External model validation and final model development}

To assess general applicability, we validated the shrunk models in the cohort that included all patients enrolled in the four other participating hospitals. For each patient in the validation cohort, the probability of a wrist fracture or of a distal radius fracture was calculated using the prediction models. The validity of the models was assessed by comparing the predicted probabilities of a fracture with the observed fractures. To estimate the ability of the models to discriminate between patients with and without a fracture, we calculated the Areas under the Receiver Operating Characteristics Curve (AUC). The AUC ranges from 0.5 to 1, with a higher score indicating more accurate predictions. The models were also evaluated for their agreement between predicted fractures and observed fractures. This is otherwise known as the model calibration and was assessed by plotting the predicted probability of a fracture and the observed frequency of fractures. The ideal slope of such a plot is 1, indicating perfect agreement between observed and predicted risks.\textsuperscript{25} As a final step, the models were fit on data from both cohorts combined to obtain robust estimates of the regression coefficients. These final models were internally validated by bootstrapping as for the initial models.

\textbf{Clinical decision rule}

A clinical prediction model provides an estimated risk of a certain outcome. A clinical decision rule goes one step further and links a recommendation to the predicted risk. In this study, the recommendation would be to request an X-ray yes or no. A clinical decision rule therefore requires a cut-off value for the predicted probability of a fracture to classify patients as low or high risk (or recommend an X-ray yes or no). We decided beforehand to select a cut-off value at which the sensitivity of the Amsterdam Wrist Rules would not drop below 98%, while maintaining the highest specificity.

\textbf{RESULTS}

\textit{Characteristics of study subjects}

We enrolled 1019 patients from five participating hospitals. A total of 137 patients (13\%) were excluded patients from the analysis for various reasons (Fig. 1). In total, 882 patients were analyzed (Table 1). In 470 patients (53\%), a fracture of the distal radius, distal ulna or one of the carpal bones was identified on conventional radiographic series. A distal radius fracture was the most common fracture (44\%).

In the derivation cohort, 487 patients were analyzed with a median age of 48 years (interquartile range, 29 - 61) and women were slightly overrepresented (57\%). A fall on outstretched hand was the most common mechanism of injury (66\%). In 251 patients (52\%) in the derivation cohort, a fracture of the distal radius, ulna or one of the carpal bones was identified.

In the validation cohort, 395 patients with similar demographic characteristics were analyzed (Table 1). In 219 of these patients (55\%), a fracture of the distal radius, distal ulna or one of the carpal bones was identified.

\textbf{External model validation and final model development}

To assess general applicability, we validated the shrunk models in the cohort that included all patients enrolled in the four other participating hospitals. For each patient in the validation cohort, the probability of a wrist fracture or of a distal radius fracture was calculated using the prediction models. The validity of the models was assessed by comparing the predicted probabilities of a fracture with the observed fractures. To estimate the ability of the models to discriminate between patients with and without a fracture, we calculated the Areas under the Receiver Operating Characteristics Curve (AUC). The AUC ranges from 0.5 to 1, with a higher score indicating more accurate predictions. The models were also evaluated for their agreement between predicted fractures and observed fractures. This is otherwise known as the model calibration and was assessed by plotting the predicted probability of a fracture and the observed frequency of fractures. The ideal slope of such a plot is 1, indicating perfect agreement between observed and predicted risks.\textsuperscript{25} As a final step, the models were fit on data from both cohorts combined to obtain robust estimates of the regression coefficients. These final models were internally validated by bootstrapping as for the initial models.

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\textbf{RESULTS}

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Model development

A clinical prediction model for all fractures was derived that included eight variables: age; sex (if male), swelling of the wrist; swelling of the anatomical snuffbox, visible deformation; distal radius tender to palpation; pain on radial deviation and painful axial compression of the thumb. The Area Under the Curve (AUC) of this model was 0.84 (95% CI: 0.81 - 0.88) and 0.82 (95% CI: 0.79 - 0.85) after correcting for model optimism by bootstrapping. The coefficient of each dichotomous variable reflects the amount of change in the probability of a fracture (Table 2). The presence of a dichotomous variable with a positive coefficient adds to the probability of a fracture. The presence of a dichotomous variable with a negative coefficient decreases the probability. The coefficient of the continuous variable age reflects the amount of change in probability for every ten-year increase in age. Except for painful axial compression of the thumb (coefficient -0.37), the presence of all variables adds to the probability of a fracture. Painful axial compression of the thumb decreases the probability of a fracture.

Table 2. Predictors in model for all fractures

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 years)</td>
<td>0.35 (0.22 - 0.49)</td>
<td>1.04 (1.02 - 1.05)</td>
</tr>
<tr>
<td>Sex (if male)</td>
<td>0.38 (-0.10 - 0.86)</td>
<td>1.46 (0.90 - 2.35)</td>
</tr>
<tr>
<td>Swelling wrist</td>
<td>1.48 (1.00 - 1.96)</td>
<td>4.40 (2.72 - 7.11)</td>
</tr>
<tr>
<td>Swelling anatomical snuffbox</td>
<td>0.47 (-0.08 - 1.02)</td>
<td>1.60 (0.92 - 2.78)</td>
</tr>
<tr>
<td>Visible deformation</td>
<td>1.32 (0.54 - 2.09)</td>
<td>3.73 (1.72 - 8.11)</td>
</tr>
<tr>
<td>Distal radius tender to palpation</td>
<td>0.88 (0.23 - 1.53)</td>
<td>2.41 (1.25 - 4.63)</td>
</tr>
<tr>
<td>Pain with radial deviation</td>
<td>0.67 (0.08 - 1.26)</td>
<td>1.95 (1.08 - 3.51)</td>
</tr>
<tr>
<td>Pain with axial compression of the thumb</td>
<td>-0.37 (-0.88 - 0.14)</td>
<td>0.69 (0.41 - 1.15)</td>
</tr>
</tbody>
</table>

The coefficient of each dichotomous variable reflects the amount of change in the log odds of a fracture. The coefficient of the continuous variable age reflects the amount of change in the log odds of a fracture for every ten-year increase in age.

Abbreviations: CI, Confidence Interval

A clinical prediction model for only distal radius fractures was derived that also included eight variables: age; swelling of the wrist; visible deformation; distal radius tender to palpation; pain on ulnar deviation; palmar flexion, supination and the painful radioulnar ballottement test (Table 3). The presence of all variables except pain on ulnar deviation increases...
the probability of a distal radius fracture. Pain on ulnar deviation (coefficient -0.67 (95% CI: -1.35 - -0.02) decreases the probability of a distal radius fracture. The Area Under the Curve (AUC) of this model was 0.91 (95% CI: 0.88 - 0.93) and 0.90 (95% CI: 0.87 - 0.92) after optimism correction by bootstrapping.

Table 4. The performance of the Amsterdam Wrist Rules at external validation (N=395)

<table>
<thead>
<tr>
<th>All Fractures</th>
<th>Amsterdam Wrist Rules indicate X-ray</th>
<th>215</th>
<th>139</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amsterdam Wrist Rules indicate no X-ray</td>
<td>4</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>219</td>
<td>176</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>98.2 (95.1 - 99.4)</td>
<td>15.7 (3.40 - 72.4)</td>
<td></td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>21.0 (15.4 - 27.9)</td>
<td>1.90 (0.86 - 4.18)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Predictors in model for distal radius fractures

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 years)</td>
<td>0.40 (0.25 - 0.54)</td>
<td>1.04 (1.02 - 1.06)</td>
</tr>
<tr>
<td>Swelling wrist</td>
<td>2.07 (1.44 - 2.70)</td>
<td>7.92 (4.24 - 14.8)</td>
</tr>
<tr>
<td>Visible deformation</td>
<td>1.38 (0.59 - 2.17)</td>
<td>3.97 (1.81 - 8.74)</td>
</tr>
<tr>
<td>Distal radius tender to palpation</td>
<td>2.75 (1.22 - 4.28)</td>
<td>15.7 (3.40 - 72.4)</td>
</tr>
<tr>
<td>Pain on palmar flexion</td>
<td>0.64 (-0.15 - 1.43)</td>
<td>1.90 (0.86 - 4.18)</td>
</tr>
<tr>
<td>Pain on supination</td>
<td>0.81 (0.15 - 1.47)</td>
<td>2.25 (1.16 - 4.37)</td>
</tr>
<tr>
<td>Pain on ulnar deviation</td>
<td>0.67 (0.13 - 0.5)</td>
<td>0.36 (0.13 - 0.98)</td>
</tr>
<tr>
<td>Pain on radioulnar ballottement test</td>
<td>0.56 (-0.02 - 1.15)</td>
<td>1.76 (0.98 - 3.16)</td>
</tr>
</tbody>
</table>

The coefficient of each dichotomous variable reflects the amount of change in the log odds of a fracture. The coefficient of the continuous variable age reflects the amount of change in the log odds of a fracture for every ten-year increase in age.

Abbreviations: CI, Confidence Interval

a. Derived from data from the academic hospital

External model validation and test characteristics

The external performance of the models was assessed in the 395 patients in the validation cohort. The Area Under the Curve at external validation of the model for all fractures was 0.81 (95% CI: 0.77 - 0.85) and the calibration slope was 0.94 (95% CI: 0.74 - 1.13). The Area Under the Curve at external validation of the model for only distal radius fractures was 0.86 (95% CI: 0.82 - 0.89) and the calibration slope was 1.07 (95% CI: 0.84 - 1.29).

The Amsterdam Wrist Rules (AWR) for all wrist fractures showed a sensitivity and specificity of 98% (95% CI: 95% - 99%) and 21% (95% CI: 15% - 28%) (Table 4). Its negative predictive value was 90% (95% CI: 81% - 99%). The sensitivity and specificity for only distal radius fractures were 98% (95% CI: 97% - 100%) and 25% (95% CI: 19% - 31%) (Table 4). The AWR was able to rule out 19% (41 / 219) of the patients without a wrist fracture and 25% (53 / 211) of the patients without a distal radius fracture. If the AWR had been used for all fractures, an X-ray would have been requested for 89.6% (354 / 395) of patients instead of 100%. This is an absolute reduction of 10.4%. The final formula to calculate the probabilities are depicted in Box 2. The AUC of the final model after bootstrapping was 0.88 (95% CI: 0.86 - 0.90).

Table 4. The performance of the Amsterdam Wrist Rules at external validation (N=395)

<table>
<thead>
<tr>
<th>Distal Radius Fractures</th>
<th>Amsterdam Wrist Rules indicate X-ray</th>
<th>179</th>
<th>158</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amsterdam Wrist Rules indicate no X-ray</td>
<td>3</td>
<td>53</td>
</tr>
<tr>
<td>Total</td>
<td>184</td>
<td>211</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%) [95% CI]</td>
<td>98.4 (96.5 - 100.0)</td>
<td>15.7 (3.40 - 72.4)</td>
<td></td>
</tr>
<tr>
<td>Specificity (%) [95% CI]</td>
<td>21.0 (15.4 - 27.9)</td>
<td>1.90 (0.86 - 4.18)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, Confidence Interval

a. Tested on data from the validation cohort

The cut-off point for X-ray yes or no was a predicted probability of 21% for all fractures and 4% for only distal radius fractures.

Box 2. Calculation of the linear predictor and probability

Linear predictor for ALL WRIST FRACTURES

0.0309 * age + 0.5862 * (if male) + 1.1486 * (if swelling wrist present) + 0.5757 * (if swelling anatomical snuff box is present) + 1.7123 * (if visible deformation present) + 0.7029 * (if distal radius tender to palpation) + 0.4963 * (if pain on palmar flexion) + 0.6567 * (if pain on supination) - 0.1793 * (if on axial compression thumb) - 3.616

Linear predictor for DISTAL RADIUS FRACTURES

0.0341 * age + 1.7298 * (if swelling of wrist present) + 1.6462 * (if visible deformation present) + 1.8117 * (if distal radius tender to palpation) + 0.4228 * (if pain on palmar flexion) + 0.6567 * (if pain on supination) - 0.2941 * (if pain on ulnar deviation) + 0.5949 * (if pain during radioulnar ballottement test) - 6.0202

All individual parameters add to the probability of a fracture.

a. Coefficients were derived from a fit of the model on both cohort combined (N = 882) and corrected for optimism by bootstrapping (N=500 replications)
DISCUSSION

We have developed a clinical prediction rule with a high sensitivity (98%) and negative predictive value (90%) for fractures of the wrist. Previous studies have illustrated that the X-ray referral policy for patients with wrist trauma is often obscure and unfounded, and to date no guidelines or criteria were available. The Amsterdam Wrist Rules can provide physicians with an externally validated screening tool trauma in the Emergency Department to select patients with acute wrist trauma for radiography.

The foremost strength of the Amsterdam Wrist Rules is that it is one of the few clinical decision rules that have been externally validated. Most clinical decision rules only undergo internal validation, often by bootstrapping. However, evaluating the performance of a prediction model or a clinical decision rule in a new patient population is essential before its implementation. The Amsterdam Wrist Rules underwent this most stringent form of external validation: the rules were tested in a patient population from different type of hospitals with different physicians. The performance of the Amsterdam Wrist Rules expressed in the AUC reflects excellent discriminative ability in a new patient population.

However, the Amsterdam Wrist Rules showed disappointing specificity at external validation. We could have developed the clinical decision rule with higher specificity and number of X-rays avoided. However, this would have resulted in a decreased sensitivity and consequently more fractures missed. Preferably, clinical decision rules in the Emergency Department have a very high sensitivity and negative predictive value. We believe that physicians will be reluctant to use any clinical decision rule with a sensitivity below 98%. In a similar way Stiell et al. devised the Ottawa Ankle Rules with a sensitivity of 100% because they felt that physicians would not accept to miss fractures. However, they also expressed the hope that society will come to accept the small price of an occasionally missed fracture that would probably have led to very little morbidity for the patients.

If the Amsterdam Wrist Rules had been applied in the external validation cohort, the 10% absolute reduction in X-rays would have been accompanied by 4 (1.6%) missed fractures: two scaphoid fractures, one intra-articular distal radius fracture and one extra-articular distal radius fracture. None of these fractures were dislocated or required surgery. Consequently, we advise caution in the use of the Amsterdam Wrist Rules before its true effects on both patient care and use of resources have been evaluated in the upcoming implementation study. After implementation of the Ottawa Ankle Rules, a relative reduction of 26% of ankle radiographies was recorded in the intervention hospital without any missed fractures or patient discontent.

Another difference between the study population of the Ottawa Ankle Rules and our study is the pre-test probability. Ankle fractures occurred in around 14% of the patients with ankle injury whereas 53% of our patients had sustained a wrist fracture. This issue was also raised by colleagues van der Brand et al., who concluded that the high percentage of patients that had sustained a fracture warrants radiography in all patients with wrist trauma. We have to agree that the low specificity of the Amsterdam Wrist Rules is somewhat disappointing. However, we feel that referring every patient for radiography would be rash and not appropriate in light of the ever-rising health care costs. Moreover, although specificity of the Amsterdam Wrist Rules was low at external validation, it is better than the current practice to refer nearly all patients for radiography. Furthermore, while a 10% reduction in X-rays may seem small, on a national level it corresponds to thousands of X-rays annually.

We decided to derive a second decision rule dedicated to the most common wrist fracture: a distal radius fracture. The performance of this model was better and therefore we recommend its use in patients who are only suspected of a distal radius fracture. We are currently also working on deriving a clinical decision rule dedicated to detecting scaphoid fractures.

To determine the actual effect of the Amsterdam Wrist Rules in clinical practice we have recently started the implementation study and currently enrolled over a 100 patients. In this study, we will evaluate the reduction in radiographs requested, costs, ED waiting times, missed fractures, patient satisfaction and clinical sensitivity to physicians. To simplify application of the Amsterdam Wrist Rules, the formula to predict the probability of a fracture (Box 2) will be made available in a smartphone application (Fig. 2). Upon entering the clinical variables, the application will calculate the probability of fracture and give a recommendation (X-ray yes/no). A secondary implementation study is scheduled to take place in general practitioner’s offices. Implementation in this more general setting, where X-ray apparatuses are not readily available, might result in a higher diagnostic yield and even more cost savings.

This study has several limitations. According to methodological standards for the development of clinical decision rules in the Emergency Department, the reliability of predictor variables should be tested by determining the intraobserver and interobserver agreement. However, we considered it unethical to subject patients with a painful wrist to two comprehensive physical examinations. Therefore we were unable to assess the consistency of the candidate predictors.
CONCLUSION
The Amsterdam Wrist Rules is a clinical prediction rule with a high sensitivity and negative predictive value for fractures of the wrist. The Amsterdam Wrist Rules can provide physicians in the Emergency Department with a useful screening tool to select patients with acute wrist trauma for radiography.

Figure 2. A screenshot of the smartphone application that will be used during the implementation study. After entering the clinical findings, the application will calculate the probability of a distal radius fracture using the formula depicted in Box 1. If the probability of a distal radius fracture is <4%, the Amsterdam Wrist Rules application will recommend no radiography. The application was built by ApplicationBuilders.

Ideally, the reference standard for this study was the presence of a distal radius fracture on Multi Slice Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans. However, considering the number of participants this was both unethical and not feasible. Therefore, the outcome used for the analysis was the radiographic diagnosis made by the attending independent skeletal radiologist based on the available radiographs at presentation. Consequently, this approach has resulted in a clinical decision rule that does not detect injuries that are not diagnosed on conventional radiography.
REFERENCES


CHAPTER 3

A CLINICAL DECISION RULE FOR THE USE OF PLAIN RADIOGRAPHY IN CHILDREN AFTER ACUTE WRIST INJURY: DEVELOPMENT AND EXTERNAL VALIDATION OF THE AMSTERDAM PEDIATRIC WRIST RULES

M.M.J. Walenkamp*
A. Slaar*
A. Bentohami
M. Maas
R.R. van Rijn
E.W. Steyerberg
L.C. Jager
N.L. Sosef
R. van Velde
J.M. Uftee
J.C. Goslings
N.W.L. Schep
* Contributed equally

INTRODUCTION
In children, wrist trauma is one of the most common reasons for visiting the emergency department. A fracture of the wrist accounts for approximately 25% to 36% of all pediatric fractures. The most common diagnosed type of injury following wrist trauma is a fracture of the distal forearm. Occurrence of carpal fractures is low, varying from 1% to 3% in children with a wrist fracture.

During the last 4 decades, an increase of distal forearm fractures in children was reported. Due to the increase in incidences, health care costs for pediatric forearm fractures in the United States currently exceed $2 billion per year. An important cause for this rise in healthcare costs is the increase in the number of radiographs requested.

Unlike ankle and cervical spine injury, no guidelines are available that indicate when children with wrist trauma require radiography. Therefore, radiographic imaging in children following acute wrist trauma is often performed routinely in most hospitals. However, in one study only 51% of radiograph studies performed in children after wrist trauma demonstrated a fracture.

Because of this routine referral for radiography, unnecessary costs are incurred, waiting time is extended and radiation exposure is increased.

The goal of this study was twofold: 1) to derive a clinical decision tool, and 2) to externally validate a clinical decision tool that physicians can use to decide whether referral for radiography in children with acute wrist trauma is required and consequently whether this would lead to a reduction in the number of radiographs requested.

MATERIALS AND METHODS
Design and setting
This study was part of a combined study in which the adult population was analysed separately from the pediatric population. The study protocol of the adult patient group has previously been published. In the pediatric population, we applied practically the same protocol. The results are addressed in this article. We performed a multicenter prospective study from April 6, 2011, to April 15, 2014, in four national hospitals - one university hospital and three non-university teaching hospitals. The children included in the university hospital formed the development cohort. The children included in the three other hospitals formed the validation cohort. We did not expect a difference in referral patterns among hospitals since the university hospital also functions as a local referral center for general practitioners.

The study consisted of three components: 1) to prospectively define a clinical decision tool, 2) to externally validate this clinical decision tool and (3) to define a clinical decision tool.

ABSTRACT
Background
In most hospitals, children with acute wrist trauma are routinely referred for radiography.

Objective
To develop and validate a clinical decision rule to decide whether radiography in children with wrist trauma is required.

Materials and methods
We prospectively developed and validated a clinical decision rule in two study populations. All children who presented in the emergency department of four hospitals with pain following wrist trauma were included and evaluated for 18 clinical variables. The outcome was a wrist fracture diagnosed by plain radiography.

Results
Included in the study were 787 children. The prediction model consisted of six variables: age, swelling of the distal radius, visible deformation, distal radius tender to palpation, anatomical snuffbox tender to palpation, and painful or abnormal supination. The model showed an area under the receiver operator characteristics curve of 0.79 (95% CI: 0.76 - 0.83). The sensitivity and specificity were 95.9% and 37.3%, respectively. The use of this model would have resulted in a 22% absolute reduction of radiographic examinations. In a validation study, 7/170 fractures (4.1%, 95% CI: 1.7% - 8.3%) would have been missed using the decision model.

Conclusion
The decision model may be a valuable tool to decide whether radiography in children after wrist trauma is required.
PART 1

The Medical Ethical Review Committees of all participating hospitals approved the study (Dutch Trial Registry number NTR2651) and waived informed consent.

Participants
All children younger than 18 years old who presented in the emergency department in one of the four participating hospitals with pain following wrist trauma were included. Children younger than 3 years old were excluded, as it is difficult to obtain an objective physical examination. We also excluded patients whose injury occurred more than 72 h previously or patients who had sustained multiple injuries (Injury Severity Score ≥16). Patients whose radiographs were requested previous to their visit to the emergency department (e.g., by their general practitioner) were excluded as well.22 Patients with pre-existing musculoskeletal disease, coagulopathy or developmental delay and patients with previous history of surgery or recent (<3 months) injury of the affected wrist were also excluded. Physicians were instructed not to include patients if they were aware of the outcome of the radiograph performed before physical examination. Since it was not mandatory to obtain radiography in all children following wrist trauma only 12 out of 897 patients (1.3%) did not undergo radiographic imaging. These children were also not included in the study.

Definitions
Wrist trauma was defined as any high or low energetic accident involving the wrist. Corresponding to the protocol of the adult study population, wrist injury was defined as injury to the proximal segment of the hand, including the carpal bones and the associated soft parts, and the distal one third of the ulnar and radial bone.22 Since the incidence of carpal fractures in children is low and since scaphoid fractures are frequently occult on plain radiography, carpal fractures were not taken into account.28-30 A fracture was defined as a disruption of one or more of the cortices of the bone. Buckle fractures or bowing fractures were also recorded as a true fracture, as were fissures and avulsions. A combined fracture of the ulna and radius, known as an antebrachii fracture, was recorded as one fracture.

Data collection and variables
We used standardized case record forms to prospectively collect our data in all four participating hospitals. The case record form consisted of 18 clinical variables, including patient characteristics, physical examination and functional testing (Appendix 1). All variables were selected after evaluation of previous studies and consensus agreement of clinical experts.24-26 All variables on the case record form, in exception of grip strength, were dichotomous (yes/no). The attending physician included eligible children after physical examination. The case record forms were filled in after physical examination. The assessors were all physicians and included consultant emergency medicine physicians, general practice registrars, and specialist registrars of the departments of (trauma) surgery, emergency medicine or orthopedics. All physicians received regular instructions and training before recruiting children to the study. Additionally, informative pocket cards and posters were provided. In order not to disrupt common practice, referral for radiography was left to the discretion of the attending physician.

Test methods
The outcome was the presence or absence of a radiologically detected fracture of the distal forearm (radius, ulna or both) diagnosed by the attending radiologist. A third-year resident in radiology (A.S.) and a clinical physician (M.M.J.W.) revised all radiographic imaging and radiologic reports. Any discrepancies in diagnosis were resolved in consensus reading. Where necessary, a pediatric radiologist (R.R.vR.) with more than 10 years of experience was consulted.

Regular clinical information was available for the radiologist, but the content of the case record form was not provided. Conforming to standard clinical practice, plain radiographic imaging consisted of at least one posterior-anterior and one lateral view and any further conventional imaging available (e.g., scaphoid series).

Sample size
A common rule of thumb to determine the sample size of the development of a prediction model is 10 events per variable.27 Since our case record form (CRF) consisted of 18 variables, the inclusion of a minimum of 180 children who sustained a fracture was required. External validation required at least 100 events (fractures) and 100 non-events.27

Statistical analysis
For efficient statistical analysis, we used imputation techniques to input the missing values (aregimpute function from the Hmisc library, R, version 3.0.1).38-30 For each missing variable, this algorithm initializes the values from a random sample from the non-missing values. Using this data, it then fits a flexible model that predicts the missing target variable while finding its optimum transformation. Each missing value is imputed with the observed value whose predicted transformed value is closest to the predicted transformed value of the missing variable. We considered an imputation model that included all potential predictor variables and the outcome. The first set of imputations was used for the analyses.

Model development and internal validation
We derived a clinical prediction model from data on patients enrolled in the university hospital.

We fitted a logistic regression model with 18 predictors, which was reduced using a stepwise backward elimination process based on a P-value of 0.15.31 We used bootstrapping to estimate the internal validity (500 replications). Bootstrapping mimics the process of sampling from the underlying population and is a method to quantify the optimism of a prediction model: the difference between performance in the bootstrap sample and performance in
the original sample.22 A shrinkage factor, also obtained by bootstrap validation, was used for multiplication of the regression coefficients.

External model validation and final model development
To assess general applicability, we validated the model in the cohort that included all children enrolled in the three other participating hospitals. For each patient in the three other hospitals (the validation cohort), the probability of a distal forearm fracture was calculated using the prediction model. To estimate the ability of the model to discriminate between patients with and without a fracture, we calculated the area under the receiver operating characteristics curve (AUC). An AUC of 0.5 means that the test is not predictive. An AUC of 1.0 means that the predictive value is very high. The agreement between observed outcomes and predictions (the calibration of the model) was determined by plotting the predicted probability of a fracture and the observed frequency of a fracture. A slope of 1 is ideal for the observed outcomes versus predicted risk.23

In order to provide a recommendation (whether to perform radiography or not), we established a cutoff value for a predicted probability. Previous literature used a threshold varying from 20% to 25% for the use of radiography in children and adolescents for detecting upper extremity injury.34 Therefore, we used a threshold probability of 23% (the mean of 20-25%), beyond which the Amsterdam Pediatric Wrist Rules recommend radiographic imaging for all children with wrist trauma and below which none would undergo radiographic imaging.

As a final step, the model was fitted on data from both cohorts combined to obtain the final estimates of the regression coefficients.

RESULTS
Participants
A consecutive series of 897 children with wrist injury was recruited in the four participating hospitals. We excluded 110 patients (12.2%) for various reasons (Fig. 1). In 364 children (46.3%), a fracture of the distal forearm was diagnosed (Table 1). In the development cohort (the university hospital), we included 408 patients. The mean age was 12 years (standard deviation: 3.0); more than half of them were male (66.7%). A fracture of the distal forearm was diagnosed in 194 patients (47.5%). In the validation cohort (three teaching hospitals), 379 patients were included. There were no significant differences between the cohorts (Table 1). The mean age in the validation cohort was 11 years (standard deviation: 2.9) and 53% were male. In 170 patients (44.9%), a fracture of the distal forearm was diagnosed. The observers had several months up to 21 years of experience in the emergency department (median: 3.5, interquartile range: 2 - 11).

