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Cast immobilization in situ versus open reduction and internal fixation of displaced medial epicondyle fractures in children between 7 and 16 years old. A study protocol for a randomized controlled trial

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ABSTRACT

Introduction

Medial epicondyle fracture of the humerus is a common injury in childhood. There is uniform agreement that minimally displaced fractures (dislocation ≤ 2mm) can be treated non-operatively with immobilization. Open fractures, fractures with joint incarceration or ulnar nerve dysfunction require surgery. There is no common consensus in treatment of closed medial epicondyle fractures with >2mm dislocation without joint incarceration or ulnar nerve dysfunction. We hypothesize that there is no difference of treatment outcomes between nonoperative and operative treatment.

Methods and analysis

This is a multicenter, controlled, prospective, randomized non-inferiority study comparing operative treatment to non-operative treatment of >2mm dislocated pediatric medial epicondyle fractures without joint incarceration or ulnar nerve dysfunction. A total of 120 patients will be randomized in 1:1 ratio to either operative or non-operative treatment. The study will have a parallel non-randomized patient preference arm. Operative treatment will be open reduction and internal fixation. Non-operative treatment will be upper limb immobilization in long arm cast for 4 weeks. Data will be collected at baseline and at each follow-up up to 2 years. Quick-DASH is used as primary outcome measure. Secondary outcomes are patient reported pain, differences in range of motion, PedsQL, Cosmetic VAS and Mayo Elbow Performance Score.

Results

The findings will be reported in 2024.

Ethics and dissemination

Ethical approval has been obtained from Helsinki University Hospital (HUS) ethical board HUS/1443/2019. A written authorization from legal guardian will be acquired and the child will be informed about the trial. Results of the trial will be disseminated as published articles in peer-reviewed journals.

Trial registration

The trial has been registered at clinicaltrials.gov with registration number NCT04531085.

STRENGTH AND LIMITATIONS OF THIS STUDY

To the best of our knowledge this is the first multicenter randomized controlled trial to examine the treatment and outcome for > 2mm dislocated medial epicondyle fractures in children and adolescents.

Blinded outcome assessor, independent of treating surgeons.

Use of several patient-reported outcome measures as well as return to sports/music.

Comparison of 2 age groups (less than 12 years vs. 12 years and over) in regards to outcome.

The results of this trial will help clinicians to select appropriate treatment method.

INTRODUCTION

The incidence of medial epicondyle fractures of the humerus in children and adolescents is ≥3:100000 and account for approximately 12-20% of all pediatric elbow fractures [1,2] 30-50% of these fractures are associated with elbow dislocation and 5-18% are incarcerated [3,4]. Dysfunction of ulnar nerve has been reported in 10-16% of cases[3].

Minimally displaced (≤ 2mm) fractures without incarceration or ulnar nerve dysfunction are treated non-operatively [5-10]. There is no common consensus between pediatric surgeons how to treat medial epicondyle fractures with > 2 mm dislocation[11-12]. It has been suggested that incarcerated fractures and fractures with elbow dislocation should be treated operatively, and that competitive athletes should be treated operatively with lower threshold than children and adolescents without sporting activities[13].

Grahn et al (2020)[1] conducted a controlled treatment trial based on prospectively collected data from ≤ 16 years old patients with more than 2 mm displaced non-incarcerated medial epicondyle fractures with a minimum follow-up of 1 year. Partial avulsion fractures were excluded, 41 were treated non-operatively and 40 operatively. They found that neither the degree of primary fracture displacement with or without concomitant elbow dislocation nor the choice of treatment (ORIF or long arm cast) affected outcome. Normal elbow function was restored in 74/81 patients. All but one primarily non-operatively treated patients had returned to the same or higher level of sport as pre-injury, whereas six surgically treated patients had down-graded their sporting activities. Pain at medial humeral epicondyle either with direct contact or under load was reported by four non-operatively and by six operatively treated children with normal sensation and elbow stability (1). According to the study of Lawrence et al. (2013)[14] there was no difference in outcome assessed by QuickDASH and elbow range of motion at 2 years from injury in 6 non-operatively and 14 operatively treated athletes. Axibal et al. (2018)[15] showed similar results with no difference in the objective outcome in less than one year follow-up between 22 operated patients matched to 22 non-operated patients.

In light of current findings we applied for ethical review board approval to conduct a randomized non-inferiority trial with the hypothesis being that conservatively treated medial epicondyle fractures fare as well as operatively treated.

