Author’s response to reviews

Title: Comparison of volar-flexion, ulnar-deviation and functional position cast immobilization in the non-operative treatment of distal radius fracture in elderly patients: a pragmatic randomized controlled trial study protocol

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Author’s response to reviews:
The authors' response letter has been included as a supplementary file.

Reviewer reports:

Valentin Neuhaus (Reviewer 1): Thank you very much for the opportunity to review this study protocol. The authors want to compare two different types of casts in distal radius fracture in elderly patients.

Some comments:

It is a very important topic. It is a prospective, multi-center study. Randomized. Blinding not possible / very difficult. Intra- and extra-articular fractures will be separately randomized (blocks). Good outcome parameters.

The authors thank for the positive comments!
1. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing? Please clearly describe "primarily stable, reducible DRF" (so, exclude DRF with ulnar styloid fracture? What is your threshold of dorsal angulation?). Please exclude patients with concomitant fractures at the same arm (finger, carpal, proximal to the DRF).

This is a pragmatic trial and thus we have decided physician to set thresholds to primarily stable, reducible DRF, as they will do in real life too. In addition, the decision to exclude patient with concomitant fracture from the study is thus decided by the physician on-call. Further, in practice stableness of reducible DRF is clinically decided and in this pragmatic RCT we investigate the outcomes of conservative management of DRFs without specific thresholds in radiologic parameters. In the manuscript we explain this as follows: “The treating physician will perform closed reduction when necessary, but specific thresholds (shortening, dorsal angulation, radial inclination) is not set” (page 7, line 146-8). The Finnish national Current Care Guidelines specify stable DRF with radiologic parameters as: dorsal angulation <15 degrees, radial shortening <3mm, volar angulation <20 degrees, intra-articular step <1mm, radio-ulnar angulation <15 degrees. We presume that the physician on-call will decide stableness of the DRF in regard to these guidelines.

2. Is the planned statistical analysis appropriate: yes. In multivariate analyses you need to control for age, sex, dorsal angulation and comminuted fractures.

The authors agree that age and sex need to be controlled in multivariate analyses but we politely disagree with the dorsal angulation. In elderly population with stable Colles fractures association with functional outcome and radiological parameters has been shown in variety of studies to be low or non-existent. Further, we expect randomisation take care of the equal frequency of dorsal angulated and comminuted fractures in both groups.

3. The topic is elderly patients. The authors chose age threshold 65 years, better 70?

Authors agree that specific threshold of age in the study is more or less trivial choice. According to our knowledge most DRF studies have chosen 65 years of age as a threshold for studies and thus it could be more comparable with the results.
Christoph Bartl (Reviewer 2): the authors address an important topic as a good cast technique is essential to have a good outcome following conservative treatment.

1. The intervention is described with the two arms: immediate post reduction x-ray is necessary to make sure that the randomized position is achieved! Also a photo after hardening of the cast is recommended for control that the aimed position was achieved.

Thank you for these comments. The authors agree for the need of an x-ray after the reduction and it will be taken (this has now been mentioned in page 7, lines 155-7). We will measure actual cast positions from x-rays.

2. Please describe the functional position: is it in slight dorsal extension? How much flexion and ulnar deviation according to the Schede/Charnley position do you aim at?

Functional position cast of wrist is typically 20 degrees in dorsal extension/angulation. We have no exact thresholds for flexion and ulnar deviation (due to pragmatic trial setting, we will compare those positions used in real life) but extensive flexion (Cotton-Loder) is not permissible due to increase in pressure of the carpal tunnel.

3. All investigators must be trained prior to the start of the study, and introduced with a booklet specifying the two positions! What is the initial material: plaster cast or light cast or is it up to the centers?

Thank you for this excellent comment. Authors have now produced the booklet showing the two casting positions for all participating centres (page 7, lines 153-4). The initial material is plaster cast (page 7, lines 154-5).


Our study is a pragmatic study, which has been structured by its principals; where the key features and important ways in which they differ from efficacy studies are (a) the questions, perspectives taken, and outcomes studies are important to practitioners and patients (b) the research is conducted in multiple, heterogenous settings similar to those in practice; (c) there are few exclusions criteria and characteristics of patients resemble those seen in typical practice; and (d) comparison conditioners are real-world alternatives- for example, current standard of care, rather than no treatment or placebo controls. (Glasgow et al. 2005, Tunis et al. 2003, Zwarenstein and Treweek 2009)
The authors agree that people could possibly rate themselves worse in QoL-scores if they had additional fractures of extremities. 15D score will be secondary outcome measure and if needed in order to make comparable groups, patients can be excluded from 15D outcome comparison. We do not exclude these patients from the whole study because we assume that these fractures do not affect remarkably the primary outcome measure of the study (PRWE). Further, according to pragmatic study principals, we assume that persons with bilateral and accompanying fractures will be randomised and allocated equally to both groups.

5. Scores: PRWE and DASH is a good choice. Is the 15D score comparable to other studies? What about SF-12 with a PCS and MCS score and the EQ-5D score? QoL-scores should also be assessed retrospectively some days after the intervention to assess the preop condition 4 weeks pre-intervention. Same with the PCS score – it should be assessed after pain control after some days to minimize bias and to negative self scoring of this population!

The authors agree that PCS score assessed at the time of acute trauma can suppress scoring. However we assume that the bias of this will be of same magnitude and direction in both groups of cast positions and thus will not affect comparison of two treatment arms.