Table 1. Clinical and Demographic Characteristics of Development Cohort, Validation Cohort and Total Cohort

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Development Cohort (n = 408)</th>
<th>Validation Cohort (n = 379)</th>
<th>Total4 (n = 787)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (SD)</td>
<td>12 (3)</td>
<td>11 (2.9)</td>
<td>11 (2.9)</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>272 (66.7)</td>
<td>201 (53.0)</td>
<td>473 (60.1)</td>
</tr>
<tr>
<td>Patients with a fracture of the distal forearm, No. (%)</td>
<td>194 (47.5)</td>
<td>170 (44.9)</td>
<td>364 (46.3)</td>
</tr>
<tr>
<td>Fractures</td>
<td>N=207</td>
<td>N=180</td>
<td>N=387</td>
</tr>
<tr>
<td>Distal radius</td>
<td>165 (79.8)</td>
<td>155 (86.1)</td>
<td>320 (82.7)</td>
</tr>
<tr>
<td>Distal ulna</td>
<td>2 (0.97)</td>
<td>0 (0.0)</td>
<td>2 (0.52)</td>
</tr>
<tr>
<td>Antebrachii</td>
<td>27 (13.0)</td>
<td>15 (8.3)</td>
<td>42 (10.9)</td>
</tr>
<tr>
<td>Other5</td>
<td>13 (6.3)</td>
<td>10 (5.6)</td>
<td>23 (5.9)</td>
</tr>
</tbody>
</table>

Abbreviations: SD, standard deviation
a. Data from the academic hospital, the initial development cohort
b. Data from the other three hospitals, the validation cohort
c. Patients included in the analysis (data from all four hospitals), the final development cohort
d. Fractures of the carpal bones and metacarpal bones.

Missing values and imputation
In both the development and validation cohorts, 83% of the cases were complete. Missing values comprised less than 5% for all variables with the exception of prehensile grip strength, which was not completed in 12.5% of the patients (Appendix 2).
Model development
The clinical prediction model derived included six variables: age, swelling of the distal radius, visible deformation, distal radius tender to palpation, anatomical snuffbox tender to palpation and painful supination (Table 2). The AUC of the model was 0.81 (95% CI: 0.76 - 0.85); after correction for optimism by bootstrapping the AUC was 0.77 (95% CI: 0.73 - 0.82). We evaluated lack of fit of the model by relaxing assumptions of linearity and additivity of predictor effects. We hereto examined non-linear transformations of the variable age, including the square term and the log transformations. We also examined interaction terms between swelling of the distal radius and painful palpation, swelling of the distal radius and visible deformation and painful palpation (Appendix 3). We found no evidence of non-linearity of the effects of age and none of the interactions terms was statistically significant.

Table 2. Contribution of variables as predictors of the presence of a distal forearm fracture in the clinical decision rule

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient (95% CI)</th>
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<tbody>
<tr>
<td>Age</td>
<td>-0.14 (-0.22 - -0.061)</td>
</tr>
<tr>
<td>Swelling of distal radius present</td>
<td>1.18 (0.706 - 1.65)</td>
</tr>
<tr>
<td>Visible deformation</td>
<td>1.58 (0.412 - 2.745)</td>
</tr>
<tr>
<td>Bone tenderness distal radius</td>
<td>1.14 (0.278 - 2.004)</td>
</tr>
<tr>
<td>Bone tenderness of anatomical snuff box</td>
<td>-1.75 (-2.37 - -1.136)</td>
</tr>
<tr>
<td>Supination painful</td>
<td>0.52 (0.006 - 1.028)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, Confidence Interval

External model validation and test characteristics
The external performance of the model was assessed in the 379 patients in the validation cohort. The AUC of the external validation was 0.79 (95% CI: 0.76 - 0.82) and the calibration slope 1.07 (95% CI: 0.82 - 1.33). After applying a threshold of 23%, the sensitivity and specificity of the Amsterdam Pediatric Wrist Rules for detecting fractures of the distal forearm in the validation cohort were respectively 95.9% (95% CI: 91.7% - 98.0%) and 37.3% (95% CI: 31.0% - 44.1%) (Table 3). The Amsterdam Pediatric Wrist Rules led to an absolute reduction of 22% of requested radiographs.

<table>
<thead>
<tr>
<th>Test characteristics and performance of the Amsterdam Paediatric Wrist Rules in the external validation cohort (95% CI)</th>
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<tbody>
<tr>
<td>Patients with fracture</td>
</tr>
<tr>
<td>Amsterdam Paediatric Wrist Rules indicate radiograph</td>
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<tr>
<td>Amsterdam Paediatric Wrist Rules indicate no radiograph</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
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<td>Specificity (%)</td>
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</table>

Abbreviations: CI, Confidence Interval

*Tested on data from the other three hospitals (the validation cohort), cut-off point for radiograph yes or no was a predicted probability of 23%.

After applying the Amsterdam Pediatric Wrist Rules, 7/170 fractures (4.1%, 95% CI: 1.7% - 8.3%) were missed in the external validation cohort (Appendix 4). They consisted of six buckle fractures of the distal radius and one non-displaced distal radius fracture with a buckle component. All these missed fractures were found in boys ages 10-15 years old.

DISCUSSION
Our derived prediction model, the Amsterdam Pediatric Wrist Rules, is a valuable tool for physicians in the emergency department in deciding if referral for radiography is required in children after acute wrist trauma. We showed that a combination of six clinical variables was able to discriminate between children with and without a fracture with an AUC of 0.79. By applying the Amsterdam Pediatric Wrist Rules, the number of requested radiographs would have been reduced by 22%. The incidence of children with a fracture in the Netherlands in 2009 was 4.465 per 100,000 children from 5-19 year old. Since approximately 50% of the children with wrist injury are diagnosed with a fracture, this resulted in 8,930 children with wrist injury per 100,000 children in 2009. By applying the Amsterdam Pediatric Wrist Rules, radiographic imaging could have been prevented in almost 2,000 children per 100,000 (22% reduction). At a price of 48 Euro/$50 per radiograph, the possible reduction of health care cost will be 96.000 euro per 100,000 children annually. This amount is probably an underestimation because the provided incidence included children ages 5-19 years old and the population that could benefit from the Amsterdam Pediatric Wrist Rules is 3-18 years old. As was the case following the implementation study of the Ottawa Ankle Rules, a reduction in waiting time may be expected after applying the Amsterdam Pediatric Wrist Rules. Additionally, we assume that applying the Amsterdam Pediatric Wrist Rules will generate a reduction in radiation exposure. Although radiation exposure of plain radiography of the wrist is low (effective dose: 0.16 μSv),
it is important to prevent unnecessary radiation exposure according to the ALARA principle (As Low As Reasonably Achievable), especially in children. Obtaining a US for detecting wrist fractures in children might also reduce radiation exposure; however, only a few studies have been performed, all with small study groups. Moreover, it is unclear if the use of sonography leads to a reduction in health care costs.

After applying the Amsterdam Pediatric Wrist Rules in seven patients (4.3%), a fracture would have been missed. The missed fractures consisted of six buckle fractures of the distal radius and one non-displaced distal radius fracture with a buckle component without displacement. According to literature and an expert panel consisting of two pediatric surgeons, one trauma surgeon and one orthopedic surgeon, none of these fractures needed closed reduction or operative treatment, but would have been treated with a splint. This type of treatment is identical to treatment for children without a fracture who are diagnosed with a contusion or sprain of the wrist. We also expect that in children in a lot of pain, physicians are more likely to give a cast for pain regulation. Therefore, we consider that the treatment and prognosis would not have been influenced by a missed or delayed diagnosis. Moreover, in children with stable buckle fractures, it is known that subacute treatment does no lead to adverse clinical outcomes. However, a follow-up evaluation by telephone, or the advice to contact the hospital if symptoms remain after 1 week, can be considered for patients who did not initially require a radiograph, according to the Amsterdam Pediatric Wrist Rules.

Because physicians were not obligated to refer patients for radiography, in 12 patients no radiograph of the wrist was obtained. These patients were not included in the study, but none of these 12 children returned to the hospital for persisting complaints in the following 4 weeks.

A limitation of the Amsterdam Pediatric Wrist Rules is its specificity of 37.3%. We could have generated a higher specificity by using another threshold, but this would have led to a decrease in the sensitivity and thus an increase of missed fractures. In accordance with Maguire et al., we judged it would not be applicable since it misses >5% of fractures in children. Since we aimed to reduce the number of requested wrist radiographs, a threshold compromise between missed fractures and reduction of radiographs was chosen. According to the literature, we determined that about three avoided radiographs outweigh one missed fracture and therefore we used a threshold value of 23.0% (1/25) for the predicted probability. The sensitivity prediction rule was 96%. Adding anamnestic variables to the model could possibly strengthen our prediction rule and result in a higher sensitivity. However, since children are not always capable or trustworthy of telling what type of trauma occurred, we did not take clinical history variables into account.

Another limitation is that some patients with wrist pain were missed due to crowding in the emergency department. This might have introduced a selection bias. However, we expect that the reasons for missing patients were mostly related to emergency department crowding and not to patient characteristic. Therefore, we consider this bias minimal.

We might have introduced another type of selection bias since this study took place in only university hospitals and non-university teaching hospitals, and not in a non-teaching hospital. We assume that in non-teaching hospitals the referral for radiography is routinely done by triage nurses, while in (university) teaching hospitals the referral for radiography is usually done by physicians. Upcoming studies should reveal if the Amsterdam Pediatric Wrist Rules could also be applied by triage nurses. Nevertheless, we expect that the clinical signs and the incidence of wrist fractures in children in non-teaching hospitals do not significantly differ from (university) teaching hospitals and therefore we do not expect that this has significantly influenced our results.

The final limitation of our study is that in 12.5% of the CRFs the valuable prehensile grip strength was not completed. In several cases, the physician wrote that this was because the patient was in too much pain to perform this test. However, the difference between patients with and without prehensile grip strength as a missing variable was small and therefore it is not likely that our results were influenced by the imputation of this variable.

Three preceding studies have considered the diagnostic value of physical findings in children with acute wrist trauma. In 1986, Rivara et al. retrospectively studied 116 children and found gross deformity and point tenderness to be the best predictors for a fracture of the upper extremity, with a sensitivity of 81% and a specificity of 82%. The sample size and, more importantly, the sensitivity of this study were much lower than in our study results. In 2000, Pershad et al. performed a prospective study in 48 children and found that a 20% or more reduction of grip strength and distal radius point tenderness were predictive values for the presence of a wrist fracture. These clinical predictors had a sensitivity of 79% and a specificity of 63%. However, this study was also limited by a small sample size.

A study performed in 2006 in 227 children showed that radial tenderness, focal swelling and abnormal supination/pronation were associated with wrist fractures in children. These predictive variables showed a sensitivity of 99.1% and specificity of 24%. The predictive variables and sensitivity of these variables were almost similar, but our specificity was higher and thus the potential reduction of the amount of requested radiographs in our study is higher (22% vs. 13%).

None of the decision rules is externally validated, which is recommended. The Amsterdam Pediatric Wrist Rules did undergo external validation in a study population with different type of hospitals and physicians. An upcoming implementation study will evaluate the impact of the Amsterdam Pediatric Wrist Rules.
Wrist Rules on the number of radiographs, emergency department waiting times and health care costs. The formula to predict the probability of a fracture (Table 4) will be made available in a smartphone application (Fig. 2). This application will give physicians a recommendation if radiography is recommended according to the probability of a distal forearm fracture.

Table 4. Linear predictors and probability

<table>
<thead>
<tr>
<th>Linear predictor</th>
<th>Coefficients</th>
<th>Linear predictor</th>
<th>Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.185* age (per year) + 1.144 * (if swelling of distal radius present) + 1.56 * (if visible deformity present) + 1.183 * (if bone tenderness of distal radius present) + -1.424 * (if bone tenderness of anatomical snuff box present) + 0.356 * (if supination painful) + 0.466</td>
<td></td>
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</tbody>
</table>

Probability of a fracture based on final model

\[
\frac{1}{1+\exp(-\text{Linear Predictor})}
\]

*Coefficients were derived from a fit of the model on both cohorts combined (n=787)

All individual parameters add to the probability of a fracture.

CONCLUSION

The derived clinical decision model (Amsterdam Pediatric Wrist Rules) may be used as a tool for physicians in the emergency department in deciding if referral for radiography in children after acute wrist trauma is necessary. Applying the model, 7/170 fractures (4.1%, 95% CI: 1.7% - 8.3%) were missed in an external validation study.

Fig. 1 Flowchart demonstrates patient selection and outcomes

Excluded n=110 (12.2%)
- No X-ray: n=12 (1.3%)
- CRF filled in by nurse/med student: n=58 (6.4%)
- X-ray requested previously to assessment: n=12 (1.3%)
- Insufficient details to identify patient: n=14 (1.6%)
- Injury > 72h previously: n=4 (0.4%)
- Other: n=10 (1.1%)

Included in analysis n=787 (87.6%)

Eligible patients n = 897

Distal forearm fracture n=364 (46.3%)

No distal forearm fracture n=423 (53.7%)
REFERENCES


32. Steyerberg E. Overfitting and optimism in prediction models, a practical approach to development, validation and updating. New York: Springer; 2009.


PART 2

TREATMENT
CHAPTER 4

THE UNSTABLE DISTAL RADIUS FRACTURE: HOW DO WE DEFINE IT?

A SYSTEMATIC REVIEW

M.M.J. Walenkamp
L.M. Vos
S.D. Strackee
J.C. Goslings
N.W.L. Schep

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THE UNSTABLE DISTAL RADIUS FRACTURE

INTRODUCTION
Unstable distal radius fractures are the subject of numerous studies. However, a prerequisite for implementing the findings of these studies is the generalizability of the results. Generalizability is the degree to which the findings in the study population can be applied to another, future population of patients. Studies that focus on the treatment of unstable distal radius fractures should therefore clearly describe what their authors regard as an unstable fracture.

However, instability is in the eye of the beholder and therefore a situation that is difficult to capture in a definition. It is often quoted that a fracture of the distal radius is considered to be unstable if it is unable to resist displacement once it has been anatomically reduced. There are various radiological and clinical criteria that would predispose distal radius fractures to instability, but it remains a subjective assessment. Nevertheless, clinical studies require established inclusion criteria and consequently a clear definition of an unstable distal radius fracture.

The absence of this definition or variability in definitions hampers apparent comparison of studies. Standardization or agreement on a definition for an unstable distal radius fracture would facilitate combining study outcomes in meta-analyses and contribute to a higher level of evidence. Therefore, we sought to examine (1) in what percentage of studies involving patients with unstable distal radius fractures the authors defined what they considered an unstable distal radius fracture; (2) what the most commonly mentioned descriptions of an unstable distal radius fracture were; and (3) whether there was one preferred definition to recommend to future authors.

METHODS
The present study was reported according to the PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses). A review protocol was drafted and registered on PROSPERO with number CRD42014011840. Two reviewers (MMJW) independently conducted a search of the Medline, EMBASE and Cochrane Central Register of Controlled trials databases on November 24, 2013 for any type of study in which the term unstable distal radius fracture occurred (see appendix for the detailed search strings). In order not to miss recently published literature, the use of Medical Subject Heading (MESH) terms was avoided. The complete search strategy is depicted in the supplementary files. The bibliographies of all articles included were reviewed for additional articles of interest.

ABSTRACT
Background
Unstable distal radius fractures are a popular research subject. However, to appreciate the findings of studies that enrolled patients with unstable distal radius fractures, it should be clear how the authors defined an unstable distal radius fracture.

Questions
In what percentage of studies involving patients with unstable distal radius fractures did the authors define unstable distal radius fracture? What are the most common descriptions of an unstable distal radius fracture? And is there one preferred evidence-based definition for future authors?

Methods
A systematic search of literature was performed to identify any type of study with the term unstable distal radius fracture. We assessed whether a definition was provided and determined the level of evidence for the most common definitions.

Results
The search yielded 2489 citations of which 479 were included. In 149 studies, it was explicitly stated that patients with unstable distal radius fractures were enrolled. In 54% (81/149) of these studies, the authors defined an unstable distal radius fracture. Overall, we found 143 different definitions. The seven most common definitions were: displacement following adequate reduction; Lafontaine’s definition; irreducibility; an AO type C2 fracture; a volarly displaced fracture; Poigenfürst’s criteria and Cooney’s criteria. Only Lafontaine’s definition originated from a clinical study (level IIIb).

Conclusion
In only half of the studies involving patients with an unstable distal radius fracture, did the authors define what they considered an unstable distal radius fracture. None of the definitions stood out as the preferred choice. A general consensus definition could help to standardize future research.

Data Sources
Two reviewers (MMJW) and (LMV) independently conducted a search of the Medline, EMBASE and Cochrane Central Register of Controlled trials databases on November 24, 2013 for any type of study in which the term unstable distal radius fracture occurred (see appendix for the detailed search strings). In order not to miss recently published literature, the use of Medical Subject Heading (MESH) terms was avoided. The complete search strategy is depicted in the supplementary files. The bibliographies of all articles included were reviewed for additional articles of interest.

Eligibility Criteria and Study Selection
Two reviewers independently reviewed all titles and abstracts for relevance. If title and ab-
stract did not provide sufficient information, full text was examined. All articles with the term unstable or instability in combination with distal radius/radial fracture were included. Publication language was restricted to English, German or Dutch. Studies were excluded if (1) they regarded paediatric patients; (2) they used the term unstable or instability in relation with carpal instability or the Distal Radioulnar Joint (DRUJ); (3) it was not clear to what the term unstable or instability referred; and (4) they regarded conference abstracts. Disagreement was resolved by discussion between the two reviewers.

Data Extraction
Two reviewers extracted data independently from eligible studies using a data collection form. Items included general information (authors, year, journal), study type and number of subjects. Additionally, they determined whether unstable distal radius fracture was used as an inclusion criterion. Subsequently, the reviewers evaluated whether a clear definition of fracture instability was described in the methods section or elsewhere in the paper. Definitions were documented word for word.

We regarded the following description as a definition: 1) radiologic criteria or patients characteristics; 2) fracture types; 3) fracture classifications. We did not consider statements that denoted a possibility of fracture instability a definition (for example: intra-articular fractures are sometimes unstable).

Data Synthesis and Quality Assessment
The primary outcome was the percentage of clinical studies involving patients with unstable distal radius fractures in which the authors defined what they considered an unstable distal radius fracture. We regarded randomised controlled trials; cohort; case-control and case series as clinical studies. Secondary outcomes included the most frequently mentioned description of an unstable distal radius fracture in any type of study (including systematic reviews, current concepts and cadaver studies) and the available evidence for these descriptions or definitions.

If applicable, we procured the full text manuscripts of the study from which each definition or description of an unstable distal radius fracture originated. Subsequently, we evaluated the overall quality of the study and determined if the primary research question was to define the term unstable distal radius fracture. If this was the case, we determined the level of evidence using the Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009).4

RESULTS
The initial search yielded 2489 citations of which 479 studies were included in this review (Figure 1, Table 1).
Table 1. Type of studies included (N=479)

<table>
<thead>
<tr>
<th>Type of study</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Meta-analysis</td>
<td>5 (1.0)</td>
</tr>
<tr>
<td>Systematic Review</td>
<td>10 (2.1)</td>
</tr>
<tr>
<td>Randomised controlled trial</td>
<td>45 (9.4)</td>
</tr>
<tr>
<td>Cohort study</td>
<td>224 (46.8)</td>
</tr>
<tr>
<td>Case-control</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Case series</td>
<td>33 (6.9)</td>
</tr>
<tr>
<td>Case report</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td>Surgical technique</td>
<td>23 (4.8)</td>
</tr>
<tr>
<td>Cadaver study</td>
<td>36 (7.5)</td>
</tr>
<tr>
<td>Biomechanical study</td>
<td>9 (1.9)</td>
</tr>
<tr>
<td>Current concepts/ nonsystematic review</td>
<td>73 (15.2)</td>
</tr>
<tr>
<td>Letter to the editor</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td>Editorial</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Othera</td>
<td>4 (0.8)</td>
</tr>
</tbody>
</table>

a. guideline (N=1), decision analytic model (N=1), translation (N=1) and interobserver study (N=1)

In what percentage of clinical studies involving patients with unstable distal radius fractures did the authors define the term?
There were 254 clinical studies and in 149 studies (59%) the authors explicitly stated that they enrolled patients with an unstable distal radius fracture. In 54% (81/149) of these studies, the authors defined what they considered an unstable distal radius fracture.

What were the most commonly mentioned descriptions of an unstable distal radius fracture in any type of study?
Overall, 213 of the 479 studies (45%) provided one or more descriptions of an unstable distal radius fracture. In total, we found 143 different descriptions. There were seven descriptions that were used most frequently to define an unstable distal radius fracture. The most commonly mentioned description was a situation in which displacement or loss of position following anatomical closed reduction had occurred (20%, 42/213, Table 2). The second most common description that was mentioned was the definition proposed by Lafontaine et al. (9%, 20/213). According to this definition, a distal radius fracture is unstable if three or more of the following factors are present: dorsal angulation exceeding 20°; dorsal comminution; intra-articular radio-carpal fracture; associated ulnar fracture and age over 60 years.

Table 2. The most common descriptions or definitions of an unstable distal radius fracture

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Definition</th>
<th>N (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Loss of position following adequate reduction</td>
<td>42 (19.7)</td>
<td>294</td>
</tr>
<tr>
<td>2</td>
<td>Lafontaine</td>
<td>20 (9.4)</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>Volarly displaced fracture (Smith’s or reversed Barton)</td>
<td>12 (5.6)</td>
<td>379</td>
</tr>
<tr>
<td>4</td>
<td>Irreducible fracture</td>
<td>11 (5.2)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>AO type C2</td>
<td>10 (4.7)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Poigenfurt</td>
<td>9 (4.2)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Cooney</td>
<td>9 (4.2)</td>
<td></td>
</tr>
</tbody>
</table>

a. percentage of total studies with definition (N=213)

The third most common description was a volarly displaced fracture (Smith or volar Barton fracture) that was defined as an inherently unstable fracture in 6% of the studies. This was followed by an irreducible fracture in 5% (11/213) of the studies.

The most frequently used classification system to describe an unstable distal radius fracture was the AO classification (8%, 18/213). An AO type C2 was the fifth most commonly mentioned description used to define an unstable distal radius fracture (5%, 10/213).

In 4% (9/213) of the studies, the description according to Poigenfurt (radial-ulnar separation; the presence of dorsal comminution and an associated ulnar fracture) was used. An equal number of studies (4%, 9/213) mentioned the definition of an unstable distal radius fracture according to Cooney (severe comminution; intra-articular components and severe displacement defined as >20° dorsal angulation and > 10 mm of radial shortening).

All other type of descriptions were mentioned in only three studies (1%) or less.

Is there one preferred definition to recommend to future authors?
Where possible, we verified the origin of the most common definitions and procured the full text manuscripts of the original studies. Four definitions did not originate from any study but were stated as expert opinions (loss of position; volar displacement; irreducibility and AO type C2 fractures). Poigenfuerst’s definition was proposed in 1980 in a narrative article as an expert opinion. According to Poigenfurt, the presence of an associated ulnar styloid fracture resulting in a rupture of the ulnar ligaments from the carpal bones, would permit further shift of the distal fracture fragment and therefore constitute fracture instability.
Cooney’s definition was first used in 1979 when Cooney et al. performed a cohort study in which 130 patients were treated with an external fixator. They included patients with an unstable distal radius fracture and defined unstable as: “the inability to maintain satisfactory fracture alignment at the time of reduction or in the presence of severe comminution; intra-articular components and severe displacement defined as >20° dorsal angulation and > 10 mm of radial shortening”. No reference or explanation as to the choice of these criteria was provided and therefore this definition is an expert opinion (Table 3).

Table 3. Level of evidence for the most commonly used definitions

<table>
<thead>
<tr>
<th>Year</th>
<th>Definition</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>radial shortening of 10 mm; dorsal angulation &gt; 20° and/or marked comminution combined with intra-articular fragments</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1980</td>
<td>reversed Barton fracture</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1980</td>
<td>radio-ulnar separation; the presence of dorsal comminution; associated ulna fracture resulting in ulnar desinsertion</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1990</td>
<td>complete articular fractures; simple articular fracture; multi-fragmentary metaphyseal component</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1989</td>
<td>At least three of the following criteria: dorsal angulation &gt; 20°; dorsal comminution; intra-articular radiocarpal fracture; associated ulnar fracture; age &gt; 60 years</td>
<td>III</td>
</tr>
<tr>
<td>1979</td>
<td>Smith fracture; Reversed Barton fracture</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1979</td>
<td>NA; NA</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1979</td>
<td>NA; NA</td>
<td>Expert opinion (V)</td>
</tr>
<tr>
<td>1979</td>
<td>NA; NA</td>
<td>Expert opinion (V)</td>
</tr>
</tbody>
</table>

a. The levels of evidence for definition of unstable distal radius fracture based in original study on the Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009). Abbreviations: NA, not applicable

Only the Lafontaine’s definition originated from a clinical study describing a retrospective cohort of 157 cases. Lafontaine et al. performed a univariate analysis for each risk factor and found a significant influence of each factor on the radiological outcome. They concluded that only patients with three or less instability factors had a satisfactory radiological outcome. Accordingly, Lafontaine considered a distal radius fracture unstable if three or more of the following factors were present: dorsal angulation exceeding 20°; dorsal comminution; intra-articular radiocarpal fracture; associated ulnar fracture and age over 60 years. Based on the Oxford Centre for Evidence-based Medicine Levels of Evidence, this study is a level 3b (non-consecutive retrospective cohort study without consistently applied reference standards).

DISCUSSION

In clinical studies, specification of the inclusion criteria for enrolment is paramount. These criteria are used to define the study population and therefore reflect if the findings in this population are generalizable to other future patients. Some criteria however, such as an unstable distal radius fracture, can be hard to capture in a definition.

The term unstable distal radius fracture describes a situation in which the distal radius fracture has an intrinsic potential for secondary displacement. It is an assessment of the probability that a fracture will lose its position and therefore it is highly subjective. However, regardless of its subjectivity, a standardized or universally accepted definition for an unstable distal radius fracture could have several benefits. It would increase awareness of the importance of specification of inclusion criteria among authors, help authors to write their study protocols and facilitate combining study outcomes in meta-analyses. Conversely, there might not exist a universal definition that all experts in the field agree upon. Moreover, defining what constitutes an unstable distal radius fracture could impact clinical practice and surgical decision-making. Nevertheless, for the sake of standardization in research we sought to examine (1) in what percentage of clinical studies involving patients with unstable distal radius fractures the authors defined what they considered an unstable distal radius fracture; (2) what the most commonly mentioned descriptions of an unstable distal radius fracture were in any type of study; and (3) whether any of these descriptions was the preferred definition that can recommend to future authors.

We found that in only 54% of the clinical studies that explicitly stated that they enrolled patients with an unstable distal radius fracture, did the authors define what they considered an unstable distal radius fracture.

Our search in any type of article resulted in 143 different descriptions of an unstable distal radius fracture. There were seven descriptions that were used most frequently to define an unstable distal radius fracture: (1) displacement of the fracture following anatomical reduction; (2) Lafontaine’s; (3) an irreducible fracture; (4) an AO type C2 fracture; (5) a fracture with volar dislocation; (6) Poigenfurst’s definition and; (7) Cooney’s definition.

The most obvious description was secondary displacement after adequate closed reduction. The occurrence of secondary displacement is what constitutes an unstable fracture and is a clear definition.
The second most common description of an unstable distal radius fracture was according to the definition from Lafontaine. It was used in 9% of the studies,11,32,34,47,99-112 of which six studies added radial shortening exceeding 5 mm to the definition.104,107-110 The definition originates from a French publication on a retrospective study of 167 cases.47 In this study the authors conclude that only patients with three or less instability predictors had a satisfactory radiological outcome. Since then, two studies have attempted to validate Lafontaine’s criteria.98,109 Of all five criteria, only age > 60 years was found to be predictive of fracture instability.106

All other definitions were expert opinions. A volarly displaced fracture for example is generally considered inherently unstable and primary operative treatment is regularly recommended.113,114 However, we found no studies that assessed fracture instability in volarly displaced fractures. The same is true for irreducibility that cannot be equalled to instability.115

Instability, or the inability of a fracture to resist displacement after closed reduction115, is often defined according to criteria regarding initial displacement such as dorsal angulation, shortening and the presence of dorsal comminution. The definition is in fact an assessment of the probability that a fracture will redisplace. Predictors of redisplacement have been studied extensively and several scoring systems to calculate the probability of instability based on initial presentation and injury films exist.48,98,116,117 The largest study to investigate predictors of instability was performed by Mackenney et al. who examined 1595 patients. They identified several significant risk factors for fracture instability with displaced fractures and found that age, the presence of any type of comminution and a positive ulnar variance compared to the uninjured radius were significant predictors of early (<2 weeks) instability.113 Other studies found that age >60 years; initial shortening and dorsal angulation exceeding 20° are significant predictors of redisplacement.32,82,117-120 Surprisingly, more than half the definitions were not based on any of these predictors.

