

Ultrasound guided radial and median nerve blocks versus haematoma block for closed reduction of distal forearm fractures; a randomised controlled trial.

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1. Personnel and inclusion sites**1.1 Initiators**

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1.3 Inclusion sites and local investigators

Patients will be included at the Emergency Departments at the following hospitals (more to be added):

Aalborg University Hospital
Hobrovej 18-22
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Local investigator: **Jakob Madsen**, MD, email: jama@rn.dk

Viborg Regional Hospital
Heibergs Allé 2-4
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1.4 Enrolling personnel

At each inclusion site, all anaesthesiologists and anaesthesiologist trainees with sufficient experience to perform acute regional anaesthesia will participate in patient screening and inclusion. They will all undergo a formal introduction to ensure conformity in injection site and injected volume, prior to their inclusion of patients.

2. Introduction and background

2.1 Patient population

Each year, approximately 40.000 patients are diagnosed with a fracture in the distal forearm in Danish hospitals(1). While the term Colles' fracture is widely used to describe all the distal forearm fractures, the Danish system for encoding of diagnosis describes a variety of fracture types in the distal forearm including three fracture types of the distal radius (code DS525); the Smith fracture (DS525A), the Colles' fracture (DS525B) and the Barton's fracture (DS525C). Among all dislocated fractures of the distal forearm only the true Colles' fracture can potentially be treated adequately with a closed reduction and a cast, while the other fracture types are unstable by definition and require surgical stabilization. Most dislocated forearm fractures, however, require a primary reduction and this procedure requires the patient to be relieved of pain and the muscle traction on the fracture to be minimal.

2.2 Anaesthetic choices for distal forearm fracture reduction

The conventional method of anaesthesia for the reduction of a distal forearm fracture is the haematoma block with the local anaesthetic agent being injected directly into the fracture line. This is performed either by using a blind technique in which the physician uses the needle to feel his way across the bone surface until the fracture line is reached, or by using x-ray to visualize the needle. In either technique blood is aspirated in

the cannula as a sign of the needle tip being in the haematoma surrounding the fracture, and the local anaesthetic is injected(2,3). The haematoma block is traditionally considered to be a safe anaesthetic option even with the risk of rapid systemic absorption and a potentially toxic systemic dose of the local anaesthetic(4,5). It has never been proven superior to other techniques in systematic reviews(6,7), nor has it been compared to an ultrasound guided analgesia technique as described in the current protocol.

2.3 Innervation of the forearm and wrist

The radial and median nerves innervate the majority of muscles in the forearm and the periosteum of the ulna and radius as the posterior and anterior interosseous nerves, respectively. Therefore, blocking of these nerves at the level of the cubital fossa should alleviate pain and decrease muscular traction allowing manipulation of fractures in the radius and ulna(8,9).

2.4 Distal nerve blocks for procedures on the forearm and hand

Although blocking the radial, median, and ulnar nerves is not a commonly used form of anaesthesia for closed reduction of forearm fractures, it is by no means an experimental anaesthetic procedure. The distal nerve blocks of the forearm have long been used both as rescue blocks in case of failed infraclavicular and supraclavicular blocks and as a primary choice in the case of surgical procedures involving one or more of the nerves innervation areas(10).

2.5 Properties of lidocaine

In the present study, lidocaine is our choice of local anaesthetic as it is well-known and widely used. Lidocaine and adrenaline in combination has been approved for medical use in Denmark for decades specifically for the indications of local infiltration and nerve analgesia(11). Lidocaine is a rapid onset local anaesthetic and in combination with adrenaline has an onset time of barely 10 minutes and a duration of at least 120 minutes when used for local infiltration and blocking of small nerves(12,13).

3. Hypothesis and outcome

3.1 Hypothesis

We hypothesize that ultrasound guided blocking of the radial and median nerves will improve fracture reduction satisfaction for the true Colles' fractures and improve analgesia for reduction of all fracture types compared to the standard haematoma block.

3.2 Primary outcome

Reduction satisfaction based on objective X-ray measures according to the National Guideline for Treatment of Distal Forearm Fractures. The primary outcome applies for the true Colles' fractures only.

3.3 Secondary outcomes

Will be evaluated for all included fracture types.