The 15D score is comparable with EQ-5D. However, 15D seems to yield better sensitivity in terms of discriminatory power and responsiveness to clinically important change. See following citation in manuscript (Vainiola et al. 2010).

6. A baseline EQ-5D and PCS score is recommended to proof if patients recover from the injury. Here also a paper addressing this question plate vs cast- an RCT from 2014 should be included, and also two other papers and reviews comparing surgical methods with casting techniques, that also looked at complications

We are a little unclear as to what the reviewer is eluding. If the reviewer is refering to specific publications, the authors politely ask the reviewer to suggest these references.

However, the main goal in this study is to compare two different cast methods after a fracture, not to address whether patient recover from the injury. Moreover, it has been suggested that, the baseline questionnaires are unreliable when baseline is measured at the time of fracture. Patients tend to answer the present status interfeared by the pain and not beeing able to focus the days prior the trauma. Hence the “baseline” is, in our opinion, considered to be far too deceptive. For this reason we didn’t want to take the baseline questionnaires in this trial.
7. Intervention: reduction control with x-ray is necessary, additional photo is recommended also for internal control. What is the acceptable range of the deviation for the cast positions?

The authors agree with the importance of an x-ray control after the reduction and it will be taken (page 7, line 155-7). Moreover, cast positions will be measured from x-rays to use these in internal control.

The acceptable range for the deviation after the reduction has been discussed more thoroughly in remark #1 of reviewer 1 (page 2 of this letter) since both reviewers suggested it.

8. Follow-up: a 1-2 week x-ray is needed to detect loss of reduction and indication for surgery.

Since this a pragmatic trial, we wish not to interfere normal treatment, only the cast position. However, based on the Finnish National guidelines, the x-rays will be arranged according to the Current Care Guidelines (page 8, lines 159-60).

9. The authors need an SAE and AE documentation - serious adverse events have to be named: cts, neurologic, ulcera etc. and these should be graded and the outcome of AE and SAE should be assessed. CRPS 1 must be added as the main complication - will there be differences (cast position, number of reductions?)

The authors agree with the need of adverse event documentation. Complications is listed now in outcome measures (page 5, line 102).

10. Statistics: the new MCRD of Walenkamp is important as it can be 11-14 points for the PRWE and DASH scores.

The study of Walenkamp et al. (2015) found the minimal clinically important difference to be 11 points and the study is cited in the manuscript (page 9, line 184).

11. Please describe exactly how much patients you need in each group. Also name the person responsible for the statistics. Add to the flow chart that after one year 40 persons in each group have to complete the 1 year FU to have enough power - 40 and 40 plus 30% drop out is not 114 or?

The power analysis of the trial for sample size is done according to the PRWE score under subchapter “Power analysis”. With the drop-out rate of 30% the sample in the beginning of the study has to be 80 (patients in the “end”) divided by 0.7 which equals 114.
Of the authors, AR, will be responsible for the statistics (page 10, lines 207-8).

The sentence explaining the number of patients needed in order to have statistical power is added to the manuscript (page 9, lines 185-6).

12. What is the primary outcome: PRWE in the ITT (intention-to-treat) setting. What about the conversion group to surgery, does it count as ITT - will it be the same in both groups? What if not?

Also an "as-treated group" should be added - only cast group 1, only cast group 2, and those with conversions to surgery - is additional statistics necessary?

The authors agree that there will be no certainty for conversion to surgery be the same in amount in both groups, but the randomization is considered to take care of it. However the primary analysis should done with ITT -fashion as described in CONSORT statement. Other analyses may be discussed after the follow-up period.

13. 12 month follow-up assessing the scores should be done in the clinic with a doctor.

The authors politely disagree with the appropriateness of physical contact with a doctor regarding to self-assessment tests that patients have done earlier during the study. The authors believe that questionnaires based on internet and regular mail on demand will result in adequate response rate and correspondence compared to physical contact in a clinic.

14. Recommended additional explanatory variables: recovery 1 y after the intervention in a QoL score eg EQ-5D, 15D, SF-12. A baseline score is mandatory in my view and easy to manage.

Complications and fracture type: use common classifications like the AO-classification.

The authors agree that in order to add 1 year QoL score recovery from baseline to explanatory variables, baseline score would be needed. However, authors suggest that baseline QoL to be unreliable due to injury itself. Moreover, we are comparing results between groups, not in groups.

The fractures will be classified with AO-classification and it has been added to the manuscript (page 5, line 104).

15. To be comparable patients must be comparable in the 2 groups: assess fracture type, age, sex, eg ASA classification for acc. illnesses, osteoporosis, bisphosphonate use etc.
Due to pragmatic trial setting, the only thing that differs between groups in this trial is cast position. What comes to osteoporosis, bisphosphonate use etc. we suspect randomisation to take care of equal distribution between groups. The authors propose that age and intra- or extra-articularness of the fracture will result in decent comparability of groups in this pragmatic trial.

16. Add photos of the cast positions in this publication to show what you mean with the 2 positions.

The authors thank for the remark of missing photos of cast positions. The photos will be added to appendix material and end of this letter.

References:


Zwarenstein, M., & Treweek, S. (2009). What kind of randomised trials do patients and clinicians need? Evidence Based Medicine, 14, 101-103