This systematic review is limited by the quality of the articles included and the subjectivity of the reviewers. The exclusion of the literature not in English, Dutch or German also introduces a source of bias. Determining the level of evidence for a definition was a subjective endeavour. Most definitions did not originate from any study and were therefore not suited to establish any level of evidence for. We have attempted to reduce subjectivity as much as possible by discussing any doubts or disagreements between reviewers. Nevertheless, we have demonstrated that there is little evidence for definitions that are most frequently used.

CONCLUSION AND RECOMMENDATION

In only half of the studies that explicitly stated to have enrolled patients with an unstable distal radius fracture, did the authors define what they considered an unstable distal radius fracture. There is an enormous variety of different descriptions of an unstable distal radius fracture circulating in the literature. Unfortunately, none of the descriptions we found stands out as the preferred definition to be used in future studies. For the sake of generalizability, we would like to urge future authors to clearly describe what they regard as an unstable distal radius fracture. We propose that the definition of an unstable distal radius fracture includes the predictors that are known to increase the probability of displacement such as comminution, initial shortening and age > 60 years. Further attempts to arrive upon a universally accepted consensus definition could possibly help to standardize distal radius fracture research.
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PART 2

THE UNSTABLE DISTAL RADIUS FRACTURE


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CHAPTER 5

VARIATION IN THE SURGICAL TREATMENT RATES OF DISTAL RADIUS FRACTURES: WHAT YOU GET IS SURGEON AND HOSPITAL DEPENDENT

M.M.J. Walenkamp
M.A. Mulders
J.C. Goslings
G.P. Westert
N.W.L. Schep
ABSTRACT

Purpose
Variations in medical practice have already been documented for a number of elective procedures. Generally, this variation is warranted if it is attributable to patient-related factors and unwarranted if it is attributable to factors such as physician’s local beliefs and preferences. Because the evidence for the optimum treatment for patients with distal radius fractures remains inconclusive, we hypothesized that there would be a considerable variation in treatment. The aim of this study was to examine the variation in surgical treatment rates of patients with distal radius fractures across Dutch hospitals.

Methods
We obtained all reimbursement data for the treatment of distal radius fractures for 2012 and 2013 categorized by hospital. The surgical rate across hospitals was corrected for possible explanatory variables using linear regression analyses.

Results
We analyzed a total of 95,754 reimbursements. The operative rate ranged from 0% to 23%, with a mean of 9.6%. Hospital type, the percentage of females, the percentage of patients over 65, the mean age, average socioeconomic status and the total number of patients treated explained only 2.6% of the observed differences in the operative rate among hospitals in 2012 and 11.6% in 2013.

Conclusions
There is considerable and possibly unwarranted variation in the treatment of patients with distal radius fractures across the Netherlands that cannot be explained by hospital type and characteristics of the patient population. Our results suggest that non-scientific influences, such as surgeon’s local beliefs and preferences, prevail and drive therapeutic decisions in patients with distal radius fractures.

Clinical relevance: the results of our study illustrate the arbitrariness of the treatment of distal radius fractures and should make surgeons critically evaluate their current practices.

INTRODUCTION

While the evidence remains inconclusive, the optimum treatment for most patients with distal radius fractures is still a matter of debate. Patient age, fracture pattern, displacement and alleged fracture instability are considered crucial to guide treatment. However, in the absence of recommendations substantiated by evidence in current guidelines, the choice of treatment is likely based on factors such as the availability of resources, surgeon density, socioeconomic circumstances and surgeon’s preference. The latter of these, surgeon’s preferences in turn vary according to surgeon’s age and background. All these factors likely result in regional variations in the treatment of patients with distal radius fractures.

Considerable variations in medical practice have already been documented for a number of elective procedures such as tonsillectomy, hip replacement and prostatectomy. Variation in healthcare practices can arise from three general factors: chance alone, patient-related factors and provider-related factors. Generally, some variation is warranted if it is attributable to patient-related factors that affect the need for surgery. Such factors include variations in regional incidence of diseases that demands surgical treatment, regional differences in patients’ willingness to undergo surgical intervention and the presence of specialized referral centers. Differences in patient-related factors are also known as the case-mix of a treatment center.

However, surgical variation can also be caused by provider-related (or care-related) factors. Primarily, physician’s local culture of beliefs and preferences about appropriateness of surgery; the extent to which physicians include patients in treatment decisions; and broader factors such as regional diffusion of developments in surgical care. Variation based on these factors is unwarranted and suggests potential to improve cost-effectiveness by reducing provision of unnecessary surgery.

Nevertheless, variation cannot be regarded as strictly unwarranted if there is no clear optimum treatment. While we await the results of several randomized clinical trials to delineate the optimum treatment for distal radius fractures, the first step in addressing potentially unwarranted variation is insight into the extent in which variation across practices exists.

Only one previous study described such variation across regions or practices concerning distal radius fractures. In this study, the authors assessed the regional variation in treatment of distal radius fractures in the United States. They studied a sample of Medicare claims and found a significant variation that was mainly driven by age and region. However, variation in the surgical treatment rate of distal radius fractures has never been investigated in a European setting. We hypothesized that, although the Dutch health care system is different from the health care system in United States and basic health insurance is mandatory, there would still be a considerable variation in practice. Hence, the aim of this study was to examine the variation in surgical treatment rates across all Dutch hospitals.
METHODS
We obtained data from the national insurance database on healthcare for the calendar years 2012 and 2013 that covers 100% of the Dutch population. This database is managed by a third party (Vektis, Zeist, The Netherlands) and contains reimbursement data of all medical treatments paid for by Dutch insurance companies. Almost 99% of Dutch inhabitants have private health care insurance (http://statline.cbs.nl/Statweb/?LA=en), which pays for treatment of a distal radius fracture. Reimbursement of hospital care is exclusively claimed using the Diagnosis Treatment Combinations Codes (Diagnose Behandeling Code [DBC]).

These codes are recorded by physicians for reimbursement purposes, similar to the internationally Disease Related Group (DRG) system. Each DBC code contains information about the diagnosis, the type of treatment and the physician. DBC codes for distal radius fractures differentiate between conservative treatment and surgical treatment. The billing for a conservatively (non-operatively) treated distal radius fracture is €506 and €6073 for a surgically treated distal radius fracture.

Our database comprised the following data arranged by each Dutch hospital: the number of patients treated conservatively, the number of patients treated surgically, the percentage of female patients, the percentage of patients over 65, the mean age and the mean socioeconomic status (SES). In the Netherlands, most patients with fractures are treated by trauma surgeons with a general surgery background. Only a small percentage is treated by orthopaedic surgeons.

Data was provided as aggregate data arranged by hospital. There are four types of hospital in the Netherlands: (1) university hospitals; (2) tertiary teaching hospitals that provide both basic and highly specialized care and train doctors in collaboration with university hospitals; (3) general hospitals that provide non-specialized care; and (4) independent single-specialty treatment centers for specialist care.

Socioeconomic status was based on patients’ residential postal codes, which were correlated to data from 2010 from the Netherlands Institute for Social Research. For a small percentage of DBCs (<0.1%), no patient characteristics were available. These DBSs were equally distributed across all hospitals.

For the purpose of our analyses, we assumed that the number of procedures (both conservative and surgical treatment) equaled the number of patients. This assumption does not account for patients with bilateral fractures, however from experience we expect this number to be negligible and estimate that it is not more than 50 patients each year.

Continuous variables were reported as mean with standard deviation (SD). We calculated Pearson’s correlation coefficients to determine the correlation between the number of patients treated operatively in 2012 and 2013. We used linear regression analyses to model the relationship between the surgical treatment rate and possible explanatory variables (hospital type, percentage of females, percentage of patients over 65, mean age, mean socioeconomic status and total number of patients). A value of p < 0.05 was considered significant in the linear regression analyses.

RESULTS
We obtained aggregated data on a total of 95,754 reimbursements for distal radius fractures: 49,615 in 2012 and 46,139 in 2013. A total of 79% of the patients was treated by a general/trauma surgeon and 21% by an orthopaedic surgeon. Overall, surgeons had an operative rate of 10% and ortopaedic surgeons a rate of 9%.

The operative rate per hospital ranged from 0% to 23%. Figure 1 and Figure 2 illustrate the spread in operative rates per hospital in 2012 and 2013. The mean operative rate was similar for 2012 and 2013, 9.6% with a standard deviation of respectively 3.9% and 3.8% (Table 1).
Regression analysis showed that hospital type, the percentage of females, the percentage of patients over 65, the mean age, the mean socioeconomic status and the total number of patients explained 2.6% of the differences in the operative rate among hospitals in 2012, and 11.6% in 2013 (adjusted R squared = 0.026 and 0.116). Except for the mean age in 2013, none of these variables was independently related to the operative rate (Table 2).

Table 2. Results of multiple linear regression analysis

<table>
<thead>
<tr>
<th>Year</th>
<th>2012 B</th>
<th>p-value</th>
<th>2013 B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>University hospital</td>
<td>0.008</td>
<td>0.686</td>
<td>0.016</td>
<td>0.345</td>
</tr>
<tr>
<td>Tertiary teaching hospital</td>
<td>0.009</td>
<td>0.382</td>
<td>-0.003</td>
<td>0.776</td>
</tr>
<tr>
<td>Percentage of females</td>
<td>-0.014</td>
<td>0.896</td>
<td>-0.003</td>
<td>0.582</td>
</tr>
<tr>
<td>Percentage of patients &gt;65</td>
<td>-0.087</td>
<td>0.528</td>
<td>-0.270</td>
<td>0.140</td>
</tr>
<tr>
<td>Mean age</td>
<td>0.004</td>
<td>0.089</td>
<td>0.005</td>
<td>0.022</td>
</tr>
<tr>
<td>Mean SES</td>
<td>0.007</td>
<td>0.391</td>
<td>-0.004</td>
<td>0.582</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>0.000</td>
<td>0.935</td>
<td>0.000</td>
<td>0.616</td>
</tr>
</tbody>
</table>

Statistically significant p-values are printed in bold. Abbreviations: SES, Socioeconomic Status

DISCUSSION

There is a considerable variation in the treatment of patients with distal radius fractures across the country with operative rates varying from 0% to as much as 23%. The high correlation between operative rates in 2012 and 2013 indicates a consistent pattern over the years. These differences could not be explained by the hospital type, the percentage of females, the percentage of patients over 65 years of age, the mean age, the mean socioeconomic status or the total number of patients in each hospital. In fact, there was not a single variable that was significantly associated with the operative rate. Only the mean age of the patients had a small significant influence on the operative rate in 2013 (B = 0.005, p-value = 0.022). Adjusted for the other factors, an increase in average age of the population of one year, results in an average increase in operative rate of 0.5%. However this relationship was not significant for 2012.

These results might suggest that the choice for operative treatment of patients with distal radius fractures is not completely attributable to patient-related factors, but also to care-related factors such as the surgeon’s beliefs and preferences. Previous studies have already indicated that younger surgeons are more likely to perform open reduction and internal fixation (ORIF) of distal radius fractures in patients over 65 years of age compared to older.
surgeons. The surgeon’s background also plays a role: orthopedic surgeons are significantly more likely to use ORIF than hand surgeons. Given the lack of evidence supporting the appropriate treatment option for most patients with distal radius fractures, these findings are not surprising. After all, in absence of an optimum treatment, a surgeon’s preference (ideally in a shared decision making process with the patient) is decisive.

Another possible explanation for differences in operative rates is the high variability in fracture patterns. Every patient is unique and every fracture is different, thus requiring a patient-tailored treatment. The higher operative rate found in university hospitals might be explained by a larger percentage of multitrauma patients who sustained high energy trauma resulting in comminuted fractures. Nevertheless, besides this, if the patient populations were similar one would not expect major differences in distribution of fracture types among hospitals. When we accounted for differences in patient population this only explained a very small percentage of the variation among hospitals.

This study has several limitations. The use of reimbursement data is limited by the depth of the data. Ideally we would have considered other case mix factors that might influence the type of treatment such as injury mechanism, fracture pattern, hand dominance, functional status of the patient and occupation. Unfortunately this data is not centrally registered, nor is it possible to receive individual patient data due to confidentiality issues. Therefore aggregated data per hospital was provided. We attempted to correct for individual differences by accounting for the percentage of females and the percentage of patients over 65 years of age in each hospital. Nevertheless, we do not expect that correcting for individual factors at hospital level would greatly reduce the practice style variation we observed.

Another limitation of the data is that the reimbursement codes do not differentiate between external fixation and ORIF. In our experience, external fixation is performed infrequently and surgeons prefer ORIF. Nevertheless, we were unable to examine any difference in the rates of external fixation among hospitals.

Although our results only regard the situation in the Netherlands, variation in surgery rates within countries appear to be similar across national boundaries. A previous study by Fauwele et al. already showed a significant regional variation in the treatment of distal radius fractures in the United States. They concluded that the type of treatment depended mostly on the patient’s age and address. We also found a substantial variation among hospital services areas, however, the patient’s age showed to be of minor importance.

Variation in treatment is not just restricted to distal radius fractures. Considerable variations in medical practice have previously been identified for a number of elective procedures such as tonsillectomy, hip replacement and prostatectomy. Some of this regional variation might be due to the presence of specialized referral centers. However, distal radius fractures are not commonly referred to specialized centers but treated locally in the nearest hospital. This is also evident from our data that shows that all hospitals, including highly specialized university hospitals, treat patients with distal radius fractures. This renders patients with distal radius fractures a valid population for a variation in treatment study.

Considering the £5500 difference in billings between conservative treatment and surgical treatment, and assuming that conservative treatment prevails in the majority of the cases, there is a substantial potential to reduce costs. If we regard an operative rate of 10% appropriate (around the mean that we observed in 2013), the annual savings from one hospital with a rate of 15% and a volume of 600 patients can be as high as £165,000 (0.05 * 600 * £5500). On a national scale, this figure could run into millions of Euros cost savings each year. Conversely, the low operative rates found in some hospitals could also be an indication of suboptimal treatment of patients with distal radius fractures. A hospital that has an operative rate of only 5% might achieve worse functional results than a hospital with a higher rate.

Our database provided a comprehensive overview of all reimbursements of distal radius fractures in the Netherlands. It also showed that there is considerable variation in the treatment of distal radius fractures among hospitals. Although these findings might not be surprising, they are alarming. The variation across the country reflects a lack of evidence and suggests that non-scientific influences, such as surgeon’s age, background and local culture, prevail and drive therapeutic decisions.

We do not know what is the appropriate rate of operative treatment of distal radial fractures, and without detailed knowledge on each individual patient it is impossible to comment on the appropriateness. Even more so because we did not investigate patients’ experiences with the provided care, Patient Reported Outcomes or other functional outcomes. Nevertheless, the variation that we observed suggests the potential for an increase in quality and appropriateness of care for patients with distal radius fractures. It also supports the notion that we require well-designed randomized studies to delineate the optimum treatment for patients with distal radius fractures.
REFERENCES


CHAPTER 6

FUNCTIONAL OUTCOME IN PATIENTS WITH UNSTABLE DISTAL RADIUS FRACTURES, VOLAR LOCKING PLATE VERSUS EXTERNAL FIXATION: A META-ANALYSIS

M.M.J. Walenkamp
A. Bentohami
M.S.H. Beerekamp
R.W. Peters
R. van der Heiden
J.C. Goslings
N.W.L. Schep

*Strategies Trauma Limb Reconstr. 2013*
INTRODUCTION

Fractures of the distal radius are common and account for an estimated 17% of all fractures diagnosed.2,3 Two-thirds of these fractures are displaced and require reduction.1 Several treatment modalities have been advocated, and decision-making is mainly based on fracture type.4,5

One possible surgical treatment method is bridging external fixation. This technique relies on ligamentotaxis to obtain and maintain fracture alignment.6 However, since the introduction of locking plates, open reduction and internal fixation (ORIF) has become increasingly popular in surgical reduction.7 This technique provides immediate stable fixation that allows early mobilization and may result in a more rapid recovery and improved regain of function.8 Conversely, bridging external fixation augmented (with or without additional Kirschner wires) is a less demanding, less invasive and faster procedure. Excellent results have been described for both techniques.9-15 However, no conclusive evidence has been published favoring ORIF with a volar locking plate over bridging external fixation or vice versa.16

Margaliot et al.11 conducted a meta-analysis of studies published between 1980 and 2004 on external and internal fixation of distal radial fractures. They concluded there was not sufficient evidence to support the use of ORIF over external fixation. However, outcome data from a large variety of different techniques of internal fixation were pooled. Studies on both locking and nonlocking implants were included resulting in considerable heterogeneity across studies.11 More recently, Wei et al.17 performed a similar meta-analysis comparing functional outcome at 1 year in patients with unstable distal radius fractures. The authors pooled data from 12 randomized and nonrandomized trials on seven different techniques of internal fixation. A secondary subgroup analysis of four studies for volar locking plates revealed a significant difference on the disabilities of the arm shoulder and hand (DASH) score in favor of this technique. Unfortunately, exact DASH scores could not be reported, and therefore, clinical relevance of these differences is difficult to evaluate.18 Moreover, this analysis included one retrospective study19 and one trial that compared volar locking plates with closed reduction and percutaneous pinning.20 The authors emphasized that their results were tempered by a substantial heterogeneity present across studies.21 However, their significant findings justify further examination regarding the benefits of volar locking plates.

Recent studies on ORIF with volar locking plate have described most benefit in the early postoperative period.21,22 In addition to improved functional results at 1 year, a more rapid recovery is of clinical interest as well. Therefore, the primary aim of this meta-analysis was to compare bridging external fixation with volar locked plating in patients with unstable distal radius fractures, regarding functional outcome as measured on the DASH score, at 3, 6 and 12 months follow-up. The secondary aim was to compare grip strength, flexion and extension and radiological parameters at 1 year follow-up.

ABSTRACT

The aim of this study was to compare bridging external fixation with volar locked plating in patients with unstable distal radial fractures regarding functional outcome. A systematic search was performed in the Cochrane Central Register of Controlled Trials, Medline and EMBASE. All randomized controlled trials that compared bridging external fixation directly with volar locked plating in patients with distal radial fractures were considered. Three reviewers extracted data independently from eligible studies using a data collection form. Studies in which the primary endpoint was measured on the disabilities of the arm shoulder and hand (DASH) score at 3, 6 and 12 months were included in the analysis. To this end, mean scores and standard deviations were extracted. The software package Revman 5 provided by the Cochrane Collaboration was used for data analysis. Three studies involving 174 patients were analyzed. Ninety patients were treated with an (augmented) bridging external fixator and 84 with a volar locking plate. Data were analyzed with the random effects model. The robustness of the results was explored using a sensitivity analysis. Patients treated with a volar locking plate showed significantly lower DASH scores at all times. A difference of 16 (p = 0.006), six (p = 0.008) and eight points (p = 0.06) was found at 3, 6 and 12 months follow-up, respectively. Patients treated with a volar locking plate showed significantly better functional outcome throughout the entire follow-up. However, this difference was only clinically relevant during the early postoperative period (3 months).
MATERIALS AND METHODS

The present study was reported according to the PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses). Eligibility criteria

All randomized clinical trials that compared (augmented) bridging external fixation with volar locking plates in adult patients with unstable distal radial fractures were considered. Publication language was restricted to English and Dutch. Studies that did not clearly define the patient population (unstable distal radius fracture) and thus did not meet the inclusion criteria for surgery were not included. Trials that compared different fixation techniques or other implants were not included either. Studies that reported functional outcome on the disability of arm, shoulder and hand score at 3, 6 and 12 months follow-up were included.

Types of outcome measures

The primary outcome measure of this meta-analysis was a functional outcome defined by the DASH score at 3, 6 and 12 months follow-up. The DASH score is a validated 30-item, self-report questionnaire designed to measure physical function and symptoms in patients with musculoskeletal disorders of the upper limb. Lower scores indicate a better functional outcome. The total scale score ranges from 0 (no disability) to 100 (most severe disability). The secondary outcome measures of this review were as follows: grip strength measured as a percentage of the uninjured side, flexion and extension in degrees, and radiological parameters including radial inclination, volar tilt, ulnar variance and radial length at a minimal of 1 year follow-up.

Data sources

We conducted a search for three electronic databases: Cochrane Central Register of Controlled Trials, Medline and EMBASE in March 2013. In order not to miss recently published literature, the use of MESH terms was avoided. The complete search strategy is depicted in Table 1. Additionally, a cross-reference check for the articles of interest was performed.

Study selection

All titles that resulted from the search strategy described above were screened independently by three reviewers. Publications reporting on completely different subjects were identified and excluded. If titles did not provide sufficient information, abstracts were examined. Cohort studies, case studies, comments and current (management) views were excluded. Eligibility with regard to the in- and exclusion criteria of the remaining articles was subsequently assessed based on full text. Disagreement was resolved by means of discussion, which included a second trauma surgeon with a master in clinical epidemiology (NS).

Data extraction

Three reviewers extracted data independently from eligible studies using a data collection form. Items include study type, number of subjects, patient characteristics, fracture type, treatment method, length of follow-up and outcome measures. Means and standard deviations were extracted for continuous outcomes or calculated from confidence intervals. Studies in which these values were not reported were excluded. If multiple treatment types were studied, only data regarding patients treated with bridging external fixation or ORIF were extracted. Risk of bias was assessed using the GRADE guidelines.

Table 1. Search Strategy

<table>
<thead>
<tr>
<th>Database</th>
<th>Search Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medline</td>
<td>(((distal[Title/Abstract]) AND fracture*[Title/Abstract]) AND {radius[Title/Abstract]) OR colles fracture*[Title/Abstract]) OR smith fracture*[Title/Abstract]) OR barton fracture*[Title/Abstract]) OR wrist fracture*[Title/Abstract]) AND (((volar[Title/Abstract]) OR palmar[Title/Abstract]) OR palmer[Title/Abstract]) AND (((external fix*[Title/Abstract]) OR fixation ext*[Title/Abstract]) OR fixateur ext*[Title/Abstract]) OR fixator ext*[Title/Abstract])</td>
</tr>
<tr>
<td>EMBASE</td>
<td>(((distal.ti,ab) AND fracture*.ti,ab) AND ((radius.ti,ab) OR radial.ti,ab)) OR (((colles’ fracture*.ti,ab) OR smith fracture*.ti,ab) OR barton fracture*.ti,ab) OR wrist fracture*.ti,ab)) AND (((volar.ti,ab) OR palmar.ti,ab) OR palmer.ti,ab) AND (((external fix*.ti,ab) OR fixation ext*.ti,ab) OR fixateur ext*.ti,ab) OR fixator ext*.ti,ab)</td>
</tr>
<tr>
<td>Cochrane Central Register of Controlled Trials</td>
<td>(distal.ti,ab,kw and fracture*.ti,ab,kw) AND (radius.ti,ab,kw or radial.ti,ab,kw) or “Colles’ fracture<em>t,ab,kw or “Smith’s fracture’t,ab,kw or “Smith’s fracture</em>t,ab,kw or wrist fracture*t,ab,kw) AND (“volar”t,ab,kw)</td>
</tr>
</tbody>
</table>
Data synthesis
The software package Revman 5 provided by the Cochrane Collaboration was used for data analysis. The mean differences in DASH scores between treatment groups at 3, 6 and 12 months were calculated with 95 percent confidence intervals. The random effects model was used to pool data. Heterogeneity was explored using the chi square test, with significance set at p<0.1. For quantification, I² was used with values less than 30% indicating low heterogeneity.

Sensitivity analysis
The stability of the results regarding the DASH scores at 3, 6 and 12 months was tested using a sensitivity analysis under different assumptions. Sensitivity analyses were performed based on methodological quality of the included studies and the meta-analytic model. In addition, the robustness of results was explored by consecutively excluding one study.

RESULTS
Literature search
The search yielded 197 results, three of which met our inclusion criteria (Fig. 1). In total, 174 patients were included, of which 90 were treated with an (augmented) bridging external fixator and 84 patients with a volar locking plate.

Description of included studies
The study characteristics are summarized in Table 2. Egol et al. randomized 88 patients with an unstable distal radial fracture to undergo either bridging external fixation (EBI, Parsippany, New Jersey or Stryker, Mahwah, New Jersey) and a K-wire construct or ORIF with a volar locking plate (Hand Innovations, Miami, Florida or Stryker). Inclusion criteria were as follows: loss of reduction following closed reduction and cast immobilization, open fractures or anticipated fracture instability. Criteria for an adequate reduction measured on conventional X-rays included residual dorsal angulation of <10° and loss of radial height of <2 mm. Randomization was performed with a random number generator. The result was handed in a sealed envelope to the treating physician. Seventy-seven patients were included in the analysis, 38 received external fixation with supplementary K-wires and 39 a volar locking plate. DASH scores were reported at a follow-up of 3, 6 and 12 months.
Patients were treated with a volar locking plate (Konigsee; Swemac, Sweden) or an external fixator (Hoffmann II Compact, Stryker). In one patient, additional augmentation with a K-wire was performed. DASH scores were reported at a follow-up of 3, 6 and 12 months.

Methodological quality
The methodological quality of the included randomized controlled trials was moderate according to the guidelines of the GRADE working group. All studies described the process of allocation concealment. Wei et al. randomized their patients into three study arms in two phases resulting in three treatment groups with unequal numbers of subjects. Patients were not blinded since the treatment involved a surgical procedure. Completion of follow-up at 1 year was 78% in Wei’s study and 100% in the two other included studies.

In the study by Wei et al., all patients were analysed based on the intention to treat principle. Egol et al. did not clearly describe crossover to other treatment arms and the type of analysis applied. In the study by Wilcke, one patient in the external fixator group was reoperated and received a supplementary volar plate. This patient was analyzed in the external fixator treatment arm. Power calculations were done for all three trials.

Functional and radiological outcome
At 3 months follow-up, there was a significant difference of 16 points in DASH score favoring the locking plate (95% CI: -24.52, -6.64). At 6 and 12 months, we found a significant difference of 6 (95% CI: -9.83, -2.58) and eight points (95% CI: -15.55, -0.44), respectively (Fig. 2a-c). A significant difference in volar tilt was observed in favor of treatment with a volar locking plate (Fig. 3). No significant differences were demonstrated in the other secondary outcomes (Table 3).