METHODS AND ANALYSIS

Study design:

The study is designed as a multicenter parallel-group non-inferiority randomized controlled trial (RCT) that complies with the CONSORT guidelines (Figure 1). A patient preference arm will be available. Patient recruitment will be done at all university hospital areas of Finland (Helsinki, Kuopio, Oulu, Tampere, Turku). The study is coordinated by Helsinki University Central Hospital, Children's Hospital pediatric orthopedic unit. Trial data analysts and person performing the recruitment will be unaware of the assigned treatment.

Patient recruitment:

All patients with a medial epicondyle fracture referred to the aforementioned hospitals will be screened for eligibility by a specialist of either hand surgery, pediatric surgery, pediatric orthopedics or orthopedics. If inclusion criteria are met, written consent is asked from the guardian. Patients and parents are given a written informed consent regarding the trial. The patient version is age adjusted for easier understanding according to the Finnish Investigators Network for Pediatric Medicines (www.finpedmed.fi)

Inclusion criteria:

Patients aged 7-16 years presenting with a ≥ 2mm displaced non-incarcerated medial epicondyle fracture with or without concomitant elbow dislocation and normal ulnar nerve function.

Exclusion criteria:

Pathological fracture, open fracture, systemic bone disease, concomitant fracture or injury of the same upper limb requiring operative intervention, other disease preventing participation in full follow-up regime and range of motion exercises.

Randomization

After agreeing to participation in the trial patients are randomized according to a computer generated randomization list[16] to either operative or non-operative treatment. Randomization ratio is 1:1. Randomization is performed by the recruiting physician who is blinded to the intervention.

Patient's choice arm:

Patients who meet inclusion criteria, but refuse participation in the randomized trial are offered to choose treatment method (operative or non-operative) and continue in a prospective parallel patient preference arm that otherwise follow the same treatment and FU protocol as the RCT.

Baseline

Standard anterior-posterior and lateral radiographs of the elbow will be obtained after closed reduction of the possible elbow dislocation. All participants in either the RCT or patient's choice arm undergo cone-beam or normal computer tomography (CT) before treatment initiation. Initial fracture dislocation will be calculated from the CT scans in three planes (anterior-posterior, cranial-caudal and medial-lateral) and both radiographs (anterior-posterior and lateral) using the method described by Edmonds et al (2010)[17]. Date of injury, method of injury, patient's age at time of injury, sex, injured side, dominant hand and main sport or musical instrument as well as level will be documented. Motor and sensory

function as well as range of motion of both upper limbs will be assessed. Carrying angle (degrees) and valgus stress test will be assessed if possible for both limbs.

Intervention

Non-operative treatment means upper limb immobilization with forearm in neutral pro-supination with a long arm cast for 4 weeks. Treatment is started after baseline examination.

Operative treatment is scheduled after baseline examination and is to be done within 7 days from injury. During sedation both elbows are stress tested using the valgus stress test, any instability is documented, carrying angle of both elbows are measured. Procedure of preference is open reduction and internal fixation (ORIF) with cannulated non-resolvable 4.0 mm screw with or without washer. If the fracture fragment is too small or fragmented for screw fixation 1.6 mm – 1.8 mm Kirshner-wires and/or bone anchor are used. After fracture fixation the injured side is again stress tested. Radiographs (anterior-posterior and lateral) documenting the fixation are taken. Long arm cast with forearm in neutral pro-supination is applied for 4 weeks. Time from injury to surgery, fixation method, length of surgery (min) and surgeon's level of training (consultant, registrar) will be documented. Hardware is not routinely removed.

All patients will receive a written exercise plan explaining the active and passive ROM exercises that are to be performed at a minimum three times per day from cast removal. Physiotherapy will be offered if guardians and/or patients feel that no progress in ROM after 2 weeks of home exercises.

Blinding

This trial tests a clinical intervention that is not suitable for protection against treatment bias. Recruiter will be blinded. Consultant on duty at will perform randomization and allocation. Non-operative

treatment will be started immediately after recruitment. ORIF will be performed by surgeon on duty. Surgeon is not blinded. Trial data is collected at each appointment at the outpatient clinic by a physician not related to the trial. Statistician analyzing trial data is blinded to treatment group.