- Pain scores using an 11-step numeric rating scale
- Time spent in the Emergency Department
- Secondary fracture dislocation

4 Study design and conduction

4.1 Selection and enrolment of participants

4.1.1 Recruitment strategy and screening

Patients eligible for screening for inclusion are identified in the Emergency Department (ED) at all recruitment sites upon primary contact. When an X-ray has revealed the relevant fracture, the ED-staff will call the available anaesthesiologist or anaesthesiologist trainee who will perform the inclusion process and randomisation. In cases where the anaesthesiologist is unable to perform inclusion due to e.g. lack of time or experience a registration of patient data, date and time as well as the reason for the missed inclusion will be made.

In case of randomisation to the control group, the anaesthesiologist/anaesthesiologist trainee will leave the ED and take no further part in the treatment or data registration. In case of randomisation to the intervention group the anaesthesiologist/anaesthesiologist trainee will perform the ultrasound guided blocks and leave the ED before the reduction procedure begins.

For all included patients a note will be made in the electronic patient journal stating that the patient meets all in- and no exclusion criteria, has given an informed consent to participation and received a copy of the signed consent form.

4.1.2 Inclusion criteria

- Presence of a closed distal forearm fracture in need of a closed reduction
- Age > 18 years
- Legally competent

4.1.3 Exclusion criteria

- Inability to give informed consent
- Allergy or intolerance towards local anaesthetics
- Infection or burns at either injection site
- Multi trauma (defined as other fractures or significant injuries)
- Known pregnancy
- Participation in other studies