Table 2. Details of included studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th>AO classification of included fractures</th>
<th>Sample Size</th>
<th>Mean age (years)</th>
<th>Country</th>
<th>Year published</th>
<th>DASH reported at</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egol et al.</td>
<td>RCT</td>
<td>A, B, C</td>
<td>38</td>
<td>39</td>
<td>USA</td>
<td>2008</td>
<td>3, 6, 12 months</td>
</tr>
<tr>
<td>Wei et al.</td>
<td>RCT</td>
<td>A3, C1, C2, C3</td>
<td>22</td>
<td>12</td>
<td>USA</td>
<td>2009</td>
<td>3, 6, 12 months</td>
</tr>
<tr>
<td>Wilcke et al.</td>
<td>RCT</td>
<td>A, C1</td>
<td>30</td>
<td>33</td>
<td>Sweden</td>
<td>2011</td>
<td>3, 6, 12 months</td>
</tr>
</tbody>
</table>

Abbreviations: RCT, randomized controlled trial

Wei et al. randomized 46 patients with an unstable distal radius fracture to be treated with augmented external fixation (n = 22), a volar locking plate (n = 12) or a radial locking column plate (n = 12). Fractures were considered unstable if fracture fragments were redisplaced following closed reduction and cast immobilization, or if three of the following criteria were met: dorsal angulation of >20o, dorsal comminution, an intra-articular fracture, an associated ulnar styloid fracture or age >60 years. Patients were randomized into three study arms in two phases. First, patients were assigned to be treated with augmented external or internal fixation. During a second randomization, the patients who had been assigned to receive internal fixation were further randomized to be treated with either a volar locking (EBI OptiLock, Parsippany, New Jersey) or a radial locking column plate. Randomization was done by computer-generated allocation using sealed, opaque envelopes. Only data on patients treated with an external fixator or with a volar locking plate were included in this meta-analysis. Treatment with external fixation (Hoffmann II Compact, Stryker) was augmented with K-wires in all patients, additional small buttress plates (n = 2) or filling of the metaphyseal void with cancellous bone allograft (n = 4) as deemed appropriate by the surgeon. Two patients who had originally been assigned to be treated with a volar locking plate received additional fixation with a dorsal plate, and four patients received supplemental bone grafting following fixation with a volar locking plate. These patients were included in the analysis in the group they were originally assigned to. DASH scores were reported at a follow-up of 3, 6 and 12 months.

Wilcke et al. randomized 63 patients under the age of 70 into volar locking plating (n = 33) or bridging external fixation (n = 30). Only dorsally displaced AO type A and C1 fractures with an axial shortening of ≥4 mm or a dorsal angulation of ≥20o were included. Randomization was performed by a sealed envelope procedure. Randomization was conducted in blocks of 20 with age stratification set on 50 years. Patients were treated with a volar locking plate (Konigsee; Swemac, Sweden) or an external fixator (Hoffmann II Compact, Stryker). In one patient, additional augmentation with a K-wire was performed. DASH scores were reported at a follow-up of 3, 6 and 12 months.
Table 3. For the secondary outcomes such as grip strength, flexion, extension, radial inclination, ulnar variance and radial length, no significant differences were demonstrated

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grip strength as percentage of uninjured side</td>
<td>3</td>
<td>-1.73 (-12.27, 15.73)</td>
</tr>
<tr>
<td>Flexion (degrees)</td>
<td>2</td>
<td>0.44 (-4.66, 5.53)</td>
</tr>
<tr>
<td>Extension (degrees)</td>
<td>2</td>
<td>4.46 (-5.21, 14.14)</td>
</tr>
<tr>
<td>Radial inclination (degrees)</td>
<td>2</td>
<td>-2.06 (-4.6, 0.49)</td>
</tr>
<tr>
<td>Ulnar variance (mm)</td>
<td>3</td>
<td>-0.086 (-1.82, 0.10)</td>
</tr>
<tr>
<td>Radial length (mm)</td>
<td>3</td>
<td>-0.96 (-1.96, 0.04)</td>
</tr>
</tbody>
</table>

Sensitivity analysis

Based on methodological quality, the study by Egol et al. was first excluded since they used a per protocol analysis. Subsequently, the trial by Wei et al. was excluded because of their considerable lost to follow-up. These analyses did not alter the findings or conclusions; all differences remained significant. This was similar when the metaanalytic model was changed. Considerable heterogeneity was found in the analysis of DASH score at 3 and 12 months. Data were homogenous for the DASH score at 6 months ($I^2 = 0\%$). When the study by Egol et al. was excluded, data were homogenous ($I^2 = 0\%$) for the analysis of DASH score at 3 months as well. The same was witnessed for the DASH score at 12 months when the trial by Wei et al. was excluded.

Complications

A complication rate of 26% in the external fixator group and 20% in the volar locking plate group was found (Table 4). These differences were not significant (Fig. 4).
be considered to be both significantly better and clinically relevant for patients treated with a volar locking plate.

Although considerable heterogeneity was found in the analysis of DASH scores at 3 and 12 months, the differences remained significant under the sensitivity analyses. No clinical or methodological issues could be identified explaining this heterogeneity.

Another significant difference between treatment methods was a slightly improved anatomical restoration of the volar tilt in the ORIF group. The mean difference between external fixation and volar locking plate was six degrees, which indicates a more accurate anatomical reconstruction. Nevertheless, we should keep in mind that radiographic parameters are surrogate endpoints and their clinical relevance remains disputed.

There are several strengths to this meta-analysis which include the comprehensive search of the literature and the inclusion of similar trials. Studies in which implants other than volar locking plates, e.g., the fragment-specific wrist fixation system, nonlocking plates or a combination of volar and dorsal plating were used, were not included.

Similarly, studies using a different form of external fixation and studies with an unclear definition of unstable fractures were excluded as well.

Therefore, the results of this meta-analysis will most likely reveal the true magnitude and direction of the differences between the treatments under study.

However, the results of this study should be interpreted with caution because of the following limitations. The power of this meta-analysis was limited since the sample size of the included studies was relatively small. Moreover, the three trials included various AO fracture types and used different definitions of fracture instability and therefore indication for surgery. Finally, unfortunately, only three trials could be included in this analysis. Nevertheless, the quality of a meta-analysis is often considered to be more susceptible to heterogeneity present across studies than the number of included trials.

A traditional argument in favor of ORIF with a volar locking plate is early mobilization, which theoretically results in less muscle weakness and therefore improved regain of wrist function. Additionally, the locking principle provides a more rigid construction in the subchondral area of the distal radius, especially in patients with osteoporosis. This theory is in accordance with the results of the current meta-analysis that revealed a significant and clinically relevant improved patient-reported functional outcome for volar locking plate at 3 months. This difference remained significant under a sensitivity analysis and can therefore be considered to be robust. A more rapid recovery might benefit high demanding patients or athletes, and therefore, treatment with volar locking plate for these types of patients with an unstable distal radius fracture is recommended.

### Table 4: Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>ORIF with volar locking plate (N)</th>
<th>Bridging external fixator (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pin tract infection</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Deep infection</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Ruptured extensor/Rexor pollicis longus tendon</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>CRPS</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Nonunion</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Painful retained hardware</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>CTS</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tenolysis for postoperative stiffness</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Malunion</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Tendinitis</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total** | 17/84 (20%) | 23/90 (26%) |

**Abbreviations:** CRPS, Complex Regional Pain Syndrome; CTS, Carpal Tunnel Syndrome
REFERENCES


32. Wilcke MK, Abbassadeh A, Adolphson PS. Wrist function recovers more rapidly after volar locked plating than after external fixation but the outcomes are similar after 1 year. Acta Orthop 2011 Feb;82(1745-3682 [Electronic]):76-81.


CHAPTER 7

SURGERY VERSUS CONSERVATIVE TREATMENT IN PATIENTS WITH TYPE A DISTAL RADIUS FRACTURES, A RANDOMIZED CONTROLLED TRIAL

In memory of Robert Wilde

M.M.J. Walenkamp
J.C. Goslings
A. Beumer
R. Haverlag
P.A. Leenhouts
E.J.M.M. Verleisdonk
R.S.L. Liem
J.B. Sinterie
M.W.G.A. Bronkorst
J. Winkelhagen
N.W.L. Schep

BMC Musculoskeletal Disorders 2014
ABSTRACT

Background
Fractures of the distal radius are common and account for an estimated 17% of all fractures diagnosed. Two-thirds of these fractures are displaced and require reduction. Although distal radius fractures, especially extra-articular fractures, are considered to be relatively harmless, inadequate treatment may result in impaired function of the wrist. Initial treatment according to Dutch guidelines consists of closed reduction and plaster immobilisation. If fracture redisplacement occurs, surgical treatment is recommended. Recently, the use of volar locking plates has become more popular. The aim of this study is to compare the functional outcome following surgical reduction and fixation with a volar locking plate with the functional outcome following closed reduction and plaster immobilisation in patients with displaced extra-articular distal radius fractures.

Design
This single blinded randomised controlled trial will randomise between open reduction and internal fixation with a volar locking plate (intervention group) and closed reduction followed by plaster immobilisation (control group). The study population will consist of all consecutive adult patients who are diagnosed with a displaced extra-articular distal radius fracture, which has been adequately reduced at the Emergency Department. The primary outcome (functional outcome) will be assessed by means of the Disability Arm Shoulder Hand Score (DASH). Secondary outcomes comprise the Patient-Rated Wrist Evaluation score (PRWE), quality of life, pain, range of motion, radiological parameters, complications and cross-overs. Since the treatment allocated involves a surgical procedure, randomisation status will not be blinded. However, the researcher assessing the outcome at one year will be unaware of the treatment allocation. In total, 90 patients will be included and this trial will require an estimated time of two years to complete and will be conducted in the Academic Medical Centre Amsterdam and its partners of the regional trauma care network.

Discussion
Ideally, patients would be randomised before any kind of treatment has been commenced. However, we deem it not patient-friendly to approach possible participants before adequate reduction has been obtained.

BACKGROUND
Fractures of the distal radius account for an estimated 17% of all fractures diagnosed. Two-thirds of these fractures are displaced and require reduction. Although extra-articular distal radius fractures are considered to be relatively harmless, inadequate treatment may result in severely impaired function of the wrist. The consequences of post-traumatic loss of function are comprehensive, both on individual and societal level, and have long been underestimated.

Several treatment modalities to obtain and maintain reduction exist and decision-making is mainly based on fracture type, region and surgeon’s preference. Although good results have been described for both conservative and surgical management, the ideal treatment method remains unknown.

According to current Dutch guidelines, standard treatment for patients with displaced extra-articular distal radius fractures consists of closed reduction and cast immobilisation for four to six weeks. Nevertheless, redisplacement occurs in up to 60% of cases and functional recovery is frequently poor. If fracture redisplacement occurs, surgical reduction and fixation is the treatment of choice.

A well-established and widely applied surgical approach is open reduction and internal fixation (ORIF). This procedure involves surgical (open) fracture reduction and internal fixation by means of locking plates. Over the past years, the use of volar locking plates has become increasingly popular. This type of osteosynthesis requires a relatively simple volar approach to the wrist, followed by fracture fixation using fixed angle implants. The technique allows more accurate reduction and immediate stable fixation. Subsequent removal of the plate is rarely necessary. The fracture stability allows for early mobilisation and may therefore result in an improved recovery of function. By 1987 already, Dias et al. concluded that patients who were encouraged to mobilise their injured wrist from the start in a modified cast which only restricted extension, recovered function more quickly than those whose who were immobilised in a conventional plaster cast.

A recent randomised controlled trial by Arora et al. compared open reduction and internal fixation with a volar locking plate with closed reduction and plaster immobilisation. They included patients of 65 years and older who had suffered all types of displaced distal radius fractures with inadequate reduction or redisplacement. The operative treatment group showed better wrist function in the early post-operative period. However, at six and twelve months there were no significant differences in wrist function between treatment groups. At all times, grip strength was significantly better in the operative group. These results are consistent with a previous retrospective cohort study among elderly patients conducted by Arora et al. as well. Future studies compare the quality of life between patients treated with a volar locking plate or closed reduction and plaster immobilisation.
Despite the high incidence of displaced distal radius fractures and the substantial possible implications of suboptimal management, no high level evidence regarding the best treatment method yet exists. To our knowledge, no studies have been performed comparing conservative treatment with ORIF in patients of all ages with displaced extra-articular distal radius fractures. Therefore, we are proposing to conduct a randomised controlled trial to compare the functional outcome, assessed with the Disability Arm Shoulder Hand Score (DASH), after ORIF with a volar locking plate with closed reduction followed by plaster immobilisation, in patients with displaced extra-articular distal radius fractures. We hypothesise that surgical reduction will result in a more rapid recovery and better functional results at one year follow up than conservative treatment consisting of closed reduction and plaster immobilisation.

The aim of this study is to compare two treatment methods for patients with displaced extra-articular distal radius fractures regarding functional outcome at one year follow up. These treatment methods include open reduction and internal fixation (ORIF) with a volar locking plate and closed reduction followed by plaster immobilisation.

METHODS/DESIGN
This single blinded randomised controlled trial will randomise between open reduction and internal fixation (ORIF) with a volar locking plate (intervention group) and closed reduction followed by plaster immobilisation (control group).

Participants
The eligible study population will consist of all consecutive adult patients who are diagnosed with a displaced extra-articular distal radius fracture, which has been adequately reduced at the Emergency Department of the Academic Medical Centre Amsterdam or one of the other participating hospitals.

Inclusion criteria
- Patients ≥ 18 years and ≤ 75 years
- Extra-articular (AO type A) displaced distal radius fracture, as classified on lateral, posterior-anterior and lateral carpal radiographs by a radiologist or trauma surgeon.
- Acceptable closed reduction obtained according to current Dutch guidelines. 8
- <15° dorsal or <20° volar angulation of the distal fracture fragment
- <5 mm loss of radial height
- ≥15° radial inclination

Exclude criteria
- Open distal radius fractures
- Multiple trauma patients (Injury Severity Score (ISS) ≥16)
- Other fractures of the affected extremity
- Patients who indicate to have had impaired wrist function prior to injury, for example due to rheumatoid arthritis, neurological disorders of the upper limb or previous malunions in the affected limb.
- Patients suffering from disorders of bone metabolism known to adversely effect fracture healing, such as osteomalacia.
- Patients suffering from connective tissue or (joint) hyperflexibility disorders known to adversely effect fracture healing and/or soft tissue and wound healing.
- Patients unable to understand the treatment information and informed consent forms as judged by the attending physician.

Interventions
All patients will initially be treated with closed reduction and cast immobilisation. This will take place under local anaesthesia by means of a haematoma block with 20 cc Lidocaine 1%. Closed reduction will be performed according to the Robert-Jones method. 19 This involves increasing the deformity first, then applying continuous traction and immobilising wrist and hand in the reduced position. Additional radiographs will be performed to verify the quality of the reduction (see inclusion criteria). After this has been confirmed, the wrist will be immobilised according to Dutch guidelines: a dorsal splint for one week. Once informed consent is obtained, patients will be randomized at one week between open reduction and internal fixation with a volar locking plate, or continuation of cast immobilization.

The intervention group will be treated with open reduction and internal fixation with a volar locking plate. The surgery will be performed by a general, trauma or orthopaedic surgeon. In order not to disturb clinical practise, and to provide an accurate comparison of two treatment modalities as they are applied in clinical practise, no specific interval to surgery is prescribed. According to the current standard treatment protocol, antibiotic prophylaxis will be administered pre-operatively. The distal radius will be approached according to Henry, which involves an incision between the tendon of the flexor carpi radialis and the radial artery. The advantage of this approach is the possibility of an easy extension to the proximal or distal part of the forearm and the fact that the plate will be optimally covered by soft tissue. 20 Moreover, the median nerve is not at risk using this technique. After the fracture site is exposed, the fracture will be reduced and provisionally fixed with K-Wires and/or reduction forceps. An appropriate volar locking plate which best suits the anatomy of the wrist and the fracture type will be selected. Screw placement and fracture reduction will be confirmed intra operatively by radiographic images. Wound closure will be performed at the discretion of the surgeon using standard techniques and no post-operative fixation or immobilisation will be applied. During the first follow up visit at five to ten days, wound
Secondary outcomes

- Wrist pain and disability expressed as change on Patient-Rated Wrist Evaluation Score (PRWE). The PRWE is a validated tool for assessing functional outcome in patients with distal radius fractures.\(^{21,22}\) This score was first described in 1998 by McDermid et al. and developed by expert surveys.\(^{22}\) The PRWE is a 15-item questionnaire designed to measure wrist pain and disability in activities of daily living. The PRWE allows patients to rate their levels of wrist pain and disability from 0 to 10, and consists of three subscales: Pain, Function, and Cosmetics.

- Quality of Life assessed using the Short Form-36 (SF-36®) questionnaire. The SF-36 is a validated multipurpose, short form health survey which contains 36 questions representing eight different health domains.\(^{23}\) These domains are combined into a mental and physical component scale. From each domain, scores ranging from 0 to 100 points are derived, with lower scores indicating poorer quality of life.

- Pain as indicated on a Visual Analogue Scale (VAS), in which 0 implies no pain and 10 the worst possible pain. Patients will be asked to give an estimation of the type and quantity of pain medication taken during all follow up visits.

- Patient satisfaction at one year by simply asking patients if they are satisfied with the result (yes/no).

- Range of motion of the wrist measured on both sides with a handheld goniometer.

- Prehensile grip strength as measured with a Baseline dynamometer.

- Radiological parameters: radial inclination, volar/dorsal tilt, comminution, ulnar variance and radial length measured digitally in the Picture Archiving and Communication System (PACS) on standard posterior anterior (PA), lateral carporadial and lateral X-rays of the wrist. Radiographs will be obtained according to standardised procedures. PA radiographs with the shoulder in 90 degrees abduction, elbow in 90 degrees flexion and the wrist in neutral position; lateral X-rays with the shoulder in neutral position and elbow in 90 degrees flexion; and the lateral carporadial radiographs will be obtained by positioning the lower arm on a 20-25 degrees angled wedge.

- Rate of cross-overs

- Complications such as: loss of reduction, fracture malunion or non-union, wound and/or plate infection, tendon irritation and/or rupture, neuropathy and the occurrence of complex regional pain syndrome according to the criteria by Veldman et al.\(^{24}\)
Side-effects reporting
All adverse events will be described in patient file during consult at any of the follow-up visits or any other moment if indicated or requested by the patient. Serious adverse events will be reported through the web portal ToetsingOnline to the Medical Ethical Review Committee of the Academic Medical Centre of the University of Amsterdam, which approved the protocol, within 15 days after the sponsor has first knowledge of the serious adverse reactions.

Data collection and follow-up
Baseline characteristics will be obtained after randomisation but before treatment takes place. During follow up patients will be asked to return to the hospital for follow up at; one, three and six weeks and three, six and twelve months, according to standard Dutch protocols. During these visits patients will be asked about any complaints and/or complications and physical and radiological examination will be performed. For details, see Table 1. Procedures additional to standard care are bold.

Table 1. Follow-up visits

<table>
<thead>
<tr>
<th>Follow-up at:</th>
<th>Tests:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 week</td>
<td>VAS, X-ray</td>
</tr>
<tr>
<td>3 weeks</td>
<td>VAS, X-ray</td>
</tr>
<tr>
<td>6 weeks</td>
<td>VAS, ROM, Grip strength, QoL, X-ray, PRWE, DASH</td>
</tr>
<tr>
<td>3 months</td>
<td>VAS, ROM, Grip strength, QoL, X-ray, PRWE, DASH</td>
</tr>
<tr>
<td>6 months</td>
<td>VAS, ROM, Grip strength, QoL, X-ray, PRWE, DASH</td>
</tr>
<tr>
<td>12 months</td>
<td>VAS, ROM, Grip strength, QoL, X-ray, PRWE, DASH</td>
</tr>
</tbody>
</table>

Examinations additional to standard care are bold

Abbreviations: VAS, Visual Analogue Scale; ROM, Range of Motion; QoL, Quality of Life; PRWE, Patient-Rated Wrist Evaluation Score; DASH, Disabilities of the Arm Shoulder and Hand Score

Sample size
This sample size calculation is based on the primary endpoint, the DASH score. The DASH score of an individual without any complaints of the wrist is 0. The mean DASH score after closed reduction and cast treatment after one year of follow up is 19 with a standard deviation (SD) of 18. This figure was measured in a patient population in which 72% suffered from a displaced extra-articular distal radius fracture. We assume that treatment with volar plating will decrease the DASH score which is achieved by conservative cast treatment by 15 points, from 19 to 4. Therefore at α = 0.05% and a power of 90%, with an estimated loss to follow-up of 10%, we would require 66 patients in total and 33 per treatment arm, to participate in the trial. This figure was calculated using the standard formula for means of superiority trials: n = (A + B)^2 * 2 * SD^2/DIFF^2, where N = the number of patients required per arm, A the level of significance, B the power, SD the standard deviation of the primary outcome and DIFF the difference between the means. For safety measures and to correct for natural deaths, 45 patients in each arm will be included. From a separate study being conducted at the Academic Medical Centre Amsterdam and two other teaching hospitals, it was established that of the 703 distal radius fractures encountered in one year, 328 were an AO type A2 and A3. Therefore we estimate that we require a maximum of two years to include and follow up the patients in this trial.

Statistical analysis
Patients will be analysed according to the intention-to-treat protocol. General descriptive statistics on patient characteristics at baseline will be performed including factors such as gender and age. The primary outcome, DASH at one year, will be corrected for age and assessed using an analysis of co-variance (ANCOVA). Trends in DASH scores among the different time points will be assessed using a repeated measures ANOVA. The secondary outcomes; PRWE, quality of life (QoL SF-36), pain as indicated on a Visual Analogue Scale (VAS) and Range of Motion (ROM) will be analysed in a similar manner. The radiological outcome, number of conversions and complication rate will be determined using either a Fisher Exact of a Chi square test, depending on the order of magnitude of the results. Subgroup analyses with regard to DASH score will be performed for gender and age for each randomisation stratum.

Ethical considerations
This study was approved by the Medical Ethical Review Committee of the Academic Medical Centre.

Regulation statement
This study will be conducted according to the principles of the Declaration of Helsinki version 59, October 2008 and in accordance with the Medical Research Involving Human Subjects Act (WMO) and other guidelines, regulations and Acts.

Recruitment and informed consent
Patients diagnosed with a displaced extra-articular distal radius fracture will be approached by the investigators and informed about this trial. Patients will receive an elaborate information sheet and contact details of both the investigator and an independent physician. Possible participants will have a period of reflection of five working days. If a patient decides to participate, written and oral informed consent will be obtained.

Benefits and risks assessment, group relatedness
The treatment that patients will receive is a component of the standard treatment of care, which currently depends on the surgeon’s preference and the complexity of the fracture. Patients will be asked to return to the hospital for follow up at one, three and six weeks,
DISCUSSION
The exact moment of inclusion and randomisation of patients with displaced distal radius fractures has proven to be a complicated issue during the design of this trial. Ideally, patients would be randomised before any kind of treatment has been commenced. However, we deem it unethical and moreover not patient-friendly to approach possible participants before adequate reduction has been obtained. Therefore, after careful collaboration and discussion, the research group has decided upon its current format.

Surgery versus conservative treatment type A distal radius fractures

Three months, six months and at twelve months. All visits are part of standard care following a fracture treated in this hospital. During these visits patients will be asked about any complaints and/or complications and physical examination will be performed. The assessment of the range of motion of the wrist will take approximately five minutes. Additional to standard care, patients will be asked to fill out three questionnaires at six weeks, three months, six months and one year. Patients will be asked to fill out a DASH form, rate their pain on a Visual Analogue Scale and give an estimation of the type and quantity of pain medication taken during all visits. This will take approximately ten minutes of their time. The PRWE score and the SF-36 will approximately take another ten minutes each. Subjects could experience mild discomfort during physical examination and testing, but this will be no different from that experienced during physical examination during routine follow-up. X-rays will be taken during every visit of which only the final radiographs at one year are additional to standard care. The burden experienced regarding time spent is difficult to estimate but will most likely not exceed 30 minutes. In the total duration of this study, patients will spend an approximate 150 minutes more. The risks are comparable to those that the standard treatment involves. This comprises the standard risk for undergoing a surgical procedure, including risks related to anaesthesia, neurovascular damage and post-operative wound infection. The risks of plaster immobilisation include redisplacement, malunion, loss of function, carpal tunnel syndrome and complex regional pain syndrome. Close follow up and a protocol of treatment, identical to the standard one, will be applied in every subject. Reduction of risks will be done according to inclusion and exclusion criteria. If complications arise, the treating physician will proportionate the adequate treatment according to the current protocols of treatment based on the published literature.

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons. This study will be terminated prematurely if and when patients experience an amount of discomfort or adverse events that is disproportionate to the benefit of the study and presents too great a risk to the participating study subjects. Since the allocated treatment is part of standard treatment of care, no interim analysis, stopping rules or data monitoring was constructed.

Indemnities
The institutional review board at the AMC has waived liability insurance, because no additional risk can be attributed to participation in this study.

Publication plan
The principal investigator, the study designer and the study coordinator will be named author. There will be a limit of ten authors. All others will obtain group authorship in the study group. All authors including group members are allowed to present the results.

Funder
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Intended date of completion: 01-11-2014.
Reporting date: 01-11-2015.
REFERENCES


CHAPTER 8

COMPUTER-ASSISTED 3D PLANNED CORRECTIVE OSTEOTOMIES IN EIGHT MAL-UNITED RADIUS FRACTURES

M.M.J. Walenkamp
R.J.O. de Muinck Keizer
J.G.G. Dobbe
G.J. Streekstra
J.C. Goslings
P. Kloen
S.D. Strackee
N.W.L. Schep

Strategies Trauma Limb Reconstr. 2015
INTRODUCTION
Malunion of a radial fracture may result in chronic pain and loss of function and occurs in around 5% of the cases. A corrective osteotomy for patients with a malunited radius fracture can improve wrist function and reduce stiffness and pain. Previous studies showed that accuracy of the anatomical reconstruction is essential to achieving an optimal outcome. Therefore, conscientious preoperative planning of the procedure and accurate surgical repositioning is required. Conventionally, planning is based on two orthogonal radiographs depicting lateral and posteroanterior views of the radius.

However, malunion of the radius commonly involves complex three-dimensional (3D) deformations in different planes, which may not be acknowledged on conventional preoperative 2D radiographs. Two-dimensional radiographic planning does not always result in adequate restoration of alignment, as was demonstrated by a recent study performed by members of our study group.

A potential solution of the challenge presented by the complex deformity of radius malunions is the use of computer-assisted 3D planning techniques. With these techniques, both physical and virtual models of the deformed radius and the mirrored contralateral radius can be created. The models are used preoperatively to conceptualise the multiple planes of deformity and to preoperatively plan the osteotomy. Preoperative 3D planning also provides the possibility to create patient-specific cutting guides to transfer the planned osteotomy plane to the patient’s bony anatomy during surgery. Patient-specific guides for cutting or drilling have been successfully introduced before. They have proven to enable accurate positioning of surgical instruments or implants with respect to bony anatomy. However, these studies mostly focus on functional results without properly evaluating residual postoperative malpositioning using 3D imaging techniques.

Therefore, the aim of this study was to assess whether computer-assisted 3D planning and the intra-operative use of personalised cutting guides improve the accuracy of bone alignment.

MATERIALS AND METHODS
All patients who underwent a computer-assisted 3D planned corrective osteotomy of the radius for the treatment of symptomatic radius malunion between January 2009 and March 2014 were eligible for inclusion. Only patients who underwent a postoperative computed tomography (CT) scan of both (full length) radii were included. Patients with a previous fracture of the contralateral radius were excluded.

Preoperative planning
Preoperative planning was based on CT scans of both the affected and the contralateral radius. The unaffected contralateral bone served as reference for determining malalignment. All
CT scans were obtained using a Brilliance 64-channel CT scanner (Phillips Healthcare, Best, The Netherlands) reconstructed to a 3D volume with a voxel spacing of 0.45 x 0.45 x 0.45 mm. Data were imported by a dedicated application program which helps quantifying pre- and postoperative malalignment. In short, the program enables segmenting the affected bone using a threshold-connected region growing algorithm that collects voxels that belong to the affected bone, followed by a binary closing algorithm to close residual gaps. A Laplacian level-set segmentation growth algorithm advances the outline towards the boundary of the bone. A polygonal mesh is finally extracted, which is used for visualisation of the bone deformity. It also serves to create a double-contour polygon by sampling the grey level image 0.3 mm towards the inside (bright) and outside (dark) for each point of the polygonal bone model. This double-contour polygon with image grey levels assigned to each point enables efficient and accurate point-to-image registration.