Outcome measure

Follow-up is set at 1, 3, 6, 12 and 24 months from initiation of treatment with the option of ending the FU at 12 months if patients is pain free with full ROM in relation to uninjured side. Elbow standard radiograph (anterior-posterior and lateral) are taken at each appointment from 3 months on until bone union is achieved or trial ends (Table 1).

Patients will be examined at the pediatric orthopedic outpatient clinic. Upon each appointment active and passive ROM of both upper limbs (elbow extension-flexion, pro-supination, wrist extension-flexion) as well as carrying angle are measured using a goniometer. Stability of both elbows are assessed using the moving valgus test[18] and the valgus stress test[19]. Distal sensation is examined by Semmes-Weinstein monofilaments[20]. Signs of cold intolerance will be assessed. Grip strength is measured with a dynamometer.

Patients and guardians are requested to answer the following patient reported outcome measures at each appointment; QuickDASH©[21], Pediatric Quality of Life Inventory™ (PedsQL), PedsQL Pediatric Pain Questionnaire[22], cosmetic visual analoque scale (VAS 0-100) and Mayo elbow performance score (MEPS)[23].

Time of returning to main sport or music and its level will be documented (weeks). Any adverse effects (wound infection, nerve damage) are documented as well as hardware problems and possible hardware removal as well as conversion of treatment during FU (cast to ORIF or ligament reconstruction).

Primary outcome:

Statistically significant difference in QuickDASH score is 6.8 (18) at 12 months FU.

Secondary outcome:

Difference in active ROM in comparison to uninjured arm, PedsQL, PEDS QL Pain module, Cosmetic VAS, MEPS, need for additional procedures.

Sample size

Based on the results of Nikolas et al (2020)[24] and Aasheim et al (2014)[25] we assume clinically significant difference between the groups to be 6,8 and the standard deviation of the QuickDASH score to be 10 points. With 0,05 significance level and 80% power a non-inferiority comparison would require 27 patients per group. Allowing a 20% dropout rate the required sample would be 30 patients per group. For subgroup analysis (less than 12 years vs. 12 years and over) 30 patients per age group needs to be collected. Assuming 50-50 split in the patients between the age groups the sample size would be 60 per ORIF and non-operated equaling a total of 120 patients.

Statistical analysis:

Data will be analyzed by using the Wilcoxon rank-sum test in Python 3.8. (Python Software Foundation, Wilmington, Delaware, U.S.A). Our hypothesis is that there is no difference in outcome between non-operative versus ORIF. Level of significance is set at $p < 0.05$.

Both treatment groups will be internally analyzed for differences in primary outcome regarding age (less than 12 years vs. 12 years and over) at time of injury and amount of initial fracture displacement (mm). Depending on group size, patient choice arm can be merged for analysis to same RCT group.

Ethics and dissemination:

There is no common consensus for dislocated (>2mm) medial epicondyle fractures. Treatment method vary by clinic and treating surgeon. Both ORIF and long arm cast are well established treatment methods for humeral medial epicondyle fractures. We have obtained ethical approval from Helsinki University Hospital (HUS) ethical board HUS/1443/2019. A permission to conduct the trial will be obtained by each study center. A written authorization from guardian will be acquired and child will be informed about the trial. Results of the trial will be disseminated as published articles in peer-reviewed journals.

Time schedule:

Last patient FU is expected by the end of 2023 and publication by the end of 2024.

CONCLUSION

The goal of this study is to compare two well-established treatment methods of dislocated non-incarcerated humeral medial epicondyle fractures in 7-16 year old patients.

COMPETING INTEREST STATEMENT

Dr. Helenius reports grants from Medtronic and Stryker. Dr. Helenius is consulting surgeon at Medtronic. Dr. Sinikumpu is consulting surgeon at Bioretec ltd. None of the other authors report any conflict of interest.