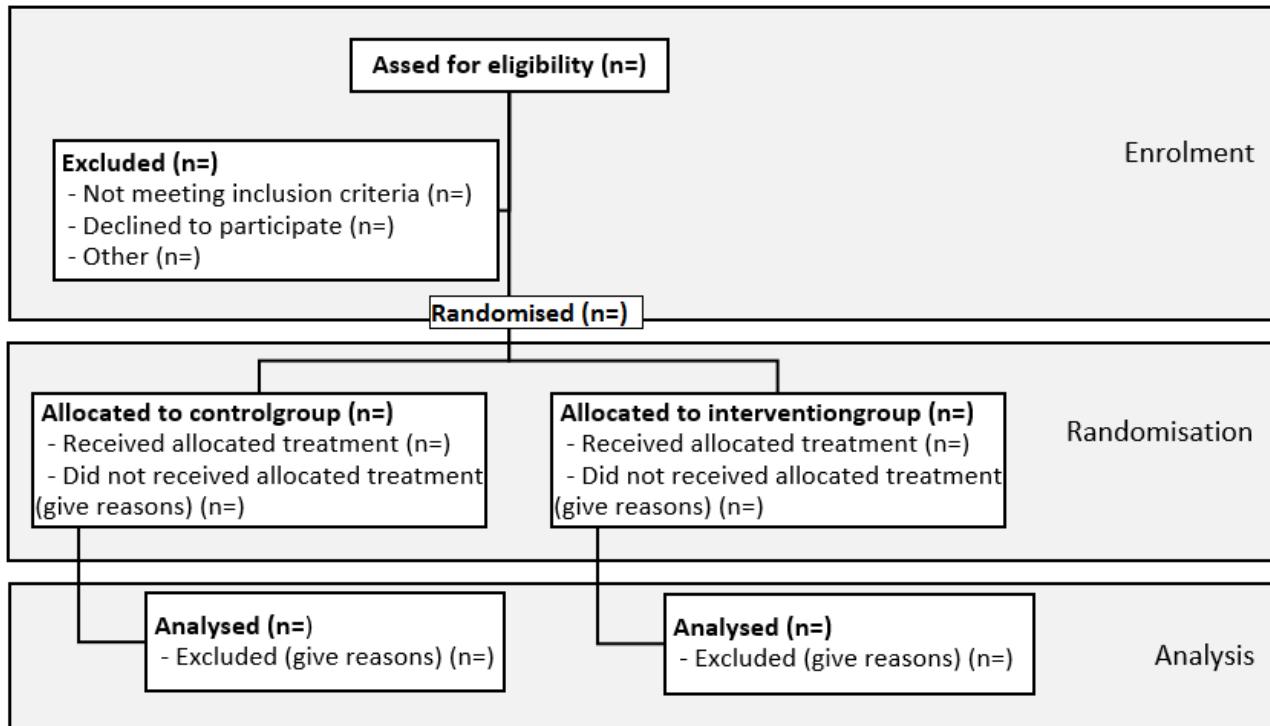
4.1.4 Information and consent

The anaesthesiologist/anaesthesiologist trainee responsible for inclusion will apply to the national regulations regarding informed consent to participation in a clinical trial. Hence, in addition to oral information the potential participant will receive written information including both the specific information on the current study as well as the general information pamphlet on participant rights when entering a clinical trial. All information and inclusion will be carried out by physicians who possess the sufficient professional prerequisites to be authorized by the sponsor to have a direct involvement in the project.

Information will be given in private and the participant will be allowed to have an assessor present. The participant will be given a brief reflection period of approximately 10 minutes before making their decision.

4.1.5 Participant flow

The following consort diagram will be continuously filled out to monitor study progress regarding primary outcome.



4.1.6 Discontinuation and withdrawal

Any participant can choose to withdraw from the study at any time. This will have no repercussions on his or her right to or quality of continuous treatment. The same applies if a discontinuation is made by the choice of the physician. In this case the patient will be informed of the reason for discontinuation. Any withdrawal or discontinuation will be noted in the consort diagram and mentioned when presenting results in future publications.

4.2 Randomisation

4.2.1 General considerations

Participants will be randomized in either the intervention or the control group using the online randomization tool Research Electronic Data Capture (REDCap, Aarhus University, Denmark).

All patients will receive an intravenous access. Monitoring of heart rate, blood pressure and oxygen saturation will be established according to local guidelines at each inclusion site before injection of local anaesthetic.

In both groups, the reduction process will begin 10 minutes after the block has been performed. The technique for the actual reduction may vary amongst physicians. To best reflect the clinical practices and to avoid the risk of an insufficient reduction due to the physician being forced to comply to a technique unfamiliar to him, no further standardisation will be made in this regard.

4.2.2 Intervention group

Using a linear probe, the medial and radial nerves will be visualized in the cubital fossa and blocked by injection of 5-7 ml lidocaine 20 mg/ml with adrenaline 5 µg/ml ('SAD').

4.2.3 Control group

Patients in the control group will receive the standard haematoma block at all inclusion sites. This will be performed using the previously described technique and local anaesthetics according to local practices.

4.3 Blinding

Only the orthopaedic surgeons evaluating the control X-ray to assess the primary outcome of fracture reduction satisfaction will be blinded to randomisation.

4.4 Data collection

In both groups, the following will be registered during the treatment period in the emergency department:

- Pain scores using an 11-step numeric rating scale (NRS) ranging from 0 (no pain) to 10 (worst pain imaginable)
 - Before local anaesthetics are given
 - During the local anaesthetic procedure
 - During reduction
- Precise amount and type of local anaesthesia used
- In plane/out of plane technique used for the ultrasound guided blocks
- Type and amount of supplementary analgesics/sedatives before and after local anaesthesia
- Fracture classification code
- Treatment plan; conservative vs. operation
- Osteoporosis yes/no
- Patients right/left hand preference
- Patient height and weight
- Any chronic use of opioids

Following casting of the fracture a control X-ray will be performed and subsequently evaluated independently by two skilled orthopaedic surgeons to establish if the reduction was satisfactory. In case of disputes a third orthopaedic surgeon will evaluate the X-ray and make a final ruling. The orthopaedic surgeons will further determine fracture type.

In cases where more than one control X-ray is performed due to re-manipulation of the fracture, only the first will be evaluated. The fracture will be deemed satisfactory using a binary outcome measure (yes/no) if all the following requirements set by the National Clinical Guideline for Treatment of Distal Radius Fractures(14) are met:

- < 10-degree dorsal angulation of the radial articular surface
- Ulnar variance < 2 mm
- Discontinuation of the articular line < 2 mm
- No incongruence of the distal radioulnar joint

Two months after the initial treatment the electronic journal will be evaluated to establish the occurrence of secondary dislocation and need for surgery.