Next, distal and proximal segments are clipped to exclude the malunited fracture region. The clipped segments are aligned with the mirrored image of the healthy contralateral bone, by point-to-image registration. This procedure provides a position matrix that brings the distal bone segment in a position that agrees with that of the mirrored contralateral bone. The matrix is used to quantify malpositioning in terms of three displacements along and three rotations about the axes of a 3D anatomical coordinate system. The centroid of the clipped bone segment polygons is used as centre of rotation. Translations are determined in the ulnar, dorsal and proximal direction. Rotations are expressed in terms of dorso-palmar tilt, radial inclination and axial rotation (pronation and supination). In case of an oblique single-cut rotation osteotomy, the matrix is used to determine the orientation of the osteotomy and the rotation angle for aligning the distal and proximal bone segments. The software further enables to create (1) both virtual and physical models of both radii on which the osteotomy planning was simulated (Fig. 1), and (2) patient-specific cutting guides and jigs for intra-operative guidance of the osteotomy (Fig. 2).

Surgical procedure

Depending on the complexity of the malunion, patients were treated with an open-wedge osteotomy or an oblique single-cut rotation osteotomy (OSCR). Both osteotomy types were planned by using virtual or physical synthetic models of both radii and/or assisted by intraoperative use of patient-specific cutting guides and jigs (Fig. 2). In the latter method, the sterilised surgical guide was positioned at the specific bone surface and was fixed with Kirschner wires, using the planned fixation holes. In the case of an oblique single-cut rotation osteotomy (OSCR), the guide was removed after the osteotomy and a stainless steel jig served to set the angle between the proximal and distal bone segment. Rotational alignment was achieved by rotating the malunited distal bone segment over the planned angle. Regular plate and screw fixation was performed to maintain the position. Postoperative management varied from direct mobilisation to 2 weeks of plaster of Paris immobilisation.
Data collection and outcome
Patients were evaluated postoperatively after a minimum follow-up of 6 months. The main outcome was residual 3D malpositioning based on a postoperative CT scan of both forearms. Residual malpositioning was again expressed in terms of six positioning parameters. These residual malpositioning parameters were quantified in exactly the same way as described for preoperative planning, with the one difference that the postoperative image was used for segmentation of the bone instead of the preoperative image. Secondary outcome was the postoperative range of motion of the wrist measured on both sides with a handheld goniometer.

This study was approved by the Medical Ethical Review Committee of the Academic Medical Centre of the University of Amsterdam. All subjects gave informed consent before participation in this study.

Statistical analysis
We reported medians and interquartile range (IQR) for nonparametric variables, and means and standard deviations (SD) for normally distributed variables. The absolute value of each malalignment parameter served to represent the residual error. The Kolmogorov-Smirnov test was used for the determination of the distribution form. The Wilcoxon signed rank test was used to compare the medians of each of the six malpositioning parameters before and after correction.

RESULTS
A total of 16 patients were treated for a symptomatic malunion with a computer-assisted 3D planned corrective osteotomy of the radius.

Five patients were treated recently, and their follow-up was shorter than 6 months. Two patients did not want to participate in postoperative position evaluation, and one patient had moved abroad. This resulted in a total of eight patients who were included in this series.

Of the included patients, three had originally developed a malunion after sustaining an extra-articular distal radius fracture. Five patients had sustained a forearm fracture (three antebrachial fractures and two isolated radius fractures), all of whom developed a diaphyseal malunion of the radius. The demographics of the study group are depicted in Table 1. We performed an opening-wedge osteotomy on four patients, and the other four patients received an oblique single-cut rotation osteotomy (OSCRO). All patients achieved primary osseous union. The median duration of follow-up was 26 months (IQR 12-34). No complications occurred.
Table 1. Demographics of study population

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Agea (years)</th>
<th>Location malunion</th>
<th>Hand affected</th>
<th>Dominant hand</th>
<th>Indication</th>
<th>Techniqueb</th>
<th>Osteotomy type</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>64</td>
<td>Distal, extra articular</td>
<td>Yes</td>
<td>Pain</td>
<td>Cutting guide</td>
<td>Opening</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>53</td>
<td>Distal, extra articular</td>
<td>Yes</td>
<td>Pain</td>
<td>Simulation</td>
<td>Opening</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>18</td>
<td>Distal, extra articular</td>
<td>No</td>
<td>Pain, DRUJ instability</td>
<td>Simulation</td>
<td>Opening</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>32</td>
<td>Diaphyseal</td>
<td>Yes</td>
<td>Restricted pronation</td>
<td>Cutting guide</td>
<td>OSCRO</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>18</td>
<td>Diaphyseal</td>
<td>Yes</td>
<td>Restricted pronation</td>
<td>Simulation</td>
<td>OSCRO</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>41</td>
<td>Diaphyseal + ulna</td>
<td>No</td>
<td>Restricted ROM (all directions)</td>
<td>Simulation</td>
<td>OSCRO</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>18</td>
<td>Diaphyseal + ulna</td>
<td>No</td>
<td>Restricted pronation/ supination</td>
<td>Cutting guide</td>
<td>OSCRO</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>13</td>
<td>Diaphyseal + ulna</td>
<td>Yes</td>
<td>Restricted supination</td>
<td>Cutting guide</td>
<td>Opening</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: F, female; M, male; ROM, Range of Motion; DRUJ, distal radioulnar joint; Opening, opening-wedge osteotomy; OSCRO, oblique single-cut rotation osteotomy

a. Age in years at time of surgery

b. Technique consisted of either pre- and intra-operative simulation of the osteotomy using virtual or physical 3D models of both radii sometimes with intra-operative use of a custom-made cutting guide and angled jig

The median pre- and postoperative malalignment per dimension is depicted in Table 2. Improvement in dorsopalmar tilt showed statistical significance (p = 0.05, Wilcoxon signed rank test). The median residual malalignment was smallest for radial length (-0.6 mm) and axial rotation (-2.6).

Table 2. Residual malalignment

<table>
<thead>
<tr>
<th>Malalignment parameter</th>
<th>Pre-op Median (IQR)</th>
<th>Post-op Median (IQR)</th>
<th>Difference Median (IQR)</th>
<th>Significancea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulnoradial shift in mm, ulnar (-), radial (+)</td>
<td>3.8 (1.4 - 9.9)</td>
<td>7.0 (1.1 - 11.0)</td>
<td>2.1 (-2.7 - 5.0)</td>
<td>0.327</td>
</tr>
<tr>
<td>Volodorsal shift in mm, volar (-), dorsal (+)</td>
<td>7.2 (-5.6 - 30.3)</td>
<td>4.0 (2.8 - 10.3)</td>
<td>3.2 (-11.6 - 11.2)</td>
<td>0.069</td>
</tr>
<tr>
<td>Proximodistal shift in mm shortened (-), lengthened (+)</td>
<td>-5.3 (-17.0 - 11.9)</td>
<td>-0.6 (-1.8 - 0.2)</td>
<td>2.9 (-0.0 - 5.4)</td>
<td>0.123</td>
</tr>
<tr>
<td>Dorsopalmar tilt in deg, dorsal (-), volar (-)</td>
<td>-9.0 (-16.8 - 13.9)</td>
<td>-6.4 (-7.9 - 0.4)</td>
<td>5.5 (-6.9 - 10.3)</td>
<td>0.050</td>
</tr>
<tr>
<td>Radial inclination in deg, ulnar (-), radial (+)</td>
<td>5.6 (0.4 - 8.8)</td>
<td>3.2 (-1.4 - 8.8)</td>
<td>-1.4 (-9.3 - 5.3)</td>
<td>0.208</td>
</tr>
<tr>
<td>Axial rotation in deg, pronation (-), supination (+)</td>
<td>7.6 (-36.4 - 2.0)</td>
<td>2.6 (-13.2 - 12.3)</td>
<td>15.0 (1.2 - 30.6)</td>
<td>0.848</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range; deg, degrees; mm, millimeter; Bold value indicates statistical significance (p≤0.05)

a. Related Samples Wilcoxon Signed Rank Test

The individual changes in preoperative and postoperative deformations are depicted in Fig. 3. In two adolescent patients (Cases 7 and 8), the radial length (translation in proximodistal direction) was not reliable due to the patients’ growing skeleton between pre- and postoperative CT scans. Volodorsal translation showed improvement (correction towards neutral) in all but one patient (88%). In six patients (75%), ulnoradial shift increased by the correction osteotomy. In two patients, this shift was corrected to nearly neutral.

Dorsopalmar tilt was improved in seven out of eight patients (88%): in one patient (Case 8), tilt was overcorrected from volar to dorsal. In one patient (Case 4), the preoperative neutral position was corrected to dorsal angulation (Fig. 4). Five patients originally had a malunion in pronation. In those five cases, rotations were corrected, although an overcorrection to supination was present in two patients (Cases 6 and 8). Radial inclination was improved in six out of eight patients (88%).
Six patients (88%) experienced a postoperative increased range of motion (Table 3). One patient (Case 3) slightly deteriorated. In addition to a distal radius fracture, this patient had sustained a triangular fibrocartilage complex (TFCC) tear that resulted in instability of the distal radioulnar joint (DRUJ). The performed correction osteotomy itself did not provide enough stability, and reinsertion of the TFCC was attempted 2 months after the corrective osteotomy, but was not successful. In one patient (Case 2), the indication for treatment was based on pain, instead of restricted ROM. The preoperative range of motion (ROM) was therefore not measured. There was no statistically significant difference in terms of malalignment parameters between the cases that were corrected with use of a cutting guide versus the corrections that were visualised (Table 4).
DISCUSSION

Postoperative 3D evaluation revealed improved positioning parameters for most patients in dorsopalmar tilt, axial rotation (pronation and supination), radial inclination, proximodistal shift and volodorsal shift. Dorsopalmar tilt significantly improved. However, ulnar radial translation was worsened by the correction osteotomy. Both over- and undercorrection occurred in individual patients. All but one patient experienced improved range of motion.

Computer-assisted 3D planning techniques are expected to optimise preoperative treatment plans and therefore minimise residual malalignment. In our study, alignment improved in five of the six positioning parameters, of which improvement in dorsopalmar tilt reached significance despite the small number of patients.

There are several explanations for the residual malalignment. Firstly, the transfer from the virtual plan to the actual realignment and fixation might leave room for error. Although in half of the patients, we used patientspecific cutting jigs to transfer the planned correction onto the patients’ radius and used a jig to indicate the angle of the osteotomy, reduction and fixation were done in a freehand manner with K-wires. Although cutting guides generally show beneficial in reconstructive surgery, based on our results we cannot yet draw conclusions on its added value. For accurate bone repositioning in future corrective osteotomy treatment, we recommend using reduction guides or patient-specific fixation plates.

The advantage of using an oblique single-cut rotation osteotomy is the correction of angular deformities in three dimensions while maintaining optimal bone contact. However, the method does not aim to correct translational displacements. Small rotational errors after corrective osteotomy of a diaphyseal malunion may scale to relatively large translational displacements at the distal articular level. This could partly explain the residual displacements in ulnarradial and volodorsal shifts.

Secondly, the preoperative plan does not take into account the soft tissue issues many of these deformed forearms have. Earlier (surgical) trauma often causes scar formation to structures like the interosseous membrane and makes the planned repositioning difficult to realise. Additionally, full geometric restoration of bony structures may hamper full mobility if there is too much stress on the soft tissue. Therefore, in some cases, complete correction was not obtained. Despite this issue, previously published data suggest a statistically significant correlation between residual malalignment and clinical outcome. When soft tissue allows, we expect that increased precision in radiological outcome will further optimise postoperative functional results.

The strength of this study is that we examined the postoperative positioning using 3D techniques. Only a few previous studies assessed postoperative results in 3D. However, they focussed on intra-articular distal radius malunions and expressed their findings in terms of radiological alignment, not functional outcome.

<table>
<thead>
<tr>
<th>Table 3. Functional results</th>
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</thead>
<tbody>
<tr>
<td>Case</td>
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<tr>
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<td></td>
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<td>1</td>
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<td>3</td>
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<td>4</td>
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<tr>
<td>5</td>
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<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>Average</td>
</tr>
</tbody>
</table>

NA, not available
a. Expressed in degrees and measured with a handheld goniometer

<table>
<thead>
<tr>
<th>Table 4. Differences in malalignment parameters compared to pre-op for patients treated with cutting guide versus visualization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malalignment parameter</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Ulnoradial shift in mm, ulnar (-), radial (+)</td>
</tr>
<tr>
<td>Volodorsal shift in mm, volar (-), dorsal (+)</td>
</tr>
<tr>
<td>Proximodistal shift in mm, shortened (-), lengthened (+)</td>
</tr>
<tr>
<td>Dorsopalmar tilt in deg, dorsal (-), volar (+)</td>
</tr>
<tr>
<td>Radial inclination in deg, ulnar (-), radial (+)</td>
</tr>
<tr>
<td>Axial rotation in deg, pronation (-), supination (+)</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range; deg, degrees, mm, millimetre
a. Independent samples Mann-Whitney U test
of postoperative articular displacement. Another study by Vroemen et al. evaluated the postoperative malalignment in 25 patients after a 2D planned corrective osteotomy using 3D imaging techniques. The median residual malalignments we presented in this study are comparable, but not per se superior to their results after a 2D planned corrective osteotomy. However, due to the lack of preoperative 3D malpositioning of their series and a potential selection of relatively complex cases in ours, full comparison is not possible.

The postoperative range of motion we found is better than previous studies with computer-assisted 3D planned corrective osteotomy in radial malunions. Athwal et al. included six patients with a distal radius malunion. They found an average postoperative range of motion of 89 of flexion-extension, 78% of pronation and 74% of supination after a mean follow-up of 25 months. Miyake et al. included 20 patients and reported a range of motion of 152 pronation and supination after a mean follow-up of 24 months.

Our functional results are also superior to published results of conventional 2D planned corrective osteotomies. A previous study that investigated the long-term results after 2D planned corrective osteotomy of distal malunions demonstrated a range of motion of 109 degrees of flexion-extension and 142 of pronation and supination after a mean follow-up of 13 years.

This study has several limitations. Due to the retrospective nature of this study, there was no predefined protocol for selecting patients. The decision to perform a computer-assisted 3D planned corrective osteotomy was made by the surgeon. Only patients with complex malunions were selected for this type of treatment. This approach has resulted in a selection bias and potentially limits the generalisability of our results. Due to the retrospective nature of this study, we were not able to acquire preoperative grip strength or functional questionnaires (e.g. DASH, PRWE), thus limiting the evaluation of functional outcome of the procedure. Another limitation is the heterogeneity of the population. We included subjects with both diaphyseal and extra-articular distal radius malunions. Distal malunions commonly show axial malalignment in pronation, whereas diaphyseal malunions typically involve angular deformation. Individual cases require different goals of correction. As mentioned, an oblique single-cut rotation osteotomy (OSCRO) aims to correct rotational deformities and is limited in providing ulnar or volodorsal shifts. This phenomenon—in combination with the low number of cases—may explain the lack of statistically significant improvement in individual directional parameters.

Some patients may benefit more from this 3D planned osteotomy than others. Future studies should focus on determining the appropriate indication for the use of 3D planning techniques in corrective osteotomy. This study suggests that virtual 3D planning of corrective osteotomies of radial malunions ameliorates alignment. Further enhancement of this technique is required to improve transfer of the preoperatively planned position to the intraoperative bone.
REFERENCES


PART 3
PROGNOSIS
CHAPTER 9

PREDICTORS OF UNSTABLE DISTAL RADIUS FRACTURES: A SYSTEMATIC REVIEW AND META-ANALYSIS

M.M.J. Walenkamp
S. Aydin
M.A.M. Mulders
J.C. Goslings
N.W.L. Schep

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INTRODUCTION

Initial treatment of patients with distal radius fractures generally consists of closed reduction and plaster immobilization. However, fracture re-displacement following closed reduction occurs in up to 64% of the patients (in part depending upon the definition). Most surgeons would agree that distal radius fractures with re-displacement outside acceptable parameters (>10° dorsal angulation, radial shortening >3mm or intra-articular step-off >) benefit from surgical fixation, taking into account patient-related factors. Patients with a distal radius fracture with a perceived high risk of re-displacement may be recommended primary surgical treatment. Unfortunately, patients with these potentially more unstable distal radius fractures are difficult to identify. In 1989, Lafontaine et al. identified five factors predictive of fracture instability: dorsal angulation exceeding 20° at presentation; dorsal comminution; extension of the fracture into the radiocarpal joint; an associated ulnar fracture; and age over 60 years. According to Lafontaine et al. a fracture can be considered potentially unstable if three or more factors are present. Since then, several studies have confirmed and refuted the importance of these five risk factors, and new clinical and radiological predictors have been identified. Other authors have quantified predictors and presented scoring systems to predict the risk of secondary displacement based on clinical and radiological variables. Although several risk factors of secondary displacement are commonly accepted, the evidence for some predictors is limited. An overview of all known predictors of fracture instability in literature, and their relative weight (pooled odds ratios), could assist physicians in decision-making regarding the optimal method of treatment for patients with distal radius fractures. The aim of this study was to perform a systematic review in order to identify predictors of secondary displacement in distal radius fractures.

METHODS

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A review protocol was drafted and registered on PROSPERO with number CRD42014010828. All of the following steps were performed by two independent reviewers (SA and MMJW). Disagreements between the two reviewers were discussed until a consensus was reached.

Eligibility criteria systematic review

Any study that could potentially provide information on predictors of secondary displacement was eligible for inclusion. Therefore, studies describing non-operative treatment in patients with distal radius fracture were also included. We anticipated that these studies would report secondary displacement during follow-up. Inclusion criteria were studies that addressed adult (18 years and older) patients with distal radius fractures initially treated with plaster immobilization, with or without closed reduction of the fracture. Reviews, animal studies, cadaver studies, case reports, surveys, current (management) concepts, edito-

ABSTRACT

The aim of this study was to perform a systematic review in order to identify predictors of secondary displacement in distal radius fractures. We performed a systematic review to identify all studies that reported secondary displacement following distal radius fractures. Where possible, we pooled the odds ratios of predictors. The initial search yielded 3178 studies of which 27 were included. Multiple studies found that age, shortening, volar comminution, loss of radial inclination, the presence of a volar hook, AO type 3 fractures (A3, B3, C3) and the Older classification were significant predictors of secondary displacement. Pooling revealed a significantly increased risk of secondary displacement in fractures with dorsal comminution, in women and in patients aged >60 years. An associated ulna fracture or intra-articular involvement does not result in an increased risk of secondary displacement. The overview provided in this study can help surgeons to inform patients of the chances of success of closed treatment regarding the radiological outcome and facilitate shared-decision making.
Synthesis of results of meta-analysis

For the meta-analysis, univariate odds ratios were pooled using the random effects model. The random effects model involves an assumption that the effects being estimated in the different studies are not identical, but follow some distribution.15 If coefficients from a logistic regression analysis were reported, odds ratios were calculated by taking the exponential. Odds ratios for instability or displacement at any point during follow-up (early or late) were added as separate odds ratios to the analysis. Data were pooled with the log odds ratio and the standard error (SE) with the generic inverse variance.

To test the robustness of the results, sensitivity analyses were performed by comparing the results obtained with the random effects model with the fixed effects models.15 Similar results imply that the results are robust.

Statistical heterogeneity for each analysis was tested with $I^2$. The $I^2$ is a statistic that indicates the percentage of variance and is qualified as follows: 0% to 40% (might not be important); 30% to 60% (may represent moderate heterogeneity); 50% to 90% (may represent substantial heterogeneity); 75% to 100% (considerable heterogeneity).15

RESULTS

Search results

The initial search yielded a total of 3178 studies, of which 2249 remained after excluding the duplicates. The full text manuscripts of 133 studies were evaluated and 27 studies were included in the systematic review (Fig 1).3,6,8-11,13,18-37 The full text manuscript of one study could not be procured, even after contacting the authors.38

Systematic review

The characteristics of the studies included are outlined in Table 2. All but three studies focused primarily on secondary displacement or radiographic outcome.20,35,37 One study excluded fractures that lost reduction within one week and assessed late secondary displacement at two months.22 Quality and risk of bias were variable (Table 1 and appendix 2). A total of 7574 patients were included. Secondary displacement occurred in 10% to 89% of the fractures. Forty-four different predictors of secondary displacement were reported. An overview of the most common predictors and in which study they were assessed is outlined in Table 3.

PREDICTORS OF UNSTABLE DISTAL RADIUS FRACTURES

Eligibility criteria meta-analysis

For the meta-analysis, an additional inclusion criterion was studies that reported odds ratios of predictors of secondary displacement, or provided sufficient information to calculate odds ratios. We required studies to have had a minimal radiological follow-up of 4 weeks for the assessment of secondary displacement.
Only a few predictors were also tested in a multivariable analysis, adjusting for other covariates. Of these, age, shortening, volar comminution, loss of radial inclination, the presence of a volar hook, AO type 3 fractures (A3, B3, C3) and the Older classification were found to be significant predictors in one or more studies.

The mechanism of the injury, the forces involved i.e. the estimated energy of the injury, the independence of a patient (defined as being able to go shopping), initial dorsal angulation >20° from neutral, the initial radial shift, the presence of an associated ulnar styloid fracture and the Frykman classification were revealed not to be significant predictors of secondary displacement in one or more studies that adjusted for other covariates.

For gender, initial ulnar variance, comminution and intra-articular involvement, there were studies that found a significantly increased risk of secondary displacement and others that did not.

**Meta-analysis**
We were able to extract or calculate odds ratios from 11 articles. We contacted the corresponding authors of four additional articles that reported $p$-values without odds ratios or only adjusted odds ratios to request additional information. The authors of two studies provided further data so we could extract or calculate odds ratios from 13 studies. Ten of these studies used a comparable definition for secondary displacement and were therefore eligible for pooling. Myderrizi et al. (2011) excluded patients with loss of reduction at one week and this study was therefore not included in the analysis. Wadsten et al. (2014) also analysed the 92 patients who went on to surgery because their post-reduction films revealed an unacceptable position and therefore we did not include this study. From the remaining eight articles we were able to pool the odds ratios of seven predictors. A total of 3807 patients were analysed. Female gender, age >60-65 years and dorsal comminution were significant predictors of secondary displacement (Figs 2-4). An associated ulnar styloid fracture, intra-articular involvement, dorsal angulation >15° from neutral and dorsal angulation >20° from neutral were not significantly associated with secondary displacement (Figure 5-8). A sensitivity analysis showed similar estimates in the random and fixed effects models (Table 4). The odds ratio of intra-articular involvement and dorsal angulation >15° from neutral were both significant only in the fixed effects model.
Figure 2. Forest plot of comparison female versus male. The four odds ratios from Mackenney et al. represent early and late instability in minimally displaced and displaced fractures. The odds ratios from Leone at al represent early and late instability in all fractures.

Figure 3. Forest plot of comparison age >60y versus <60-65y. Mackenney et al. represent early and late instability in minimally displaced and displaced fractures.

Figure 4. Forest plot of comparison dorsal comminution versus no comminution. The four odds ratios from Mackenney et al. represent early and late instability in minimally displaced and displaced fractures. The odds ratios from Leone at al represent early and late instability in all fractures.

Figure 5. Forest plot of comparison presence of associated ulnar styloid fracture versus intact ulnar styloid. The odds ratios from Leone et al. represent early and late instability in all fractures.

Figure 6. Forest plot of comparison intra-articular fracture involvement versus no involvement.

Figure 7. Forest plot of comparison dorsal angulation >15° from neutral versus dorsal angulation ≤15° from neutral.

Figure 8. Forest plot of comparison dorsal angulation >20° from neutral versus dorsal angulation ≤20° from neutral.

PART 3

PREDICTORS OF UNSTABLE DISTAL RADIUS FRACTURES

Figure 9. Forest plot of comparison dorsal angulation <15° from neutral versus dorsal angulation ≥15° from neutral.
DISCUSSION

This systematic review provides an overview of all predictors of secondary displacement of distal radius fractures in literature. We have demonstrated that not all popular predictors of instability that are persistently used in the literature have indeed been identified as significantly associated with secondary displacement. For instance, several studies that also adjusted for other covariates in their analyses did not find an increased risk of secondary displacement in fractures with an initial dorsal angulation exceeding 20° from neutral and neither in fractures with an associated ulnar styloid fracture.

For other popular risk factors such as the female gender, dorsal comminution and intra-articular involvement, the results were inconclusive. Some studies with adjusted analyses did find a significant influence on secondary displacement and others did not.

In an attempt to provide a definite answer, we pooled the odds ratios of seven predictors including gender, age >60-65, dorsal comminution, associated ulnar styloid fracture, intra-articular involvement and dorsal angulation exceeding 15° and 20° from neutral. Our results show a significantly increased risk of secondary displacement in fractures with dorsal comminution and in women. Additionally, the pooled results confirm the importance of age demonstrating a significantly increased risk of secondary displacement of distal radius fractures in patients older than 60-65 years.

Conversely, our analysis reveals no significantly increased risk of secondary displacement in fractures with a dorsal angulation exceeding 15° or 20° from neutral, an associated ulna fracture or intra-articular involvement.

Intra-articular involvement is often mentioned as an indication for surgery and is one of Lafontaine’s often cited risk factors. Nevertheless, we found no significant effect on secondary displacement of intra-articular fractures (0.52, p=0.07). When the fixed effects model was used, risk of secondary displacement in intra-articular fractures was significantly lower (OR: 0.5, p=0.03). An explanation for this is that in the fixed-effects analyses, studies are weighted less equally than in the random-effects. Therefore, the larger study of the two (that found a significant OR) has greater weight. Another possible reason could be that patients with more severe intra-articular fractures received primary operative treatment, resulting in less severe intra-articular fractures in the study population. The same reason may explain why dorsal angulation >15° from neutral was significant in the fixed-effects model and not in the random-effects model.

Another of Lafontaine’s risk factors is the presence of an associated ulnar styloid fracture, which is believed to result in injuries of the unocarpal ligaments and therefore constitute fracture instability. However, despite its popularity, this predictor was not identified as significantly associated with secondary fracture displacement in multiple studies. This is confirmed by the results of our meta-analysis that do not show an increased risk of secondary displacement for an associated ulnar styloid fracture.

The strength of this study is that it provides a complete and comprehensive overview of all predictors known in literature. There is a considerable advantage to the novel approach we took in this study to pool odds ratios of predictors. This is especially demonstrated by the pooled results for gender and dorsal comminution. Table 3 shows evidence for both predictors seems inconclusive; however, by pooling we found that both are significantly associated with secondary displacement. Gender is not commonly addressed in popular definitions of an unstable distal radius fracture. Moreover, gender has been refuted as a predictor by several studies (Table 3). It is possible that by pooling, we identified a predictor that did not previously reach significance due to small study sizes. Nevertheless, the effect of female gender could be mitigated when accounting for age because women reach a higher age than men and are more prone to suffer from osteoporosis. Thus the association between gender and fracture instability is probably indirect and should not be interpreted as direct causality.

This study has several limitations. The majority of studies that we included focused primarily on secondary displacement. Consequently, these studies only described patients who were treated conservatively. Patients treated initially with an operation were probably not included. This last group is likely to include the most unstable fractures. In our opinion, this limitation mostly applies to studies performed after the introduction of volar locking plates in 2000. Conversely, some patients might have been treated operatively who would have achieved excellent results with conservative treatment. Unfortunately, the decisions to perform primary surgical fixation and exclude these patients were only reported in a few studies. Intra-articular involvement, volar fracture displacement or open fractures were most commonly mentioned.

A limitation regarding the meta-analysis is the variation among study populations: four studies provided one common odds ratio for both non-displaced and displaced fractures; one study only provided odds ratios for displaced fractures; and one study reported separate odds ratios for displaced and minimally displaced fractures. We were unable to extract separate odds ratios for non-displaced and displaced fractures and therefore combined these data.

Of particular note is the definition of secondary displacement varied considerably across studies (Table 2). All studies included an alteration in dorsal angulation as a criterion of displacement in their definition. However, cut-off values varied from an absolute dorsal angulation of 10° or 15° from neutral to a change of 5°. The pooled odds ratios we found should therefore be interpreted with some caution.