REFERENCES

1. Grahn P, Hämäläinen T, Nietosvaara Y, Ahonen M. Comparison between non-operative and operative treatment of medical epicondyle fracture: functional and patient reported outcome. Acta Orthop. 2020 Article in press.
2. Flynn J, Skaggs D, Waters P. Rockwood & Wilkins` Fractures in Children, Eight edition. Wolters Kluwer 2014.
3. Louahem D, Bourelle S, Cottalorada J. Displaced medial epicondyle fractures of the humerus: surgical treatment and results. A report of 139 cases. Arch Orthop Trauma Surg. 2010;130:649-655.
4. Hyvönen H, Korhonen L, Hannonen J, Serlo W, Sinikumpu JJ. Recent trends in children's elbow dislocation with or without a concomitant fracture. BMC Musculoskelet. 2019;20:294.
5. Gottschalk H, Eisner E, Hosalkar H. Medial epicondyle fractures in the pediatric population. J Am Acad Orthop Surg 2012;20:223-232.
6. Smith F. Medial epicondyle injuries. J Am Med Assoc. 1950;142:396-402.
7. Blount W. Fractures in Children. London: Williams & Wilkins; 1955.
8. Maylahn D, Fahey J. Fractures of the elbow in children: Review of three hundred consecutive cases. J Am Med Assoc. 1958;166:220-228.
9. Bede W, Lefebvre A, Rosman M. Fractures of the medial humeral epicondyle in children. Can J Surg. 1975;18(2):137-142.
10. Tarollo L, Mugani R, Catani F. Pediatric medial epicondyle fractures with intra-articular elbow incarceration. J Orthop Trauma. 2015;16:117-123.
11. Lee H, Shen H, Lee C, Wu S. Operative treatment of displaced medial epicondyle fractures in children and adolecents. J Shoulder Elb Surg. 2005;14(2):178-85.

12. Pezzutti D, Lin J, Singh S, Rowan M, Samora J. Pediatric medial epicondyle fracture management: A systematic review. J Pediatr Orthop. 2020;40(8):e697-e702.
13. Baety J, Kasser J. Chapter 15 in Rockwood & Wilkins`Fractures in Children 8th edition. Philadelphia, PA : Lippicott Williams & Wilkins; 2014.
14. Lawrence J, Patel N, Macknin J, Flynn J, Cameron D, Wolfgruber H, Ganley T. Return to competitive sports after medial epicondyle fractures in adolescent athletes: results of operative and nonoperative treatment. Am J Sports Med. 2013;41(5):1152–1157
15. Axibal D, Carry P, Skelton A, Mayer S. No Difference in return to Sport and Other Outcomes Between Operative and Nonoperative Treatment of Medial Epicondyle Fractures in Pediatric Upper-Extremity Athletes. Clin J Sport Med. 2018; 1;10.1097/JSM.0000000000000666
16. Urbaniak, G. C., & Plous, S. Research Randomizer. 2011;Retrieved from http://www.randomizer.org.
17. Edmonds E. How displaced are “nondisplaced” fractures of the medial humeral epicondyle in children? Results of a three-dimensional computer tomography analysis. J Bone Joint Surg Am. 2010;92:2785-2791.
18. O'Driscoll S, Lawton R, Smith A. The "moving valgus stress test" for medial collateral ligament tears of the elbow. Am J Sports Med. 2005;33(2):231-239.
19. Flynn T. User's 220 guide to the musculoskeletal examination: Fundamentals for the evidence-based clinician. Buckner, Kentucky: Evidence in Motion. 2008.
20. Bell-Krotoski J. “Pocket filaments” and specifications for the semmes-weinstein monofilaments. J Hand Ther. 1990;3(1):26-31.
21. Beaton D, Wright J, Katz J. Development of the Quick-DASH: comparison of three item-reduction approaches, J Bone Joint Surg Am. 2005;87:1038-46.

22. Varni J, Seid M, Rode C. The PedsQL: Measurement model for the pediatric quality of life inventory. Med Care 1999;37(2):126-39.

23. Morrey B. The Elbow and Its Disorders. Philadelphia: WB Saunders; 1993.

24. Kazmers N, Qiu Y, Yoo M, Stephens A, Tyser A, Zhang Y. The Minimal Clinically Important Difference of the PROMIS and QuickDASH Instruments in a Nonshoulder Hand and Upper Extremity Patient Population. J Hand Surg Am. 2020;45(5):399-407.e6.

25. Aasheim T, Finsen V. The DASH and the QuickDASH instruments. Normative values in the general population in Norway. J Hand Surg Eur Vol. 2014;39(2):140–144.