4.5 Data handling

4.5.1 Data management

All primary registration of data will be performed on paper by the ED staff. To ensure a simple procedure for data collection the registration sheet will be present on a specified location in the ED and each section on the sheet marked according to the staff member in charge of each registration. All registration sheets will subsequently be collected by the coordinating investigator and entered online in the REDCap database. Access for data registration and access to already submitted data will be granted to all the initiating investigators.

4.5.2 Confidentiality

All data will be handled in accordance with the act on processing of personal data and no identifiable data will be included in the analysis. When the study is concluded all person-sensitive data will be destroyed.

4.6 Data analysis

4.6.1 Sample size estimation

The number of included patients is calculated using data from an unpublished quality database at Viborg Regional Hospital. Approximately 15 percent of the true Colles' fractures are currently being satisfactorily reduced, and we consider an increase to 30 percent to be clinically relevant. With $\alpha = 0.05$ and $\beta = 0.8$, 121 patients are needed in each group to detect a statistically significant difference in reduction satisfaction. From the same local database we found that the true Colles' fracture comprises approximately 90 % of the total number of fractures and we anticipate a total inclusion of 268 patients ($2 \times 121 + 10\%$).

4.6.2 Statistics

Binary data, including primary endpoint will be analysed using chi squared test. For normally distributed measurements the differences between groups will be compared using Student's *t*-test. Variables considered not to be normally distributed will be analysed by Mann-Whitney's *U*-test. Two-tailed *P*-values < 0.05 will be considered statistically significant.

5. Ethical concerns

5.1 Approvals

Permission for conduction of the study and gathering of information in the electronic patient journal will be received from the Ethical Committee and the Danish Data Protection Agency through the common Regional system in the Central Denmark Region.

We specifically seek permission to access all relevant journal entries in the participants electronic journal regarding the current forearm fracture and its treatment from the point of primary contact to the ED and for the remainder of the study period. This includes any X-ray information available in different electronic systems.

5.2 Risks and safety considerations

Regardless of a patient being treated within the study or declined participation, a fracture reduction is needed as is analgesia prior to this reduction. As both the haematoma and the ultrasound guided blocks are well established methods of analgesia and as lidocaine is well established as a local anaesthetic agent, no significant ethical concerns are found with conduction of the study. The establishment of an i.v. access poses no significant risks.

5.3 Adverse reactions

Regardless of injecting technique and site the adverse reactions to local anaesthetic use include allergy and toxicity. Both are rare when small doses of local anaesthetics are used, as is the case in the current study, and most often occur if the local anaesthetic is vascularly injected as it increases the risk of rapid systemic distribution. Symptoms of toxicity include tinnitus, tingling lips, heart palpitations, altered mental status and in extreme cases loss of consciousness, severe heart arrhythmias and cardiac arrest. The intervention group is not thought to face a greater risk of adverse effects than the control group, and the ultrasound procedure poses no additional risk. As with conduction of all clinical trials, there may be unforeseen risks and adverse effects. All patients included in the study are covered by the common patient insurance.

5.4 Gain and benefits

Participants have the possible benefit of a reduced pain with regards to both the local anaesthetic and reduction procedures as well as the possible gain of a more satisfactory reduction. To our knowledge there are no long-term benefits from participation. The gain for future patients in the potentially increased pain relief and reduction satisfaction far outweighs the minimal disadvantages of study participation including establishment of an i.v. access and two injection sites when randomized to the intervention group as opposed to one, when randomized to the control group or treatment outside the study.

None of the investigators benefits personally from conducting the study nor from any results and conclusions.

6. Funding

All initiative for the current study have been taken by the previously stated physicians. They have no personal economic involvement, no possible economic gain from any outcome and no ties to the medical industry or corporations gaining from study outcomes.

Funding for the purchase of iPads for data registration and statistical assistance in the analysis phase will be sought from relevant private and public funds. Due to the modest running expenditures comprising only lidocaine and injection equipment already present at all inclusion sites the study will be conducted regardless of any successful funds applications.

7. Publication

Upon approval from all relevant committees the protocol will be made public at clinicaltrials.gov. All results and conclusions both positive, negative and inconclusive, drawn from the study will be sought internationally published regardless of any discrepancies with our primary hypothesis.

8. References

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