Despite the obvious variability among studies, the statistical heterogeneity tests showed an I² of 48% or less for all analyses but one. The heterogeneity for dorsal comminution was
considerable ($I^2 = 78\%$). A possible explanation for this could be that the assessment of the presence of dorsal comminution was more subjective and variable across studies than other predictors such as age and gender.

These limitations emphasize the need for consistency of definitions, measurement methods and a structured follow-up for patients with distal radius fractures. Standardization would allow easier comparison of studies and contribute to a higher level of evidence.

This systematic review provides a comprehensive overview of all known predictors and non-predictors of secondary displacement in patients with distal radius fractures. We have demonstrated that, despite their popularity as predictors of secondary displacement, distal radius fractures with an associated ulna fracture, a dorsal angulation $>15^\circ$ or $>20^\circ$ from neutral, and intra-articular fractures do not have an increased risk of secondary displacement. We did find a significantly increased risk of secondary displacement for patients older than 60-65, women and fractures with dorsal comminution. Our results can provide a good basis for surgeons to inform patients on the probability of secondary displacement and therefore the chances of success from conservative treatment. This will facilitate shared-decision making between patient and surgeon. Nevertheless, since secondary displacement does not always entail poor functional results after conservative treatment, especially in elderly patients (Bartl et al., 2014) future studies should focus on pooling important predictors of functional outcome.
REFERENCES


CHAPTER 10

VALIDATION OF A PREDICTION MODEL FOR INSTABILITY IN DISTAL RADIAL FRACTURES

M.M.J. Walenkamp
J. van Hilst
J.C. Goslings
N.W.L. Schep

Submitted
INTRODUCTION
Instability of distal radius fractures has often been subject of investigation in an attempt to timely select those patients requiring surgery. Non-displaced fractures generally tend to be stable and can be managed conservatively. However, treatment of displaced and potentially unstable fractures continues to stimulate debate. Preferably, patients with a displaced distal radius fracture with a high risk of early loss of reduction are selected for preemptive surgical treatment. Unfortunately, these potential unstable distal radius fractures are difficult to identify.

Mackenney et al. published a prediction model to predict early instability in distal radius fractures. Based on age, the presence of comminution and ulnar variance, the model predicts the probability of instability occurring within the first two weeks after the injury. The study was very well-designed and the model was based on data of over 4,000 patients. However, although the model is available as an online calculator and can thus be used in clinical practice, it has never been externally validated. External validation, or evaluating the performance of a prediction model in a new patient population, is essential before its implementation elsewhere.

The aim of this study was to externally validate this model in a different patient population with displaced distal radius fractures. We sought to examine how the model would perform in a new patient population and what its sensitivity and specificity for correctly identifying an unstable fracture would be.

METHODS
Source of data and participants
For this retrospective cohort study, we included all consecutive adult patients with a displaced distal radius fracture who were treated conservatively between 2009 and 2014. The primary outcome was early (<2 weeks) instability. The validity of the model was assessed by comparing the predicted probabilities of early instability with the observed early instability. We calculated the ability of the model to discriminate between patients with and without early instability (Area under the Receiver Operating Characteristics Curve [AUC]). Additionally, we determined its sensitivity and specificity.

Results
Ninety-nine patients were included and early instability occurred in 61 patients (62%). The AUC of the model was 0.53 (95% CI: 0.41 - 0.64), indicating poor discrimination. The sensitivity and specificity for correctly identifying an unstable fracture were 1.6% (95% CI: 0.9% - 9.9%) and 94.7% (95% CI: 80.9% - 99.1%) respectively.

Conclusions
External validation of Mackenney’s prediction model for early instability in displaced distal radius fractures revealed a disappointing performance. Therefore we conclude that the model in its current form is unsuitable for a population other than the population from which it was derived.
injury. Because Mackenney's criteria for an unacceptable position differ from Dutch guidelines, we evaluated two definitions of early instability: According to Mackenney et al., an unacceptable position is a fracture with dorsal angulation of >0° and/or an ulnar variance of >3 mm. According to Dutch guidelines, an unacceptable position is defined as ≥15° dorsal angulation or ≥20° volar angulation of the distal fracture fragment, ≥5mm shortening or <15° radial inclination.

Predictors
According to hospital protocol, patients were evaluated clinically and radiographically at presentation, following closed reduction, and at approximately one week and six weeks after injury. Radiographic evaluation comprised standard posteroanterior and lateral radiographs. The first author retrospectively determined the following criteria on all X-rays: AO fracture classification, dorsal or volar angle, radial inclination, radial height, ulnar variance and radial shift (in millimetres), and the presence of any comminution. Mackenney et al. expressed ulnar variance as difference between the injured side and the normal (uninjured) side. However, since we do not regularly image the uninjured wrist, ulnar variance was calculated as the difference between the injured side and the normal value (0.49 mm). All radiographs were measured using the functions available on the computerised radiographical system (IMPAX) with a digital ruler and protractor.

Analysis
We reported medians and interquartile range (IQR) for non-parametric variables, and means and standard deviations (SD) for normally distributed variables. The Shapiro-Wilk test was used for testing normality.

For each patient, the probability of early instability was calculated according to the published formula: X = 0.03 * age + 0.38 * (if comminution is present) + 0.21 * ulnar variance -3.12. The probability of instability equals (ex / [1 + ex]) * 100.

To estimate the ability of the model to discriminate between patients with and without instability, we calculated the Area under the Receiver Operating Characteristics Curve (AUC). The AUC ranges from 0.5 to 1, with higher score indicating better discrimination. The calibration of the model (the agreement between observed outcomes and predictions) was assessed by plotting the predicted probability of instability and the observed frequency of occurrence of instability. The ideal is a slope of 1 for the observed versus predicted risks.

Decision-making in the treatment of displaced distal radius fractures requires a binary outcome: is the fracture stable or unstable? The predictive formula of Mackenney et al. generates a percentage risk of instability. The authors demonstrated that for the prediction of malunion in displaced fractures, the cut-off is best set at approximately 70% (<70% probability of instability constitutes a stable fracture, ≥70% probability constitutes an unstable fracture). Therefore, we calculated the sensitivity and specificity for a cut-off of 70%.

Data entry and analysis were performed with the Statistical Package for Social Sciences (SPSS) version 20.0 for Windows (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) and R Gui version 3.1.2 (R Development Core Team (2008,R Foundation for Statistical Computing, Vienna, Austria). A p-value of ≤0.05 was considered statistically significant.

RESULTS
During the study period there were 515 patients with a distal radius fracture. A total of 99 patients were eligible and included in the analysis (Figure 1). The characteristics of the study population are outlined in Table 1. The probability of early instability according to the model ranged from 5% to 89% with a median probability of 33%. Early instability occurred in 61 patients (62%).
DISCUSSION

External validation of Mackenney’s prediction rule for early instability showed poor discrimination and calibration. The AUC of 0.53 represents a discriminative ability that is equal to a coin toss. Applying a 70% cut-off for the predicted probability (a probability of <70% constitutes a stable fracture, ≥70% probability constitutes an unstable fracture) resulted in good specificity (95%) but very low sensitivity (<2%) for predicting instability.

This study has several limitations. Due its retrospective nature, selection of patients for surgery did not follow a protocol. As discussed above, this has resulted in a study population that is not clearly defined and therefore limits the generalizability of our results. We also had to exclude a considerable number of patients due to missing radiographs. Our hospital is situated in a city that is frequently visited by tourists who are followed up elsewhere. The follow-up evaluation radiographs of these patients were missing and therefore the occurrence of early instability could not be determined.

Another study limitation and possible reason for the model’s poor performance is the method we used to determine the ulnar variance. Mackenney et al. calculated the ulnar variance

### Table 1. Characteristics of study population (N=99)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, IQR)</td>
<td>63 (54 - 74)</td>
</tr>
<tr>
<td>Sex (female), No. (%)</td>
<td>73 (74)</td>
</tr>
<tr>
<td>AO fracture classification, No. (%)</td>
<td>55 (56)</td>
</tr>
<tr>
<td>A</td>
<td>20 (20)</td>
</tr>
<tr>
<td>B</td>
<td>24 (24)</td>
</tr>
<tr>
<td>C</td>
<td>61 (62)</td>
</tr>
<tr>
<td>Early instability Dutch, Number (%)</td>
<td>18 (18)</td>
</tr>
</tbody>
</table>

a. Instability according to the Dutch guidelines: 15˚dorsal angulation or ≥20˚volar angulation of the distal fracture fragment, ≥5mm shortening or <15˚radial inclination.

The ability of the model to discriminate between patients with and without early instability expressed as the AUC was 0.53 (95% CI: 0.41 - 0.64). The calibration slope of the model was -0.10 (95% CI: -0.62 - 0.41).

When applying the suggested 70% cut-off (≥70% probability of instability constitutes a stable fracture, <70% probability constitutes an unstable fracture), the model showed a sensitivity of 1.6% (95% CI: 0.9% - 9.9%) and a specificity of 94.7% (95% CI: 80.9% - 99.1%) for correctly identifying an unstable fracture (Table 2).

### Table 2. Performance of the model to when cut-off was applied (N=99)

<table>
<thead>
<tr>
<th></th>
<th>Unstable fracture</th>
<th>Stable fracture</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted probability ≥70%</td>
<td>1 (3)</td>
<td>60 (96)</td>
<td>99</td>
</tr>
<tr>
<td>Predicted probability &lt;70%</td>
<td>2 (2)</td>
<td>36 (38)</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (95% CI)</td>
<td>1.6% (0.9% - 9.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity (95% CI)</td>
<td>94.7% (80.9% - 99.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, Confidence Interval

According to the more liberal Dutch guidelines, only 18 patients (18%) showed early fracture instability. Using this definition as the predicted outcome, the AUC of the model was 0.71 (95% CI: 0.58 - 0.84) for predicting this type of instability (Figure 2). The calibration slope was 0.85 (95% CI: 0.14 - 1.6). The model showed a sensitivity of 0% (95% CI: 0% - 21.9%) and a specificity of 96.3% (95% CI: 88.9% - 99.0%) for correctly identifying an unstable fracture.
CONCLUSION

Unfortunately, external validation of Mackenney’s prediction rule for early instability in a different population showed poor discrimination and calibration. Recalibration of the model by adjusting the intercept for a new population would not have led to better results. Our results do not discredit the model itself, merely its performance in another patient population. Surprisingly, the model performed better when it was used to predict early instability according to the more liberal Dutch guidelines. Nevertheless, its sensitivity remained equally low. Therefore we conclude that the model in its current form is unsuitable for a population other than the population from which it was derived.

The poor performance of the model could also be explained by the differences between the study populations. In our population, primary operative treatment was selected for most displaced intra-articular fractures, and some displaced extra-articular distal radius fractures based on surgeons’ preference. In Mackenney’s population, primary operative treatment was selected for all intra-articular fractures or volarly displaced fractures. Of the 1595 displaced fractures they included, early instability occurred in 682 (43%). Our more conservative selection of patients for operative treatment may have resulted in a less favourable population with a higher a priori probability of instability. The higher percentage of patients with early instability in our sample (62% versus 43%) supports this theory.

Predictors of loss of reduction or instability in distal radius fractures have been studied extensively. However, the definition of loss of acceptable reduction varies across studies. In general, the Dutch definition is more liberal, allowing up to 15 degrees of dorsal angulation or 20 degrees of volar angulation, and 5 mm of shortening. Surprisingly, the model performed better when it was used to predict early instability according to the Dutch guidelines. Although the model was not designed to predict this outcome, both the discrimination and the calibration were higher. Nevertheless, decision-making in the treatment of displaced distal radius fractures requires a binary outcome: is the fracture stable or unstable? When applying the cut-off of 70% (<70% stable, ≥70% unstable), specificity of the model was good (96%), but its sensitivity was very low (0%).

Clinical prediction models can assist and support shared decision making between patients and physicians. Especially well-designed models derived from large samples such as the model from Mackenney, can provide a useful tool. However, evaluating the validity of a prediction model in a new patient population is essential before its implementation. The validity of a model can be assessed by comparing the observed outcomes with the predicted probabilities. Subsequently, the model may be updated to improve predictions in the population examined.
REFERENCES


CHAPTER 11

THE MINIMUM CLINICALLY IMPORTANT DIFFERENCE OF THE PATIENT-RATED WRIST EVALUATION SCORE FOR PATIENTS WITH DISTAL RADIUS FRACTURES

M.M.J. Walenkamp
L.M. Vos
R.J.O. de Muinck Keizer
J.C. Goslings
M.P. Rosenwasser
N.W.L. Schep

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ABSTRACT

Background
The Patient-rated Wrist Evaluation (PRWE) is a commonly used instrument in upper extremity surgery and in research. However, to recognize a treatment effect expressed as a change in PRWE, it is important to be aware of the minimum clinically important difference (MCID) and the minimum detectable change (MDC). The MCID of an outcome tool like the PRWE is defined as the smallest change in a score that is likely to be appreciated by a patient as an important change, while the MDC is defined as the smallest amount of change that can be detected by an outcome measure. A numerical change in score that is less than the MCID, even when statistically significant, does not represent a true clinically relevant change. To our knowledge, the MCID and MDC of the PRWE have not been determined in patients with distal radius fractures.

Questions/Purposes
We asked: (1) What is the MCID of the PRWE score for patients with distal radius fractures? (2) What is the MDC of the PRWE?

Methods
Our prospective cohort study included 102 patients with a distal radius fracture and a median age of 59 years (interquartile range [IQR], 48-66 years). All patients completed the PRWE questionnaire during each of two separate visits. At the second visit, patients were asked to indicate the degree of clinical change they appreciated since the previous visit. Accordingly, patients were categorized in two groups: (1) minimally improved or (2) no change. The groups were used to anchor the changes observed in the PRWE score to patients’ perspectives of what was clinically important. We determined the MCID using an anchor-based receiver operator characteristic method. In this context, the change in the PRWE score was considered a diagnostic test, and the anchor (minimally improved or no change as noted by the patients from visit to visit) was the gold standard. The optimal receiver operator characteristic cutoff point calculated with the Youden index reflected the value of the MCID. Results in our study, the MCID of the PRWE was 11.5 points. The area under the curve was 0.54 (95% CI: 0.37 - 0.70) for the pain subscale and 0.71 (95% CI: 0.57 - 0.85) for the function subscale. We determined the MDC to be 11.0 points.

Conclusions
We determined the MCID of the PRWE score for patients with distal radius fractures using the anchor-based approach and verified that the MDC of the PRWE was sufficiently small to detect our MCID.

Clinical Relevance
We recommend using an improvement on the PRWE of more than 11.5 points as the smallest clinically relevant difference when evaluating the effects of treatments and when performing sample-size calculations on studies of distal radius fractures.

INTRODUCTION
A frequently used outcome measure in distal radius fracture studies is the Patient-rated Wrist Evaluation (PRWE) score. The PRWE is a 15-item questionnaire designed to measure a patient’s wrist pain and disability. It consists of two subscales (pain and function) and has a score range from 0 (no disability) to 100 (severe disability).

To recognize a treatment effect expressed as a change in PRWE score, it is important to be aware of the minimum clinically important difference (MCID) of the PRWE score. The MCID represents the smallest change in score that would be perceived by the patient as beneficial. Consequently, a numeric change in score that is less than the MCID, even if statistically significant, does not represent a true clinically relevant change. Because the MCID defines a difference that is considered important to patients, the MCID also serves as the basis for estimating the necessary sample size in designing future studies.

Another important instrument is the minimum detectable change (MDC). The MDC is the smallest amount of change that falls outside the measurement error of an instrument. Therefore, any change smaller than the MDC could be the result of the variability of the questionnaire. To ensure that the MDC is sufficiently small to detect the MCID, the MDC should be greater than the MDC.

The MCID and the MDC of the PRWE have been examined in patients with chronic wrist conditions; however, to our knowledge, they have not been determined in patients with a distal radius fracture. Therefore, the purpose of our study was to determine the MCID and MDC of the PRWE score in patients with distal radius fractures.

PATIENTS AND METHODS
Our prospective cohort study was conducted alongside two ongoing clinical trials that are coordinated from our institution, an academic Level-1 trauma center in The Netherlands. The medical ethical review committee granted approval before initiation of this parallel study, without the need for informed consent from patient participants.

Patients for our cohort study were recruited from the two ongoing clinical trials between January 2011 and July 2014, during their first visit to the outpatient clinic. To increase the size of our cohort study population, we also recruited patients with distal radius fractures at the outpatient clinic who were not enrolled in the clinical trials. The patients who were not participants of the clinical trial were enrolled in our study between January 2014 and July 2014.

Our study population consisted of 102 patients with distal radius fractures. Patients were excluded if they: (1) did not want to complete the questionnaire at the outpatient clinic; (2) did not complete the anchor questions; (3) were unable to understand the study information; or (4) had sustained their distal radius fracture more than 1 year before their visit to the outpatient clinic.
Of the two concurrent clinical trials occurring during our prospective cohort study, the first trial included 42 patients who underwent a study of two- and three-dimensional imaging. This trial provided 42 adult patients with intraarticular distal radius fractures who were treated with open reduction and internal fixation with a volar locking plate.

The second trial randomized patients with displaced extraarticular distal radius fractures (AO types A2 and A3) between treatment with either open reduction and internal fixation with a volar locking plate or plaster immobilization. This trial provided 39 patients.

Additionally, during the first 6 months of 2014, we identified 55 patients who were not enrolled in either clinical trial but who were eligible for participation in our study. All adult patients with a distal radius fracture were eligible for inclusion, regardless of the type of treatment they received. After exclusion, an additional 21 patients with a distal radius fracture who were not enrolled in either of the two trials were included in our study cohort.

There are two methods to define the MCID: (1) a distribution-based and (2) an anchor-based approach. The distribution-based approach is used to evaluate if the observed effect is attributable to true change or simply the variability of the questionnaire. It examines the distribution of observed scores in a group of patients. The magnitude of the effect is interpreted in relation to variation of the instrument. In other words, is the observed effect attributable to true change or simply the variability of the questionnaire?

The anchor-based approach uses an external criterion (the anchor) to determine the MCID. Possible anchors include objective measurements, such as prehensile grip strength and ROM, or patient-reported anchor questions. The purpose of a patient-reported anchor question is to “anchor” the changes observed in the PRWE score to patients’ perspectives of what is clinically important.

Anchor-based methods to determine the MCID are preferred because an external criterion is used to define what is clinically important; however, the anchor-based method does not take into account the measurement error of the instrument, so it is valuable to use the anchor- and distribution-based approaches. To avoid confusion, the distribution-based method generally is referred to as minimum detectable change (MDC), and the anchor-based method as MCID. We use the same terms to identify the methods.

Data were collected prospectively. Patients completed the Dutch version of the PRWE questionnaire during two visits at approximately 6 to 12 weeks and approximately 12 to 52 weeks after distal radius fracture injury.

At the second visit, patients were asked to indicate the degree of clinical change they had noticed since the previous visit for each domain (pain and function). Patients noted their answers on a global rating of change scale (GRC) from -5 (much worse) to +5 (much better) (Fig. 1). The purpose of this question was to “anchor” the changes observed in the PRWE score to patients’ perspectives regarding what is clinically important.

There is no consensus regarding the required sample size to determine the MCID. We made a sample size estimation based on a conservatively estimated MCID of 12 points, with a SD of ± 14. To achieve an a of 0.05 and a power of 80%, we required 18 data points representing no change, and 18 data points representing minimal improvement.

Fig. 1 The global rating of change (GRC) scale used in the Patient-rated Wrist Evaluation (PRWE) questionnaire is shown. The anchor questions allowed patients to assess their current health status regarding wrist function and wrist pain, and compare their status with that of their previous visit.

1. Pain

Rate the pain in your wrist compared to your previous visit. Please indicate your answer on the scale below.

\[
\begin{align*}
\text{Much worse} & \quad \text{No change} & \quad \text{Much better} \\
-5 & \quad -4 & \quad -3 & \quad -2 & \quad -1 & \quad 0 & \quad 1 & \quad 2 & \quad 3 & \quad 4 & \quad 5
\end{align*}
\]

2. Function

Rate your wrist function compared to your previous visit. Please indicate your answer on the scale below.

\[
\begin{align*}
\text{Much worse} & \quad \text{No change} & \quad \text{Much better} \\
-5 & \quad -4 & \quad -3 & \quad -2 & \quad -1 & \quad 0 & \quad 1 & \quad 2 & \quad 3 & \quad 4 & \quad 5
\end{align*}
\]

Statistical Methods

The number of questions not answered by patients comprised less than 5% for all items and were replaced with the mean score of the subscale according to the PRWE user manual. PRWE scores were calculated for both subscales (pain and function) using the published algorithm. The change in outcome was calculated as the difference between the last and the first scores. The change in score between visits was transformed such that improvement was indicated by a positive value. We reported medians and interquartile ranges (IQR) for nonparametric variables, and means (± SD) for normally distributed variables. The Kolmogorov-Smirnov test was used to determine if a variable was normally distributed. A p value of 0.05 or less was considered statistically significant. Data entry and analysis were performed using SPSS (Version 20.0; IBM Corp, Armonk, NY, USA) and R Studio Version 3.1.2; R Studio, Boston, MA, USA), with the package coefficient alpha.
**Determination of MDC**

We calculated the MDC for the pain and function subscales separately and summed them to obtain the total MDC.\(^1\) The MDCs were calculated as:

\[
z \text{ score}_{0.90} = \sqrt{2} \times \text{Standard Error of Measurement}_{\text{PRWE}}
\]

A z score of 1.65 was chosen to reflect a 90% one-sided CI, similar to previous studies.\(^6,7\) The standard error of measurement is a measure of the instrument variability and takes into account the distribution of repeated measures on a questionnaire around the “true” score of a patient. For our study, the standard error of measurement was calculated by multiplying the SD (σ) of the PRWE score at the second follow-up, by the square root of 1, minus the reliability coefficient (r) of the instrument, or, in formula\(^15,19.\):

\[
\text{Standard Error of Measurement} = \sigma \times \sqrt{1 - r}
\]

The reliability coefficient is the overall consistency of an instrument. We used Cronbach’s alpha as a parameter of reliability.\(^20\) Cronbach’s alpha is used to measure the internal consistency of a (sub)scale. Its value can range from 0 to 1.0, where greater than 0.7 indicates good internal consistency.\(^20\)

**Determination of the MCID**

We calculated the MCID according the receiver operating characteristic (ROC) curve method.\(^7,21\) In this context, the change in PRWE score was considered a diagnostic test and the anchor was the gold standard.\(^21\) The ROC curve plots the sensitivity against 1-specificity for all possible cutoff points of the change in PRWE score. The optimal ROC cutoff point is the value for which the sum of percentages of false positive and false negative classifications is smallest \((1 - \text{sensitivity}) + (1 - \text{specificity})\).\(^21\) This value represents the MCID. The area under the ROC curve reflects the ability of the change in PRWE score to differentiate between patients with and without clinically important change. The area under the ROC curve ranges from 0.5 to 1; a higher score indicates better discrimination.

Consistent with previous studies\(^8,22\), patients were categorized in five groups according to their answer to the anchor question: -5 to -4 (marked worsening); -3 to -2 (minimal worsening); -1 to 1 (no change); 2 to 3 (minimal improvement); and 4 to 5 (marked improvement). We calculated the MCID by plotting the ROC of the change in PRWE score for patients in the minimal-improvement group compared with patient scores in the no-change group.

We tested for significant score changes among patients who indicated they had experienced marked worsening, minimal worsening, no change, minimal improvement, and marked improvement, using the Kruskal-Wallis test. Nonsignificant differences among the five patient categories could suggest that the improvement categories were not sufficiently discrimina-
### RESULTS

#### MCID of the PRWE for Patients with Distal Radius Fractures

The overall MCID was 11.5 points on the PRWE (Table 2). For the pain subscale, 20% of the patients (20/102) indicated they had experienced minimal improvement and 37% (38/102) experienced no change. The area under the ROC curve of the change in PRWE score to differentiate between patients with minimal improvement in pain and patients with no change in pain was 0.54 (95% CI: 0.37-0.70). For the function subscale, 24% of the patients (24/102) reported minimal improvement in function and 34% (35/102) experienced no change. The area under the ROC curve of the change in PRWE score to differentiate between patients with minimal improvement in function and no change in function was 0.71 (95% CI: 0.57-0.85).

#### MDC of the PRWE

The MDC was 11.0 points. The majority of patients reported marked improvement (Table 3) and the PRWE scores between the first and the second measurements differed (p< 0.001; Wilcoxon signed rank test). For the pain subscale, 40 patients reported marked improvement (change in PRWE, 9.5; IQR, 5.0 - 16.0), and 20 patients had minimal improvement (change in PRWE, 5.0; IQR, -1.8 to 10.7). For the function subscale, 41 patients reported marked improvement (change in PRWE, 12.5; IQR, 5.8 - 19.7), and 24 patients had minimal improvement (change in PRWE, 10.8; IQR, 3.6 - 18.8).

There were significant differences in the changes in PRWE scores among patients who indicated they had experienced marked worsening, minimal worsening, no change, minimal improvement, or marked improvement in pain (p = 0.001, Kruskal-Wallis test), suggesting sufficiently discriminative categories (Table 3). There also were significant differences in the changes in PRWE scores among the categories of the function subscale (p<0.001, Kruskal-Wallis test).

There was correlation between the change in PRWE scores for the pain subscale and the GRC categories, confirming the adequacy of the GRC (correlation coefficient = 0.39; two-tailed p<0.001). The correlation between the change in PRWE score and GRC categories for function was similar (correlation coefficient = 0.34; two-tailed p = 0.001). Reliability coefficients (Cronbach’s alpha) were 0.98 for the pain subscale and 0.95 for the function subscale, indicating good internal consistency of the questionnaire.

#### DISCUSSION

The PRWE score is a well-accepted measure of patient functional outcome after distal radius fracture. Knowledge of the MCID of the PRWE provides a useful benchmark to interpret study results and a basis for sample size calculations. Three previous studies have examined the MCID of the PRWE; however, to our knowledge, no such study has examined patients with distal radius fractures. Some authors advocate that the MCID is not a universal fixed attribute and cannot be applied across patient populations or disease-specific states. The MCID can fluctuate based on what is interpreted as important to the patient; therefore,
The MDC is the smallest change in score that likely reflects true change rather than measurement error. It shows which changes fall outside the measurement error of the health status measurement (based on, for instance, internal validity or test-retest reliability).\(^1\) To ensure that the MDC is sufficiently small to detect the MCID, it should be greater than the MDC. We found an MDC of 11.0 points, similar to the MDCs reported by Kim and Park (7.7 points)\(^7\) and Schmitt and Di Fabio (12.2 points).\(^6\) This value for the MDC indicates that the PRWE questionnaire is able to detect changes as small 11.0 points, therefore the PRWE should be able to detect the MCID we determined.

In our prospective cohort study, we determined the MCID of the PRWE for patients with distal radius fractures using the anchor-based approach and verified that the MDC of the PRWE was sufficiently small to detect our MCID.

The MCID is not a value that can be used to classify individual treatment results, but rather a method to put group level treatment effects in perspective. We recommend using an improvement on the PRWE of more than 11.5 points as the smallest clinically relevant difference when evaluating the effects of treatments and when performing sample-size calculations on studies of distal radius fractures.

The MCID for our patients was 11.5 points, which was lower than previously determined MCIDs. Three previous studies have examined the MCID of the PRWE. Schmitt and Di Fabio\(^6\) reported a MCID of 24 points in a cohort of 211 patients, however their patients predominately had shoulder pain, and the PRWE is not intended for patients with shoulder injuries. The second study, by Sorensen et al.\(^8\), included 102 patients with a traumatic upper-extremity conditions such as isolated tendinitis, arthritis, and nerve compression syndrome. The MCID in that study was 14 points. The third study included 31 patients who underwent ulnar-shortening osteotomy for ulnar impaction syndrome and the MCID was 17 points.\(^7\)
REFERENCES


25. Wright JG. The minimal important difference: who’s to say what is important? J Clin Epidemiol 1996 Nov;49(11):1211-1222.