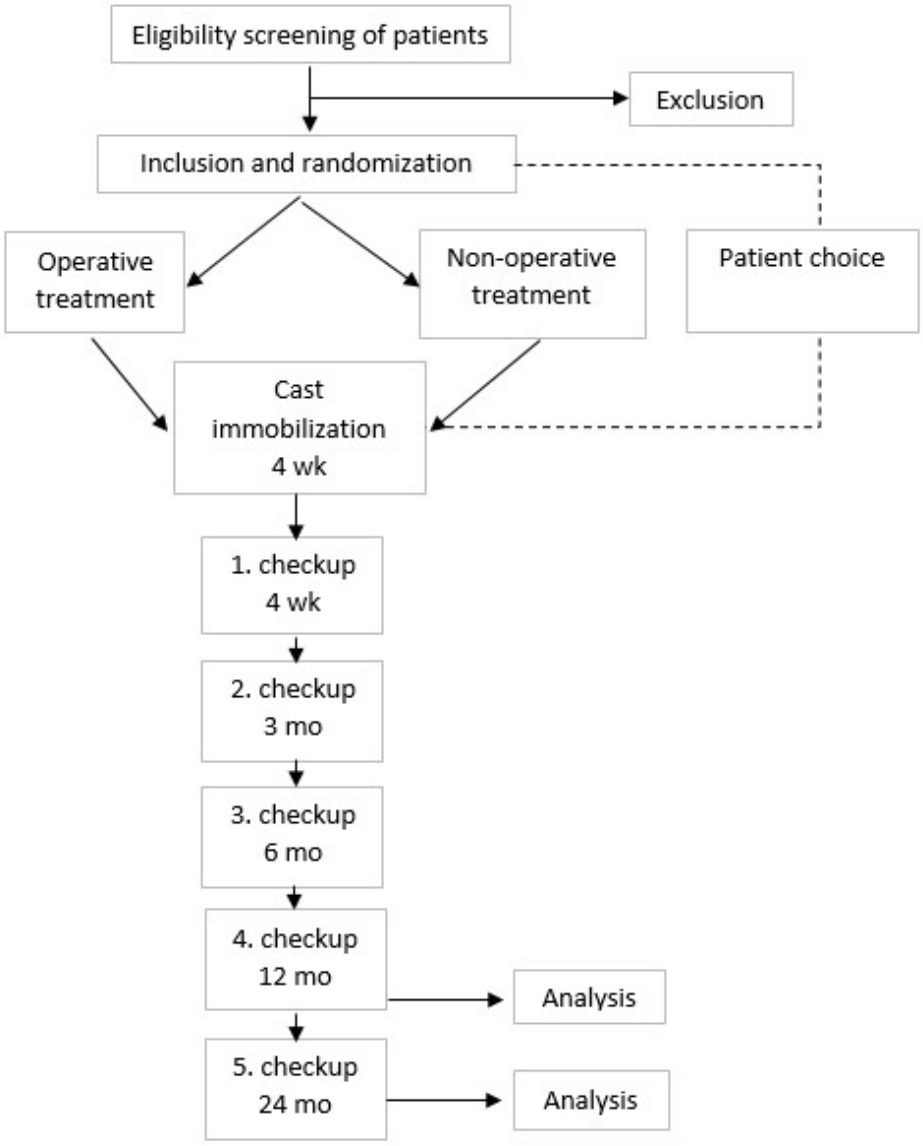

Figure 1 caption: Flow chart of the study

132x161mm (96 x 96 DPI)

	Baseline	Treatment day 0	1. Checkup 4 wk	2. Checkup 3 mo	3. Checkup 6 mo	4. Checkup 12 mo	5. Checkup 24 mo
Diagnosis, eliqibility	x						
Randomisation	x						
Surgery or non-operative treatment		x					
Physical examination	x		x	x	x	x	x
Questionnaires			x	x	x	x	x
Computer tomography	x						
Standard radiograph	x		x	x	x	x	x

Table 1 **Data collection time points**

	Baseline	Treatment day 0	1. Checkup 4 wk	2. Checkup 3 mo
Diagnosis, eliqibility	x			
Randomisation	x			
Surgery or non-operative treatment		x		
Physical examination	x		x	x
Questionnaires			x	x
Computer tomography	x			
Standard radiograph	x		x	x

3. Checkup 6 mo	4. Checkup 12 mo	5. Checkup 24 mo
x	x	x
x	x	x
x	x	x

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First version of protocol.

ABSTRACT

Introduction

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Blinded outcome assessor, independent of treating surgeons.

Use of several patient-reported outcome measures

Comparison of 2 age groups (less than 12 years vs. 12 years and over) in regards to outcome.

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elbow range of motion at 2 years from injury in 6 non-operatively and 14 operatively treated athletes. Axibal et al. (2018)[16] showed similar results with no difference in the objective outcome in less than one year follow-up between 22 operated patients matched to 22 non-operated patients.

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Patient recruitment:

All patients with a medial epicondyle fracture referred to the aforementioned hospitals will be screened for eligibility by a specialist of either hand surgery, pediatric surgery, pediatric orthopedics or orthopedics. If inclusion criteria are met, written consent is asked from the guardian. Patients and parents are given a written informed consent regarding the trial. The patient version is age adjusted for easier understanding according to the Finnish Investigators Network for Pediatric Medicines (www.finpedmed.fi)

Inclusion criteria

Patients aged 7-16 years presenting with a ≥ 2mm displaced non-incarcerated medial epicondyle fracture with or without concomitant elbow dislocation and normal ulnar nerve function.

Exclusion criteria

Pathological fracture, open fracture, systemic bone disease, concomitant fracture or injury of the same upper limb requiring operative intervention, other disease preventing participation in full follow-up regime and range of motion exercises.

Randomization

After agreeing to participation in the trial patients are randomized according to a computer generated randomization list[17] to either operative or non-operative treatment. Randomization ratio is 1:1, block size 10. Prior to recruitment assigned arm of the RCT trial has been placed in sealed envelops. Each study center receives a set of 10 consecutive envelopes at a time. Allocation sequence is kept at the main study center (HUS, New Children's hospital) where it is unavailable to recruiting physicians. Patient allocation in the trial is determined as the patient opens the assigned envelope.

Patient's choice arm

Patients who meet inclusion criteria, but refuse participation in the randomized trial are offered to choose treatment method (operative or non-operative) and continue in a prospective parallel patient preference arm that otherwise follow the same treatment and FU protocol as the RCT.

Baseline

Standard anterior-posterior and lateral radiographs of the elbow will be obtained after closed reduction of the possible elbow dislocation. All participants in either the RCT or patient's choice arm undergo cone-beam or normal computer tomography (CT) before treatment initiation. Initial fracture dislocation will be calculated from the CT scans in three planes (anterior-posterior, cranial-caudal and medial-lateral) and both radiographs (anterior-posterior and lateral) using the method described by Edmonds et al (2010)[18]. Date of injury, method of injury, patient's age at time of injury, sex, injured side, dominant hand and main sport or musical instrument as well as level will be documented. Motor and sensory function as well as range of motion of both upper limbs will be assessed. Carrying angle (degrees) and valgus stress test will be assessed if possible for both limbs.

Intervention

Non-operative treatment means upper limb immobilization with forearm in neutral pro-supination with a long arm cast for 4 weeks. Treatment is started after baseline examination.

Operative treatment is scheduled after baseline examination and is to be done within 7 days from injury. During sedation both elbows are stress tested using the valgus stress test, any instability is documented, carrying angle of both elbows are measured. Procedure of preference is open reduction and internal fixation (ORIF) with cannulated non-resolvable 4.0 mm screw with or without washer. If the fracture fragment is too small or fragmented for screw fixation 1.6 mm – 1.8 mm Kirshner-wires and/or bone anchor are used. After fracture fixation the injured side is again stress tested. Radiographs (anterior-posterior and lateral) documenting the fixation are taken. Long arm cast with forearm in neutral pro-supination is applied for 4 weeks. Time from injury to surgery, fixation method, length of surgery (min)

and surgeon's level of training (consultant, registrar) will be documented. Hardware is not routinely removed.

All patients will receive a written exercise plan explaining the active and passive ROM exercises that are to be performed at a minimum three times per day from cast removal. Physiotherapy will be offered if guardians and/or patients feel that no progress in ROM after 2 weeks of home exercises.

Blinding

This trial tests a clinical intervention that is not suitable for protection against treatment bias. Recruiter will be blinded. Consultant on duty at will perform randomization and allocation. Non-operative treatment will be started immediately after recruitment. ORIF will be performed by surgeon on duty. Surgeon is not blinded. Trial data is collected at each appointment at the outpatient clinic by a physician not related to the trial. Statistician analyzing trial data is blinded to treatment group.

Outcome measure

Follow-up is set at 1, 3, 6, 12 and 24 months from initiation of treatment with the option of ending the FU at 12 months if patients is pain free with full ROM in relation to uninjured side. Elbow standard radiograph (anterior-posterior and lateral) are taken at each appointment from 3 months on until bone union is achieved or trial ends (Table 1).