APPENDIX

Chapter 2

Number of patients with missings according to variable

<table>
<thead>
<tr>
<th>Variables</th>
<th>Derivation cohort</th>
<th>Validation cohort</th>
</tr>
</thead>
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<td></td>
<td>(n = 487), No. (%)</td>
<td>(n = 395), No. (%)</td>
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<td>320 (81.0)</td>
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<td>0</td>
</tr>
<tr>
<td>Sex</td>
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<td>0</td>
</tr>
<tr>
<td>Mechanism of injury</td>
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</tr>
<tr>
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<td>7 (1.8)</td>
</tr>
<tr>
<td>Distal radius tender to palpation</td>
<td>0 (0.6)</td>
<td>1 (0.3)</td>
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<tr>
<td>Dorsiflexion</td>
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<td>2 (0.5)</td>
</tr>
<tr>
<td>Palmar flexion</td>
<td>3 (0.6)</td>
<td>7 (1.8)</td>
</tr>
<tr>
<td>Supination</td>
<td>3 (0.6)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Pronation</td>
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<td>4 (1.0)</td>
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<td>5 (1.3)</td>
</tr>
<tr>
<td>Radial deviation</td>
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</tr>
<tr>
<td>Radioulnar ballottement test</td>
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<td>17 (4.3)</td>
</tr>
<tr>
<td>Axial compression of forearm</td>
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<td>14 (3.5)</td>
</tr>
<tr>
<td>Prehensile grip strength</td>
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<td>45 (11.4)</td>
</tr>
<tr>
<td>Distal radius fracture (outcome)</td>
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Characteristics of patients with and without prehensile grip strength as missing variable

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<th>Non-missing (N=782)</th>
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<td>49 (31-63)</td>
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<tr>
<td>Female, No. (%)</td>
<td>59 (59.0)</td>
<td>473 (60.5)</td>
</tr>
<tr>
<td>Patients with distal radius fracture, No. (%)</td>
<td>57 (57.0)</td>
<td>327 (41.8)</td>
</tr>
<tr>
<td>Patients with other wrist fracture than distal radius No. (%)</td>
<td>13 (13.0)</td>
<td>73 (9.3)</td>
</tr>
<tr>
<td>Patients with multiple wrist fractures No. (%)</td>
<td>13 (13.0)</td>
<td>73 (9.3)</td>
</tr>
<tr>
<td>Complete cases</td>
<td>92 (92.0)</td>
<td>753 (96.3)</td>
</tr>
</tbody>
</table>

a. Patient without a distal radius fracture but with an isolated fracture of the ulna or one of the carpal bones.
b. Patients that sustained a fracture of distal radius and one of the carpal bones.
c. Patients with and without fractures
d. Not recorded in patients files

APPENDIX

Chapter 2

Number of patients with missings according to variable

<table>
<thead>
<tr>
<th>Variables</th>
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<th>Validation cohort</th>
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<td>320 (81.0)</td>
</tr>
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<td>Age</td>
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<td>0</td>
</tr>
<tr>
<td>Sex</td>
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</tr>
<tr>
<td>Mechanism of injury</td>
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<td>0</td>
</tr>
<tr>
<td>Swelling of distal radius</td>
<td>1 (0.2)</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Visible deformation</td>
<td>4 (0.8)</td>
<td>7 (1.8)</td>
</tr>
<tr>
<td>Distal radius tender to palpation</td>
<td>0 (0.6)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Dorsiflexion</td>
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<td>2 (0.5)</td>
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<tr>
<td>Palmar flexion</td>
<td>3 (0.6)</td>
<td>7 (1.8)</td>
</tr>
<tr>
<td>Supination</td>
<td>3 (0.6)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Pronation</td>
<td>3 (0.6)</td>
<td>4 (1.0)</td>
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<tr>
<td>Ulnar deviation</td>
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<td>Radial deviation</td>
<td>3 (0.6)</td>
<td>8 (2.0)</td>
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<tr>
<td>Radioulnar ballottement test</td>
<td>16 (3.3)</td>
<td>17 (4.3)</td>
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<tr>
<td>Axial compression of forearm</td>
<td>11 (2.3)</td>
<td>14 (3.5)</td>
</tr>
<tr>
<td>Prehensile grip strength</td>
<td>55 (11.3)</td>
<td>45 (11.4)</td>
</tr>
<tr>
<td>Distal radius fracture (outcome)</td>
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</table>

a. Data from the academic hospital.
b. Data from the other four hospitals.
### Appendix 1: Clinical Variables of the CRF

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
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<tr>
<td>Sex</td>
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<td>Age</td>
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<tr>
<td>Swelling of distal radius</td>
<td></td>
</tr>
<tr>
<td>Swelling of distal ulna</td>
<td></td>
</tr>
<tr>
<td>Swelling of anatomical snuff box</td>
<td></td>
</tr>
<tr>
<td>Visible deformation</td>
<td></td>
</tr>
<tr>
<td>Bone tenderness</td>
<td></td>
</tr>
<tr>
<td>- distal radius</td>
<td></td>
</tr>
<tr>
<td>- distal ulna</td>
<td></td>
</tr>
<tr>
<td>- anatomical snuff box</td>
<td></td>
</tr>
<tr>
<td>Active mobility painful</td>
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</tr>
<tr>
<td>- dorsiflexion</td>
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<td>- palmar flexion</td>
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</tr>
<tr>
<td>- supination</td>
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</tr>
<tr>
<td>- pronation</td>
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<td>- ulnar deviation</td>
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<tr>
<td>Functional tests painful</td>
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<tr>
<td>- radio ulnar ballottement test</td>
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<td>- axial compression of forearm</td>
<td></td>
</tr>
<tr>
<td>Prehensile grip strength</td>
<td></td>
</tr>
</tbody>
</table>

a. Items were scored positive if the patient experienced pain, if they were unable to perform the test or if they refused to perform the test.

b. Test is positive if pain or tenderness occurs when the ulna is translated from volar to dorsal while the radius manually fixated.

c. Both sides assessed three times with a Baseline Hydraulic Hand Dynamometer, expressed in percentage of decrease in grip strength between the healthy and the mean affected side.

### Appendix 2: Missing variables

<table>
<thead>
<tr>
<th>Missing variables</th>
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<tr>
<td>Swelling of distal radius present</td>
<td>1 (0.1)</td>
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<tr>
<td>Swelling of distal ulna present</td>
<td>32 (4.1)</td>
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<tr>
<td>Visible deformation</td>
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</tr>
<tr>
<td>Bone tenderness distal radius</td>
<td>2 (0.3)</td>
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<tr>
<td>Bone tenderness distal ulna</td>
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</tr>
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<td>Bone tenderness anatomical snuff box</td>
<td>3 (0.4)</td>
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<tr>
<td>Dorsiflexion painful</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>Palmar flexion painful</td>
<td>4 (0.5)</td>
</tr>
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<td>Supination painful</td>
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<td>Pronation painful</td>
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<td>Ulnar deviation painful</td>
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<td>Radial deviation painful</td>
<td>5 (0.6)</td>
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<tr>
<td>Radioulnar ballottement test painful</td>
<td>25 (3.2)</td>
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## Appendix 3: Interaction of the variables

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<th>Bone tenderness distal ulna</th>
<th>Bone tenderness anatomical snuff box</th>
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<th>Palmar flexion</th>
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<th>Radial deviation</th>
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<td>Ulnar deviation</td>
<td>294</td>
<td>141</td>
<td>61</td>
<td>54</td>
<td>510</td>
<td>301</td>
<td></td>
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<td>Radial deviation</td>
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<td>135</td>
<td>54</td>
<td>49</td>
<td>464</td>
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<tr>
<td>Radio ulnar ballottement test</td>
<td>253</td>
<td>121</td>
<td>50</td>
<td>48</td>
<td>450</td>
<td>277</td>
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<td>161</td>
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</table>

### Other Tests
- Axial compression of forearm: 253, 121, 50, 48, 450, 277
- Dorsi flexion: 319, 162, 65, 55, 561, 351
- Palmar flexion: 267, 137, 60, 48, 487, 307
- Supination: 274, 141, 51, 55, 489, 306
- Pronation: 258, 131, 47, 49, 464, 291
- Ulnar deviation: 295, 144, 54, 52, 453, 311
- Radial deviation: 294, 141, 61, 54, 510, 301
- Radio ulnar ballottement test: 263, 135, 54, 49, 464, 295
- Axial compression of forearm: 253, 121, 50, 48, 450, 277
Appendix 4:
Radiographs of patients with a potentially missed fracture after applying the Amsterdam Paediatric Wrist Rules in the external validation cohort.

Patient 1: boy, 15 years old, buckle fracture of the distal radius.

Patient 2: boy, 10 years old, buckle fracture of the distal radius.
Patient 3: boy, 12 years old, subtle buckle fracture of the distal radius.

Patient 4: boy, 10 years old, buckle fracture of the distal radius.
Patient 5: boy, 11 years old, fracture of the distal radius with buckle component dorsal.

Patient 6: boy, 10 years old, buckle fracture of the distal radius.
Chapter 4

Box 1. Search string

Medline:
(((radius[Title/Abstract]) OR radial[Title/Abstract]) AND ((distal[Title/Abstract]) AND fracture*[Title/Abstract]) OR (radius fracture[MeSH Terms]) AND distal[Title/Abstract]) OR (colles fracture[MeSH Terms]) OR (((((colles[Title/Abstract]) OR colles[Title/Abstract]) OR barton[Title/Abstract]) OR barton[Title/Abstract]) OR bartons[Title/Abstract]) OR barton’s[Title/Abstract]) OR hutchinson[Title/Abstract]) OR hutchinsons[Title/Abstract]) OR hutchinson’s[Title/Abstract]) OR chauffeur[Title/Abstract]) OR chauffeurs[Title/Abstract]) OR chauffeur’s[Title/Abstract]) OR smith[Title/Abstract]) OR smiths[Title/Abstract]) OR smith’s[Title/Abstract]) OR wrist[Title/Abstract]) AND (fracture*[Title/Abstract])) AND (((unstable) OR instability) OR instable)

EMBASE:
radius.ti,ab OR radial.ti,ab AND distal.ti,ab AND fracture OR colles.ti,ab OR colles’.ti,ab OR barton.ti,ab OR bartons.ti,ab OR barton’s.ti,ab OR Hutchinson.ti,ab OR hutchinsons.ti,ab OR hutchinson’s.ti,ab OR chauffeur.ti,ab OR chauffeurs.ti,ab OR chauffeur’s.ti,ab OR smith.ti,ab OR smiths.ti,ab OR smith’s.ti,ab OR wrist.ti,ab AND fracture. ti,ab OR Exp wrist fracture/ Exp colles fracture/Exp radius fracture/ AND distal AND (instable or unstable or instability).af

Cochrane:
radius.ti,ab,kw OR radial.ti,ab,kw AND distal.ti,ab,kw AND fracture OR Colles fracture*.ti,ab,kw OR colles’ fracture*.ti,ab,kw OR Barton fracture*.ti,ab,kw OR Barton’s fracture*.ti,ab,kw OR Colles fracture*.ti,ab,kw OR Hutchison fracture*.ti,ab,kw OR Hutchinson’s fracture*.ti,ab,kw OR chauffeur fracture*.ti,ab,kw OR chauffeurs fracture*.ti,ab,kw OR chauffeur’s fracture*.ti,ab,kw OR Smith fracture*.ti,ab,kw OR Smiths fracture*.ti,ab,kw OR Smith’s fracture*.ti,ab,kw OR wrist fracture*.ti,ab,kw OR distal radius fracture*. AND (instable or unstable or instability)

APPENDIX

Patient 7: boy, 9 years old, buckle fracture of the distal radius.
Search string

MEDLINE


EMBASE

(displac* or redisplac* or dislocat* or redislocat* or instab* or unstab* or loss of reduction or loss of posit*.ti,ab.) and (((radius or radial).ti,ab.) and (((distal and fracture*).ti,ab.) or (distal.ti,ab. and radius fracture/)) or (*Colles' Fracture*/ or colles fracture*.ti,ab. or wrist fracture*.ti,ab. or (oblique fracture* and radial).ti,ab. or barton fracture*.ti,ab. or smith fracture*.ti,ab. or hutchinson fracture*.ti,ab. or chauffeur fracture*.ti,ab.)) (displac* or redisplac* or dislocat* or redislocat* or instab* or unstab* or loss of reduction or loss of posit*.ti,ab.)
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<th>First author</th>
<th>Bias due to study participation</th>
<th>Bias due to study attrition</th>
<th>Bias due to prognostic factor measurement</th>
<th>Bias due to confounding</th>
<th>Bias due to analysis</th>
<th>Bias due to outcome measurement</th>
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<td>Abbaszadegan</td>
<td>Moderate (eligibility criteria and recruitment not described. Not clear if patients without initial anatomical reduction were excluded)</td>
<td>Moderate (attrition not reported)</td>
<td>Low (measurements illustrated, although definition of dorsal compression is unclear)</td>
<td>Low (all major predictors were tested)</td>
<td>Moderate (only univariate analyses were performed, analysis done seems linear regression although outcome was binary)</td>
<td>Moderate (used combined outcome and did not clearly describe definitions, duration of follow-up adequate)</td>
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<td>Adolphson</td>
<td>Moderate (eligibility criteria and recruitment not described. Not clear if patients without initial anatomical reduction were excluded)</td>
<td>Moderate (attrition not reported)</td>
<td>Low (measurements illustrated)</td>
<td>Low (all major predictors were tested)</td>
<td>Moderate (an algorithm was tested that was not described)</td>
<td>Moderate (used combined outcome and did not clearly describe definitions, duration of follow-up adequate)</td>
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<tr>
<td>Alemdaroglu</td>
<td>Moderate (not clear if patients without initial anatomical reduction were excluded)</td>
<td>Low</td>
<td>Low (measurements described)</td>
<td>Low (all major predictors were considered)</td>
<td>Moderate (univariate analysis not adjusted for other factors)</td>
<td>Low (outcome clearly defined and adequate follow-up)</td>
</tr>
<tr>
<td>Altissimi</td>
<td>Moderate (eligibility and recruitment not described)</td>
<td>Moderate (attrition not reported)</td>
<td>Moderate (measurements partly described)</td>
<td>Moderate (age was not considered)</td>
<td>Moderate (univariate analysis not adjusted for other factors)</td>
<td>High (outcome was not defined)</td>
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<td>Bartl</td>
<td>Low</td>
<td>Low</td>
<td>Moderate (prognostic factor was AO fracture type determined by a single surgeon)</td>
<td>Moderate (predictors were not investigated in this study but observed in the conservative treatment arm)</td>
<td>Moderate (unadjusted relative risk)</td>
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<td>Benoist</td>
<td>NA (no clinical data described)</td>
<td>NA (no clinical data described)</td>
<td>NA (no clinical data described)</td>
<td>High (prognostic factor was merely described)</td>
<td>NA (no clinical data described)</td>
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<td>Moderate (analysis not clearly described)</td>
<td>Moderate (outcome defined but follow-up not reported)</td>
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<td>Low</td>
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<td>Moderate (combined outcome as either poor radiologic result or progression to surgery)</td>
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<td>Low</td>
<td>Low</td>
<td>Low (most important predictors were considered)</td>
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<tr>
<td>Clayton</td>
<td>Moderate (not clear if patients without initial anatomical reduction were excluded)</td>
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<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>High (outcome was not observed instability but instability calculated with algorithm)</td>
</tr>
<tr>
<td>Einsiedel</td>
<td>High (eligibility criteria, recruitment and treatment not described. Not clear if patients without initial anatomical reduction were excluded)</td>
<td>Not reported</td>
<td>Low</td>
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<td>Moderate (univariate correlations without adjusting for other factors)</td>
<td>Low</td>
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<td>Fenyo</td>
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<td>High (investigated result of primary reduction as predictor but this was not defined)</td>
<td>High (only result of primary reduction and immobilisation technique were considered)</td>
<td>High (analyses not described)</td>
<td>High (outcome not defined)</td>
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<td>Hove</td>
<td>High (excluded patients with a second reduction during the immobilisation period)</td>
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<td>Low</td>
<td>Low (most important predictors were considered)</td>
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<td>Not reported</td>
<td>Moderate (measurements partly described)</td>
<td>Moderate (only AO type was considered)</td>
<td>Moderate (univariate analysis not adjusted for other factors)</td>
<td>High (outcome undefined, duration of follow-up not reported)</td>
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<td>Low</td>
<td>Low</td>
<td>Moderate (univariate analysis not adjusted for other factors)</td>
<td>High (outcome was result on Stewart score (a summation of points for OA, radial angle and radial length))</td>
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<td>LaMartina</td>
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<td>Low</td>
<td>Moderate (multivariate analysis but unclear with which factors, coefficients not reported and referred to as correlations)</td>
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<td>Makhni</td>
<td>Moderate (not clear if patients without initial anatomical reduction were excluded)</td>
<td>Not reported</td>
<td>Low</td>
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<td>Moderate (univariate analysis not adjusted for other factors)</td>
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<tr>
<td>Myderrizi</td>
<td>Moderate (excluded early unstable fractures that lost reduction within one week)</td>
<td>Not reported</td>
<td>Moderate (measurements not described)</td>
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<td>Moderate (univariate analysis not adjusted for other factors)</td>
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<td>Nesbitt</td>
<td>Moderate (patients with &lt;3 instability factors were excluded)</td>
<td>Low</td>
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<td>Moderate (univariate analysis not adjusted for other factors)</td>
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<td>Oskarsson</td>
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<td>Moderate (measurements not described)</td>
<td>High (univariate analysis not adjusted for other factors, significance reported but corresponding p-values not)</td>
<td>High (outcome was defined as poor functional outcome)</td>
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<td>Moderate (measurements not described)</td>
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<td>Low</td>
<td>Moderate (only a few predictors considered)</td>
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<td>Robin</td>
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<td>Low</td>
<td>Moderate (measurements not described)</td>
<td>Moderate (only T-scores were considered)</td>
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<td>Tahririan</td>
<td>Moderate (patients with &lt;3 instability factors were excluded, duration of immobilisation unclear)</td>
<td>Low</td>
<td>Moderate (measurements not described and unclear if loss of radial height and inclination were defined as relative to uninjured side)</td>
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<td>Wadsten</td>
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<td>Moderate (not all predictors defined)</td>
<td>Moderate (age was not considered)</td>
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THEESIS SUMMARY & FUTURE PERSPECTIVES
Thesis Summary

Wrist trauma is one of the most common Emergency Department attendances. Around 40%-50% of the patients with wrist trauma has sustained a distal radius fracture. Annually, this amounts to 286 distal radius fractures per 100,000 persons. Although a distal radius fracture might appear to be a quite innocent condition, immobilisation of the wrist causes substantial disability. This does not only affect the patient but also their family and friends. Moreover, insufficient treatment may result in definitive impairment of the wrist.

This thesis aimed to improve diagnosis, treatment and prognosis of patients with wrist injury. To this end, we performed several multicentre prospective and retrospective studies that focussed on diagnosing wrist fractures, treating distal radius fractures and determining the prognosis of distal radius fractures.

Part 1: Diagnosis

In Chapter 1, we performed a multicentre cross-sectional observational study in five Emergency Departments and included all consecutive adult patients with wrist trauma. Physicians were asked to perform a standardized examination of the wrist and to subsequently indicate the probability of a distal radius fracture. We found that physicians were able to accurately discriminate between patients with and without a distal radius fracture based on their physical findings. Despite this, the majority of the 924 included patients were referred for radiography (99.6%). We concluded that a validated clinical decision rule could reinforce physician’s clinical judgment and support them in their decision not to routinely request radiography.

The aim of Chapter 2 was to derive and externally validate such a clinical decision rule for adult patients with wrist trauma. We performed a multicentre prospective study that consisted of three components: (1) derivation of a clinical prediction model for detecting wrist fractures in patients following wrist trauma; (2) external validation of this model; and (3) design of a clinical decision rule. A total of 882 patients was analysed; 487 in the derivation cohort and 395 in the validation cohort. Subsequently, we derived a clinical prediction model with six variables: age; sex; swelling of the wrist; swelling of the anatomical snuffbox, visible deformation; distal radius tender to palpation; pain on radial deviation and painful axial compression of the thumb. The Area Under the Curve (AUC) at external validation of this model was 0.81 (95% CI: 0.77 - 0.85).

We named this clinical decision rule the Amsterdam Wrist Rules (AWR). If the AWR had been applied in the external validation cohort, its sensitivity for detecting fractures of the wrist would be 98% (95% CI: 95% - 99%) and its specificity 21% (95% CI: 15% - 28%). The negative predictive value would be 90% (95% CI: 81% - 99%). Use of the AWR could result in a 10.4% absolute reduction in X-rays requested. We concluded that the Amsterdam Wrist Rules can provide physicians in the Emergency Department with a useful screening tool to select patients with acute wrist trauma for radiography.

In Chapter 3, we aimed to derive and externally validate a similar clinical decision rule for paediatric patients with wrist trauma and named it the Amsterdam Paediatric Wrist Rules (APWR). We analyses a total of 787 children; 408 in the derivation cohort and 379 in the validation cohort. A prediction model was derived with six variables: age; swelling of the wrist; visible deformation; distal radius tender to palpation; anatomical snuffbox tender to palpation and painful or abnormal supination. The model showed good discriminative ability (AUC 0.79, 95% CI: 0.76 - 0.83) at external validation. If the APWR had been applied to the external validation cohort, its sensitivity and specificity would be 95.9% (95% CI: 91.7% - 98.0%) and 37.3% (95% CI: 31.0% - 44.1%) respectively. The use of the APWR would have resulted in a 22% absolute reduction of radiographs, however at the cost of missing a fracture (without therapeutical consequences) in 4.3% of the patients. We concluded that the Amsterdam Pediatric Wrist Rules can provide a valuable tool for physicians to decide if radiography in children after wrist trauma is required. Implementation of the APWR may avoid unnecessary waiting time for children and result in a reduction of radiation exposure.

Part 2: Treatment

Treatment of distal radius fractures is a popular area of research, especially in patients with unstable distal radius fractures for whom the optimal treatment remains inconclusive. However, to appreciate the findings of studies that enrolled patients with unstable distal radius fractures, it should be clear how the authors defined an unstable distal radius fracture. In Chapter 4, we described a comprehensive systematic review to assess what the most common definition of an unstable distal radius fracture was in literature, and to examine if there is one preferred evidence-based definition for future authors. The search yielded 2489 citations of which 479 studies were included. We found that of the 149 studies in which it was explicitly stated that patients with unstable distal radius fractures were enrolled, the authors only provided a definition of what they considered an unstable distal radius fracture in 81 studies (54%). Moreover, there was an abundance of definitions circulating in literature: overall we found 143 different definitions for unstable distal radius fractures. The seven most common definitions were: displacement following adequate reduction; Lafontaine’s definition; irreducibility; an AO type C2 fracture; a volarly displaced fracture; Poigenfürst’s criteria and Cooney’s criteria. Only Lafontaine’s definition originated from a clinical study (Level of Evidence IIb). We concluded that none of the definitions stood out as the preferred choice.

In addition to a substantial amount of variation in definitions used in literature, variation is also present in the actual treatment of distal radius fractures. In Chapter 5 we performed a study to examine the variation in surgical treatment rate across all Dutch hospitals. Therefore we obtained all reimbursement data for the treatment of distal radius fractures categorised by hospital for a period of two years. This resulted in a total of 95,754 reimbursements;
described a case series of eight patients who were treated with a computer-assisted 3-D planned corrective osteotomy. We analysed the postoperative residual malpositioning on 3-D reconstructions that were expressed in six positioning parameters (three translations along three orthogonal axes and three rotations about these axes). In this small case series, dorsopalmar tilt was significantly improved (p = 0.05). However, ulnar radial shift was worsened by the correction osteotomy (in 6 of 8 cases). Postoperative 3-D evaluation revealed improved positioning parameters for patients in axial rotational alignment radial inclination, proximodistal shift and volodorsal shift, although the group was not large enough to reach statistical significance. All but one patient experienced improved range of motion. We concluded that computer assisted 3-D planning can ameliorate alignment of radial malunions, especially in rotational deformity.

PART 3: PROGNOSIS
To help surgeons to inform patients on chances of success of closed treatment and facilitate shared decision making, it is important to consider prognostic factors for patients with distal radius fractures. In Chapter 9, we performed a systematic review and meta-analysis to provide an overview of risk factors secondary displacement in distal radius fractures. The initial search yielded 3178 studies of which 27 were included in the systematic review. Multiple studies found that age, shortening, loss of radial inclination and AO type 3 fractures (A3, B3, C3) were significant predictors of secondary displacement. Conversely, the mechanism of trauma, energy of the injury, the Frykman classification, intra-articular involvement, radial shift and an associated ulnar styloid fracture were found non-significant predictors of secondary displacement. For sex, dorsal comminution and dorsal angulation, the studies seem inconclusive.

Because the majority of studies in distal radius fracture research regard relatively small sample sizes, we decided to pool the odds ratios of the predictors in a meta-analysis. We were able to pool the odds ratios of seven predictors and found a significantly increased risk of secondary displacement in fractures with dorsal comminution and in female patients. Additionally, the pooled results confirmed the importance of age demonstrating a significantly increased risk of secondary displacement of distal radius fractures in patients older than 60-65 years. Our results did not show an increased risk of secondary displacement for fractures with intra-articular involvement, nor for fractures with an associated ulnar styloid fracture.

Another method to review the radiological prognosis of a patient is by using a clinical prediction model that predicts the probability of secondary displacement. In Chapter 10, we performed a retrospective cohort study to externally validate an existing clinical prediction model in our patient population with displaced distal radius fractures. We included 99 patients who had been treated conservatively. Early secondary displacement (within two weeks) occurred in 61 patients (62%). Unfortunately, the performance of the model was disappointing with an AUC of 0.53 (95% CI: 0.41 - 0.64), indicating poor discrimination. The sen-
sitvity and specificity were 1.6% (95% CI: 0.9% - 9.9%) and 94.7% (95% CI: 80.9% - 99.1%) for correctly identifying an unstable fracture. We concluded that the model in its current form is unsuitable for a population other than the population from which it was derived.

Ultimately, secondary displacement does not always result in poor functional outcome. For this reason it is important to regard patient-reported outcome measures such as the DASH and the PRWE score. To interpret results expressed in patient-reported outcome scores, one should be aware of the minimal numeric change in score that constitutes a clinical change for the patient. This value is called the minimum clinically important difference (MCID). In Chapter 11, we determined the MCID of the PRWE for patients with distal radius fractures. We included 102 patients with a distal radius fracture and asked them to complete the PRWE questionnaire during each of two separate visits. At the second visit, patients were asked to indicate the degree of clinical change they appreciated since the previous visit. Accordingly, patients were categorized in two groups: (1) minimally improved or (2) no change. The groups were used to anchor the changes observed in the PRWE score to patients’ perspectives of what was clinically important. We found that the MCID of the PRWE for patients with distal radius fractures is 11.5 points. We recommend using this value as the smallest clinically relevant difference when evaluating the effects of treatments and when performing sample-size calculations on studies of distal radius fractures.

**FUTURE PERSPECTIVES**

The true effect of the clinical decision rules that were designed in Chapter 2 and Chapter 3 can only be evaluated after their implementation. Do the Amsterdam Wrist Rules and the Amsterdam Paediatric Wrist Rules really result in a reduction of X-rays requested? Will patients still be satisfied with the care they have received? And will physicians be content with using the AWR and the APWR? These and other questions are the subject of the Amsterdam Wrist Rules implementation study that is currently being conducted. Should the AWR and APWR prove to be effective, a nationwide implementation in both General Practitioners’ offices and Emergency Departments is indicated. We expect to have the results of the implementation study at the end of 2016.