Table 1, data collection time points

	Baseline	Treament Day 0	1. Checkup 4 wk	2. Checkup 3 mo	3. Checkup 6 mo	4. Checkup 12 mo	5. Checkup 24 mo
Diagnosis, eliqibility	x						
Randomisation	x						

Surgery or non-operative treatment		x					
Physical examination	x		x	x	x	x	x
Questionnaires			x	x	x	x	x
Computer tomography	x						
Standard radiograph	x		x	x	x	x	x

Patients will be examined at the pediatric orthopedic outpatient clinic. Upon each appointment active and passive ROM of both upper limbs (elbow extension-flexion, pro-supination, wrist extension-flexion) as well as carrying angle are measured using a goniometer. Stability of both elbows are assessed using the moving valgus test[19] and the valgus stress test[20]. Distal sensation is examined by Semmes-Weinstein monofilaments[21]. Signs of cold intolerance will be assessed. Grip strength is measured with a dynamometer.

Patients and guardians are requested to answer the following patient reported outcome measures at each appointment; QuickDASH©[22], Pediatric Quality of Life Inventory™ (PedsQL), PedsQL Pediatric Pain Questionnaire[23], cosmetic visual analoque scale (VAS 0-100) and Mayo elbow performance score (MEPS)[24].

Time of returning to main sport or music and its level will be documented (weeks). Any adverse effects (wound infection, nerve damage) are documented as well as hardware problems and possible hardware removal as well as conversion of treatment during FU (cast to ORIF or ligament reconstruction).

Primary outcome

Statistically significant difference in QuickDASH score is 6.8[25-26] at 12 months FU.

Secondary outcome

Difference in active ROM in comparison to uninjured arm, PedsQL, PEDS QL Pain module, Cosmetic VAS, MEPS, need for additional procedures.

Sample size

Based on the results of Nikolas et al (2020)[25] and Aasheim et al (2014)[26] we assume clinically significant difference between the groups to be 6,8 and the standard deviation of the QuickDASH score to be 10 points. With 0,05 significance level and 80% power a non-inferiority comparison would require 27 patients per group. Allowing a 20% dropout rate the required sample would be 30 patients per group. For subgroup analysis (less than 12 years vs. 12 years and over) 30 patients per age group needs to be collected. Assuming 50-50 split in the patients between the age groups the sample size would be 60 per ORIF and non-operated equaling a total of 120 patients.

Statistical analysis

Data will be analyzed by using the Wilcoxon rank-sum test in Python 3.8. (Python Software Foundation, Wilmington, Delaware, U.S.A). Our null hypothesis is that there is no difference in outcome between non-operative versus ORIF. Level of significance is set at $p < 0.05$.

Both treatment groups will be internally analyzed for differences in primary outcome regarding age (less than 12 years vs. 12 years and over) at time of injury and amount of initial fracture displacement (mm). Depending on group size, patient choice arm can be merged for analysis to same RCT group.

Patient and Public Involvement

Patients, caregivers or public were neither involved in the development of the research questions nor the planning of the study design. They are neither involved in the recruitment nor conduct of the study. Results of the study are published only in peer-reviewed journals, no other information of the results of the study are provided to the patients or caregivers. Patients or caregivers will not take part in assessment regarding possible burden of the interventions of this study.

ETHICS AND DISSEMINATION

There is no common consensus for dislocated (>2mm) medial epicondyle fractures. Treatment method vary by clinic and treating surgeon. Both ORIF and long arm cast are well established treatment methods for humeral medial epicondyle fractures. If at any point an imminent problem in healing is observed, warranting a change in the treatment regimen, this will be done at the discretion of the treating physician regardless of the initial treatment allocation. The participants will be treated according to our best knowledge during and after the trial. Patients will not receive any compensation for participiation. The Finnish Patient Insurance Centre will provide compensation for treatment injuries.

We have obtained national ethical approval from Helsinki University Hospital (HUS) ethical board HUS/1443/2019. A local permission to conduct the trial will be obtained by each study center (Kuopio University Hospital, Oulu University Hospital, Tampere University Hospital and Turku University Hospital). A written authorization from guardian will be acquired and child will be informed about the trial. Results of the trial will be disseminated as published articles in peer-reviewed journals. Authorship will follow the ICMJE recommendations[27].