Not only diagnosis, but also the treatment of distal radius fracture also requires further clarification. First, a general consensus definition of what constitutes an unstable distal radius fracture could help to standardize future research. We are planning on conducting a Delphi study in an attempt to reach such a conclusion among experts in the field of upper extremity surgery.

Second, the substantial variation in treatment of patients with distal radius fractures in the Netherlands is a phenomenon that is hard to explain to the public. For an individual patient, the probability of receiving operative treatment seems to be driven more by a surgeon’s local beliefs and preferences than by scientific influences. This variation across the country calls for a standardized and transparent reporting of outcomes of different health care providers. Health care insurance companies already require some providers to transparently report the clinical outcomes they achieve. The considerable variation in the treatment of distal radius fractures should especially urge providers to systematically collect patient-reported outcomes of their patient population in order to benchmark their quality of care.

Third, the results of the VIPER-trial will solve many of the so far unanswered questions regarding the treatment of patients with displaced extra-articular distal radius fractures. The results of its sequel and equivalent study, the VIPAR trial, will provide these answers for patients with intra-articular distal radius fractures. Should both surgical and conservative treatment turn out to achieve similar acceptable results, the costs might prove to be of paramount importance. Since the direct costs of operative fixation of distal radius fractures are approximately tenfold that of conservative treatment, health insurance companies might narrow the indications for which they reimburse surgical treatment. Nevertheless, a possible earlier return to work after operative fixation should also be considered when evaluating costs. These costs could surmount the direct costs of surgical fixation from a societal point of view. The economic evaluation that runs parallel to both the VIPER-trial and the VIPAR-trial will provide more insight into these issues.

Fourth, the use of computer-assisted 3-D planned corrective osteotomies for treatment of malunions of the radius is still in its infancy. Accurate pre-operative planning does not always result in equally accurate post-operative reconstruction. Further development is required to improve transferral of the planned position into post-operative results. Moreover, computer-assisted technology is currently mainly applied in patients with complex deformations. This renders comparison of clinical outcomes to the results of conventional corrective osteotomies for less complex malunions an intricate endeavour. Once the technique has been optimised, a computer-assisted 3-D planning might become standard of care for all patients with corrective osteotomies.

Finally, as the importance of patient-reported outcome measures is increasing, so should the number of studies that have determined the minimum clinically important difference (MCID) in various populations. Future sample-size calculations on studies with distal radius fractures should not be based on predetermined arbitrary differences in PRWE score, but rather on the minimum clinically important difference. The MCID should also be used as a tool when comparing health care outcomes among providers. Therefore, health care insurance companies should encourage providers and researchers to determine the MCIDs for various patient populations. This will help ensure that not statistics, but rather patients’ perception of the quality of the health care they received is of paramount importance.
SAMENVATTING & TOEKOMSTPERSPECTIEVEN
SAMENVATTING
Polstrauma is een van de meest voorkomende redenen voor een bezoek aan de Spoedeisende Hulp. Ongeveer 40% tot 50% van de patiënten met polstrauma heeft een distale radius fractuur opgelopen. Jaarlijks resulteert dit in 286 distale radius fracturen per 100.000 personen. Hoewel een distale radius fractuur ogenzienlijk een onschuldige aandoening is, veroorzaakt immobilisatie van de pols een aanzienlijke belemmering. Bovendien kan onjuiste of onvoldoende behandeling leiden tot blijvende schade aan het polgewricht.

Het doel van dit proefschrift was om de diagnose, behandeling en prognose van patiënten met polstrauma te verbeteren. Daartoe hebben wij verschillende multicenter prospectieve en retrospectieve studies uitgevoerd die zich richtten op de diagnose, de behandeling en de prognose van distale radius fracturen.

DEEL 1: DIAGNOSE
In Hoofdstuk 1 hebben wij een multicenter cross-sectionele observationele studie op vijf Spoedeisende Hulp afdelingen uitgevoerd en alle opeenvolgende volwassen patiënten met polstrauma geïncludeerd. Artsen werden gevraagd een gestandaardiseerd lichamelijk onderzoek van de pols te verrichten en aansluitend de waarschijnlijkheid van een distale radius fractuur aan te geven. Wij vonden dat artsen op basis van het lichamelijk onderzoek goed in staat waren om een onderscheid te maken tussen patiënten met en patiënten zonder een distale radius fractuur. Desondanks bleek het merendeel (99,6%) van de 924 patiënten die de tabatière anatomique, standsafwijking, drukpijn over de distale radius, drukpijn over het tabatière anatomique en pijnlijke of abnormale supinatie. Dit model toonde bij externe validatie een goed discriminatorend vermogen (AUC 0.79, 95% BI: 0.76- 0.83). De regel had in het externe validatiecohort een sensitiviteit van 95.9% (95% BI: 91.7% - 98.0%) en een specificiteit van 37.3% (95% BI: 31.0% - 44.1%). Het gebruik van de APWR zou geresulteerd hebben in een vermindering van het aantal aangevraagde Röntgenfoto’s van 22%. Daarentegen zou gelijk tijdig 4,3% van de fracturen zijn gemist. Dit betrof echter klinisch niet relevante fracturen en onderbehandeling zou geen therapeutische consequenties hebben gehad.

Wij concludeerden dat ook de Amsterdam Pediatric Wrist Rules een nuttig screeningsinstrument is om kinderen met polstrauma te selecteren voor een Röntgenfoto. Implementatie van de APWR heeft de potentie om de wachtijd voor kinderen te doen verminderen en resulteert in een vermindering van de stralenbelasting.

DEEL 2: BEHANDELING
De behandeling van distale radius fracturen is een populair onderzoeksgeweld. In het bijzonder geldt dit voor patiënten met een instabiele distale radius fractuur. Voor deze groep patiënten bestaat nog geen overtuigend bewijs van de optimale behandeling. Echter, om de bevindingen van de vele studies, die patiënten met een instabiele distale radius fractuur hebben geïncludeerd op waarde te kunnen schatten, is het van belang dat auteurs het begrip “instabiele distale radius fractuur” duidelijk hebben gedefinieerd. In Hoofdstuk 4 beschreven wij een grootscheeps literatuuronderzoek, waarin wij trachten te bepalen wat de meest gebruikelijke definitie van een instabiele distale radius fractuur was in de literatuur. Daarnaast onderzochten wij of er een definitie werd gebruikt, die de voorkeur geniet voor toekomstige auteurs. De zoektocht leverde 2489 citaties op, waarvan 479 studies werden geïncludeerd. Wij vonden dat de 149 studies, waarin expliciet werd vermeld dat patiënten met een instabiele distale radius fractuur waren geïncludeerd, de auteurs slechts in 81 studies (54%) een definitie gaven van wat zij als een instabiele distale radius fractuur beschouwden. Bovendien was er een grote verscheidenheid aan definities: wij 143 verschillende definities van een instabiele distale radius fractuur. De zeven meest voorkomende definities waren: isolocatie van de fractuur met adequate repositie, Lafontaines definitie, een niet reduceerbare fractuur, aan AO type C2 fractuur, een volaar gedisloceerde fractuur,
Poigenförst’s criteria en Cooney’s criteria. Van deze zeven definities was alleen Lafontaine’s definitie afkomstig uit een klinische studie (Level of Evidence IIIb). Wij concludeerden dat geen van de gevonden definities een goede beschrijving geeft van een instabiele distale radius fractuur.

Naast een aanzienlijke variatie in verschillende definities die worden gebruikt in de literatuur, is variatie ook aanwezig in de behandeling van distale radius fracturen. In Hoofdstuk 5 onderzochten wij de variatie in het percentage operatief behandelde patiënten met een distale radius fractuur in alle Nederlandse ziekenhuizen. Daartoe verkregen wij alle vergoedingsdata voor de behandeling van distale radius fractures in Nederland voor een periode van twee jaar, gecategoriseerd per ziekenhuis. Dit resulteerde in 95,754 vergoedingen; 49,615 in 2012 en 46,139 in 2013.

Wij constateerden dat de ratio’s patiënten die geopereerd werd per ziekenhuis varieerden van 0% tot 23%. Het type ziekenhuis, het percentage vrouwelijke patiënten, het percentage patiënten boven de 65, de gemiddelde leeftijd, de gemiddelde sociaal economische status en het totaal aantal behandelde patiënten verklaarden slechts 2,6% van de geobserveerde verschillen tussen ziekenhuizen in 2012 en 11,6% in 2013 (adjusted R squared = 0,026 en 0,116). Behoudens de gemiddelde leeftijd van de patiënten in 2013, was geen van de bovengenoemde variabelen onafhankelijk gerelateerd aan de ratio geopereerde patiënten. Wij concludeerden dat er een aanzienlijke variatie is in de behandeling van patiënten met distale radius fractures in Nederland, die niet volledig kan worden verklaard door het type ziekenhuis en karakteristieken van de patiëntpopulatie.

Een van de chirurgische behandelmethoden voor distale radius fractures is fixatie met een overbruggende fixateur externe. De werking van deze techniek berust op ligamentotaxis, waardoor de fractuurvelden in positie blijven. In Hoofdstuk 6 beschreven wij een meta-analyse waarin wij de functionele uitkomst na overbruggende fixateur externe vergeleken met een hoekstabiele volaire plaat in patiënten met een instabiele distale radius fractuur. De functionele uitkomst was uitgedrukt in de Disability of the Arm Shoulder and Hand Score (DASH). De zoektocht van de literatuur leverde 197 citaties op, waarvan drie studies konden worden geselecteerd. De primaire uitkomstmaat is polsfunctie, geme- ten met de DASH score en de Patient-Rated Wrist Evaluation score (PRWE). De resultaten van de VIPER-trial zullen een definitief antwoord geven op de vraag wat de optimale behandeling is voor patiënten met een gedisloceerde extra-articulaire distale radius fractuur. Als beide behandelmethoden gelijke functionele resultaten bereiken, zullen de resultaten van de parallelle economische evaluatie mogelijk doorslaggevend zijn.

Een mogelijke gevolg van inadequate behandeling van een distale radius fractuur is een malunion, welke kan resulteren in pijn en functieverlies. Een nauwkeurige preoperatieve planning is essentieel om de functionele uitkomsten na een correctie-osteoïomie te optimaliseren. In Hoofdstuk 8 beschreven wij een serie van acht patiënten die werden behandeld met een computer-geassisteerde 3-D geplande correctie-osteoïomie. Wij analyseerden de postoperatieve raderende malpositionering op 3-D reconstructies en drukten deze uit in zeson positionerings parameters (drie translaties langs drie orthogonalen assen en drie rotaties om deze assen). Wij constateerden in het merendeel van de patiënten een verbetering in de positionering parameters volaire kanteling, radiale inclinatie, radiale lengte en sagittale shift (volair - dorsaal), hoewel niet statistisch significant. De dorsopalmare tilt afwijking was wel significant verbeterd na de ingreep (p=0,05). De ulnoradiale shift werd juist verslechterd door de correctie-osteoïomie (in 6 van de 8 casus). Behoudens één, hadden alle patiënten een verbeterde range of motion. Wij concludeerden dat computer-geassisteerde 3-D planning de postoperatieve stand bij radiale malunions kan verbeteren, en in het bijzonder bij rotatieafwijkingen.

**DEEL 3: PROGNOSE**

Om chirurgen te ondersteunen bij het informeren van patiënten over de kans op een succesvolle conservatieve behandeling is het van belang verschillende prognostische factoren in ogenschouw te nemen. In Hoofdstuk 9 beschreven wij een literatuuronderzoek en meta-analyse waarin wij een overzicht gaven van belangrijke risicofactoren voor secundaire dislocatie in distale radius fractures. De initiële zoektocht leverden 3178 citaten op waarvan 27 studies werden geïncludeerd in het literatuuronderzoek. Meerdere studies hadden aangetoond dat leeftijd, verkorting, verlies van radiale inclinatie en AO type 3 fractures (A3 ,B3, C3) significante voorspellers waren van secundaire dislocatie. Daarentegen waren het traumamechanisme, hoog energetisch trauma, de Frykman classificatie, intra-articulaire be-
trokkenheid, radiale shift en een geassocieerde fractuur van het processus styloideus ulnae geen significante voorspellers. Voor de factoren het vrouwelijk geslacht, dorsale comminutie en dorsale angulatie waren de studies onbeslist.

Omdat de meerderheid van de studies met patiënten met distale radius fracturen relatief kleine groepen betreft, besloten wij de odds ratios van de risicofactoren gezamenlijk te analyseren in een meta-analyse. We waren in staat om de odds ratios van zeven risicofactoren samen te voegen en een gewogen gemiddelde te berekenen. Hieruit bleek dat er een significante verhoogd risico is op secundaire dislocatie in patiënten met dorsale comminutie en in vrouwelijke patiënten. Bovendien bevestigde deze analyse het belang van leeftijd als risicofactor, want wij vonden ook dat patiënten ouder dan 60-65 jaar een verhoogd risico hadden voor secundaire dislocatie. Daarnaast toonden onze resultaten dat er geen verhoogd risico is bij fracturen met intra-articulaire betrokkenheid en ook niet bij aanwezigheid van een geassocieerde fractuur van het processus styloideus ulnae.

Een andere methode om de radiologische prognose van patiënten te bepalen, is met behulp van een klinisch predictiemodel dat de kans op secundaire dislocatie voorspelt. In *Hoofdstuk 10* beschreven wij een retrospectieve cohortstudie waarin wij een bestaande klinisch predictiemodel extern validateerden in onze patiëntenpopulatie met gedisloceerde distale radius fracturen. Hiervoor includeerden wij 99 conservatief behandelde patiënten. In deze groep trad in 61 patiënten (62%) binnen 2 weken secundaire dislocatie op. Helaas pres- teerde het predictiemodel teleurstellend in onze populatie. De AUC was 0,53 (95% CI: 0,41 - 0,64), een waarde die aangeeft dat het model slecht kan discrimineren tussen patiënten waarin secundaire dislocatie zal optreden en patiënten waarbij dit niet zal optreden. De sensitiviteit en specificiteit van het correct identificeren van een instabile fractuur waren 1,6% (95% CI: 0,9% - 9,9%) en 94,7% (95% CI: 80,9% - 99,1%) respectievelijk. Wij concluderen dat het model in zijn huidige vorm niet geschikt is voor een populatie anders dan de populatie waaruit het is afgeleid.

Uiteindelijk resulteert secundaire dislocatie niet altijd in een slechte functionele uitkomst. Om deze reden is het van belang ook patient-reported outcome measures zoals de DASH en de PRWE score in ogenschouw te nemen. Interpretatie van studiesresultaten uitgedrukt in patient-reported outcome measures vereist echter bewustzijn van de minimale numerieke verandering in score die een klinisch verschil voor de patiënt vormt. Deze waarde is het kleinste verschil in de PRWE score die door patiënten als klinisch relevant wordt beschouwd. Wij adviseren dan ook om dit getal in gedachte te houden bij het interpreteren van studieresultaten, en te hanteren als basis voor sample-size berekening van toekomstige studies.

**TOEKOMSTPERSPECTIEVEN**

De waar effecten van de klinische beslisseregels die in Hoofdstuk 2 en Hoofdstuk 3 zijn beschreven kunnen pas geëvalueerd worden na hun implementatie. Resulteert het gebruik van de Amsterdam Wrist Rules en de Amsterdam Paediatric Wrist Rules werklik in een reductie van het aantal aangevraagde Röntgenfoto’s? Zijn patiënten nog steeds tevreden met de zorg die zij ontvangen? En zijn artsen die de AWR en de APWR gebruiken ook tevreden? Deze en andere vragen zijn het onderwerp van de Amsterdam Wrist Rules implementatie studie die momenteel loopt. Indien blijkt dat de AWR en de APWR effectief zijn, is een landelijke implementatie van de beslissregels op zowel de Spoedeisende Hulp als in de huisartsenprak- tijk aangewezen. Wij verwachten eind 2016 de resultaten van de implementatieteste te kunnen presenteren.

Niet alleen de diagnose, maar ook de behandeling van distale radiusfracturen vereist in de toekomst meer verduidelijking. Ten eerste zou een algemene consensus definitie van een instabile distale radius fractuur kunnen bijdragen aan het standaardiseren van toekomstige studies. Wij werken momenteel aan een Delphi studie in een poging een dergelijke consensus definitie onder experts op het gebied van de bovenste extremiteit te bereiken.

Ten tweede is de aanzienlijke variatie in de behandeling van patiënten met distale radiusfracturen een fenomeen dat lastig uit te leggen is aan de maatschappij. Voor een individuele patiënt is de kans om geopereerd te worden aan een distale radiusfractuur meer gebaseerd op lokale gebruiken en voorkeuren van de chirurg dan op wetenschappelijke invloeden. Deze variatie in Nederland vereist een gestandaardiseerde en transparante rapportage van de uitkomsten van verschillende zorgaanbieders. Zorgverzekeraars vragen momenteel al enkele zorgaanbieders hun klinische resultaten transparant te maken. Juist de aanzienlijke variatie in de behandeling van patiënten met distale radiusfracturen zou zorgaanbieders moeten aanzetten tot het systematisch verzamelen van patient-reported outcome measures van hun patiëntenpopulatie om zo een benchmark te creëren van de kwaliteit van de door hun geleverde zorg.

Ten derde zullen de resultaten van de VIPER-trial een oplossing bieden voor de vele, tot op heden onbeantwoorde, vragen over de optimale behandeling van patiënten met een gedisloceerde extra-articulaire distale radius fractuur. De resultaten van haar opvolger, de VIPAR-trial, zullen deze vragen voor patiënten met intra-articulaire distale radius fracturen

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**NEDERLANDSE SAMENVATTING EN TOEKOMSTPERSPECTIEVEN**

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beantwoorden. Indien zowel chirurgische als conservatieve behandeling gelijke en acceptabele resultaten bereiken, zullen de kosten doorslaggevend zijn. Gezien de directe kosten van operative fixatie van distale radiusfracturen ongeveer het tienvoudige zijn van de conservatieve behandeling, zullen zorgverzekeraars mogelijk de indicaties vernauwen waarvoor zij chirurgische therapie vergoeden. Echter, bij het evalueren van de kosten moet ook de mogelijksnelere herstelling van betaald werk na operative fixatie overwogen worden. Deze kosten zouden vanuit een maatschappelijk oogpunt de directe kosten van chirurgische fixatie kunnen overstijgen. De economische evaluatie die parallel loopt aan zowel de VIPER-trial als de VIPAR-trial biedt mogelijk meer inzicht in dit vraagstuk.

Ten vierde staat het gebruik van computer-geassisteerde 3-D geplande correctie-osteotomie voor behandeling van malunions van de radius nog in de kinderschoenen. Een accurate preoperatieve planning leidt niet altijd tot even accurate postoperatieve reconstructie. Er is behoefte aan nieuwe ontwikkelingen die zich richten op het verbeteren van de overdracht van de geplande positie naar de postoperatieve resultaten. Dit kan bijvoorbeeld geeffectueerd worden met aparte reductie mallen. Daarnaast wordt deze techniek momenteel voornamelijk toegepast bij patiënten met complexe deformaties. Dit bemoeilijkt de vergelijking met conventionele correctie osteotomieën. Zodra de techniek geoptimaliseerd is zou een computer-geassisteerde 3-D geplande correctie-osteotomieën de standaard kunnen worden voor alle patiënten met een malunion.

Tot slot, met het toenemende belang van de patient-reported outcome measures in wetenschappelijk onderzoek zou ook het aantal studies dat zich richt op het bepalen van de MCID in verschillende populaties moeten stijgen. Toekomstige sample-size berekeningen voor patiënten met distale radius fracturen kunnen niet meer slechts gebaseerd zijn op een vooraf bepaalde arbitrair verschil in PRWE score, maar op het minimaal klinisch relevante verschil voor patiënten. De MCID zou daarnaast ook gebruikt moeten worden als instrument om zorguitkomsten onder verschillende zorgaanbieders te vergelijken. Hiertoe moeten zorgverzekeraars zorgaanbieders stimuleren de MCIDs te bepalen voor verschillende patiëntenpopulaties. Dit zal ervoor zorgen dat niet statistieken, maar vooral de perceptie van patiënten van de kwaliteit van zorg doorslaggevend is.
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2014 0.5

De Amsterdam Wrist Rules, een klinische beslisregel
Traumadagen, Amsterdam, Nederland
2014 0.5

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2012 0.5

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2015 1

Annual Meeting of the Federation of European Societies for Surgery of the Hand (FESSH), Milan, Italy
2015 0.75

Spring meeting of the Dutch Society for Surgery of the Hand, Amsterdam, The Netherlands
2015 0.25

16th European Federation of National Associations of Orthopaedics and Traumatology annual congress, Prague, Czech Republic
2015 0.75

16th European Congress for Trauma and Emergency Surgery, Amsterdam, The Netherlands
2015 0.75

Spring Scientific meeting of the British Society for Surgery of the Hand, Bath, England
2015 0.5

Instructional Course American Society for Surgery of the Hand, Maui, Hawaii, United States of America
2015 0.75

Annual Meeting of the American Association for Hand Surgery, Paradise Island, Bahamas
2015 1

Najaarsdag van de Nederlandse Vereniging voor Heelkunde, Utrecht, Nederland
2014 0.25

1. PhD training

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Presentations

The Minimal Clinically Important Difference of the PRWE Annual Meeting of American Society for Surgery of the Hand (ASSH), Seattle, Washington, United States of America
2015 0.5

Predictors of Instability in Distal Radius Fractures, a systematic review and meta-analysis
Annual Meeting of the Federation of European Societies for Surgery of the Hand (FESSH), Milan, Italy
2015 0.5

The Minimal Clinically Important Difference of the PRWE
Spring meeting of the Dutch Society for Surgery of the Hand, Amsterdam, The Netherlands
2015 0.5

The Minimal Clinically Important Difference of the PRWE
16th European Federation of National Associations of Orthopaedics and Traumatology annual congress, Prague, Czech Republic
2015 0.5

Outcomes scores in distal radius fracture research (invited lecture)
16th European Congress for Trauma and Emergency Surgery, Amsterdam, The Netherlands
2015 0.5

The Minimal Clinically Important Difference of the PRWE
Spring Scientific meeting of the British Society for Surgery of the Hand, Bath, England
2015 0.5

The Amsterdam Wrist Rules, A Clinical Decision Rule
Instructional Course of the American Society for Surgery of the Hand (ASSH), Maui, Hawaii, United States of America
2015 0.5

The Amsterdam Wrist Rules, A Clinical Decision Rule
Annual Meeting of the American Association for Hand Surgery, Paradise Island, Bahamas
2015 0.5

Een multicenter cross-sectionele studie om te evalueren of artsen op basis van het lichamelijk onderzoek in staat zijn een distale radiusfractuur te voorspellen
Najaarsdag van de Nederlandse Vereniging voor Heelkunde, Utrecht, Nederland
2014 0.5

LIST OF PUBLICATIONS
### 2. Teaching

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<td>Dorien Salentijn, Radiological criteria for acceptable reduction in intra-articular distal radius fractures and their relation to patient-reported functional outcome, Trauma Training Center, Columbia University Medical Center, New York</td>
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<td>Anna Heijne, the correlation of clinically utilized outcome instruments and the DASH score in distal radius fractures, Trauma Training Center, Columbia University Medical Center, New York</td>
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<td>Kasper Roth, Functional Outcome after Corrective Osteotomy for Malunited Forearm Fractures in Children: a Systematic Review and Meta-Analysis of Individual Participant Data, Department of Orthopedic Surgery, Erasmus University Medical Centre, Rotterdam</td>
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<td>Iris Westra, Carpal alignment in distal radius fractures, Trauma Training Center, Columbia University Medical Center, New York</td>
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<td>Bente Dubois, External validation of a clinical decision model to predict the presence of a wrist fracture in children</td>
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<td>Niels Hakkens, Costs of distal radius fracture treatment, Trauma Unit, AMC</td>
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<td>Sema Aydin, Predictors of instability in distal radius fractures, Trauma Unit, AMC</td>
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<td>Jony van Hilst, External validation of clinical prediction model for instability in distal radius fractures</td>
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<td>Initiation and coordination of a hand surgery research fellowship program at the Trauma Training Center in Columbia University Medical Center, New York</td>
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### 3. Parameters of Esteem

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<td>Top 15 best posters of the Instructional Course American Society for Surgery of the Hand, Maui, Hawaii, United States of America</td>
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DANKWOORD
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Velen hebben direct of indirect bijgedragen aan de totstandkoming van dit proefschrift. Hierbij wil ik iedereen dan ook graag hartelijk danken en een aantal in het bijzonder:


Dr. Schep, Niels, ouwe, je bent een fantastische co-promotor! Met je tomeloze energie en optimisme weet je me altijd te motiveren. Je hebt me vanaf het begin af aan de ruimte en het vertrouwen gegeven om zelfstandig tot oplossingen te komen. De afgelopen jaren ben ik bijzonder gesteld op je geraakt, inclusief je ongenuanceerde opinies, je myosynge opmerkingen (waarbij je soms lijkt te vergeten dat ik ook tot die groep behoor) en je mailtjes waarin je geen enkele leestekens gebruikt. Ik ben heel blij dat ik jou jaren geleden in het Erasmus MC heb ontmoet en we samen in het AMC onderzoek zijn gaan doen. Ik hoop dat ik zowel in de kliniek als in de wetenschap nog lang met je mag samenwerken en veel van je mag leren. Heel veel dank voor alles!

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Secretaresse van G4 en in het bijzonder Jacq, dank voor al je hulp en de gezellige momenten!

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Alle patiënten die hebben deelgenomen aan de onderzoeken van dit proefschrift en in het bijzonder aan de VIPER-trial.

Chirurgen van de deelnemende centra van Amsterdam Wrist Rules (Romuald van Velde, Nico Sosef en Jan Uitee) en de VIPER-trial (Berry Cleffken, Egbert-Jan Verleisdonk, Robert Haverlag, Ronald Liem, Jan Bernard Sintenie, Maarten Bronkhorst, Jasper Winkelhagen, Mark de Vries, Gerald Kraan, Bas Twigt, Alexander van Marle, Ewan Ritchie, Sanne Kleinveld en Bart van Dijkman), hartelijk dank voor uw inzet!

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ABOUT THE AUTHOR
ABOUT THE AUTHOR
Monique Margaretha Jozefa Walenkamp was born in Leiderdorp on January 31st 1986. She grew up in Oegstgeest where she graduated from bilingual Gymnasium at the Rijnlands Lyceum. She initially wanted to become an engineer and went to the Technical University of Delft to study Life Science & Technology. However, after completing her first year she decided to switch to medicine at the Erasmus University of Rotterdam.

Monique combined her 4th and 5th year of medical school with a research master Clinical Epidemiology at the University of Utrecht. Her research project led her to the Academic Medical Centre (AMC) in Amsterdam, where she helped design and initiate the Amsterdam Wrist Rules study and the VIPER-trial. Her efforts were rewarded with a PhD scholarship for which she paused her clinical rotations in Rotterdam. After starting the VIPER-trial in multiple hospitals, Monique resumed her rotations and combined this with her PhD research. She did her final rotation at the Trauma Unit in the AMC and graduated in February 2014 as a Medical Doctor.

In 2013, she managed to secure a large government grant (ZonMW Doelmatigheidssubsidie) for the implementation study of the Amsterdam Wrist Rules. This allowed a new PhD researcher who is currently running this study to be appointed.

Monique loves travelling. During medical school, she did a six months trauma research fellowship in Cape Town followed by a two month journey through Southern Africa. She also did a three months research fellowship at Columbia University Medical Centre in New York (supervisor Dr. Melvin Rosenwasser) in 2015. During this period, she initiated a research fellowship program for Dutch students and young doctors who want to do research in hand surgery at Columbia University Medical Centre.

Monique is currently working as a surgical resident (ANIOS) at the Department of Surgery in Maasstad Hospital Rotterdam (supervisor Dr. R.A. Klaassen).