Time schedule

Last patient FU is expected by the end of 2023 and publication by the end of 2024.

CONCLUSION

The goal of this study is to compare two well-established treatment methods of dislocated non-incarcerated humeral medial epicondyle fractures in 7-16 year old patients.

CONTRIBUTORSHIP STATEMENT

Dr. Hämäläinen, Dr. Ahonen and Dr. Grahn have conceived and designed the study, performed the analysis and written the paper. Dr. Helenius, Dr. Jalkanen, Dr. Lastikka, Dr. Nietosvaara, Dr. Salonen and Dr. Sinikumpu have participated in writing the paper.

COMPETING INTEREST STATEMENT

Dr. Helenius reports grants from Medtronic and Stryker. Dr. Helenius is consulting surgeon at Medtronic. Dr. Sinikumpu is consulting surgeon at Bioretec ltd. None of the other authors report any conflict of interest.

FUNDING

This research did not receive grants from any funding agency in the public, commercial or not-for-profit sectors. No direct or indirect funding will be acquired from industry related to this study.

DATA SHARING

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Figure 1: flowchart of the study.

REFERENCES

1. Grahn P, Hämäläinen T, Nietosvaara Y, Ahonen M. Comparison of outcome between nonoperative and operative treatment of medial epicondyle fractures Acta Orthop. 2020 Online ahead of print.
2. Flynn J, Skaggs D, Waters P. Rockwood & Wilkins` Fractures in Children, Eight edition. Wolters Kluwer 2014.
3. Louahem D, Bourelle S, Cottalorada J. Displaced medial epicondyle fractures of the humerus: surgical treatment and results. A report of 139 cases. Arch Orthop Trauma Surg. 2010;130:649-655.
4. Hyvönen H, Korhonen L, Hannonen J, Serlo W, Sinikumpu JJ. Recent trends in children's elbow dislocation with or without a concomitant fracture. BMC Musculoskelet. 2019;20:294.
5. Gottschalk H, Eisner E, Hosalkar H. Medial epicondyle fractures in the pediatric population. J Am Acad Orthop Surg 2012;20:223-232.
6. Smith F. Medial epicondyle injuries. J Am Med Assoc. 1950;142:396-402.
7. Blount W. Fractures in Children. London: Williams & Wilkins; 1955.
8. Maylahn D, Fahey J. Fractures of the elbow in children: Review of three hundred consecutive cases. J Am Med Assoc. 1958;166:220-228.
9. Bede W, Lefebvre A, Rosman M. Fractures of the medial humeral epicondyle in children. Can J Surg. 1975;18(2):137-142.
10. Tarollo L, Mugani R, Catani F. Pediatric medial epicondyle fractures with intra-articular elbow incarceration. J Orthop Trauma. 2015;16:117-123.
11. Lee H, Shen H, Lee C, Wu S. Operative treatment of displaced medial epicondyle fractures in children and adolecents. J Shoulder Elb Surg. 2005;14(2):178-85.

12. Pezzutti D, Lin J, Singh S, Rowan M, Samora J. Pediatric medial epicondyle fracture management: A systematic review. J Pediatr Orthop. 2020;40(8):e697-e702.
13. Baety J, Kasser J. Chapter 15 in Rockwood & Wilkins`Fractures in Children 8th edition. Philadelphia, PA : Lippicott Williams & Wilkins; 2014.
14. Kamath A, Baldwin K, Horneff J, Hosalkar H. Operative versus non-operative management of pediatric medial epicondyle fractures: a systematic review. J Child Orthop. 2009;3(5):345-357.
15. Lawrence J, Patel N, Macknin J, Flynn J, Cameron D, Wolfgruber H, Ganley T. Return to competitive sports after medial epicondyle fractures in adolescent athletes: results of operative and nonoperative treatment. Am J Sports Med. 2013;41(5):1152–1157.
16. Axibal D, Carry P, Skelton A, Mayer S. No Difference in return to Sport and Other Outcomes Between Operative and Nonoperative Treatment of Medial Epicondyle Fractures in Pediatric Upper-Extremity Athletes. Clin J Sport Med. 2018; 1;10.1097/JSM.0000000000000666
17. Urbaniak, G. C., & Plous, S. Research Randomizer. 2011.
18. Edmonds E. How displaced are “nondisplaced” fractures of the medial humeral epicondyle in children? Results of a three-dimensional computer tomography analysis. J Bone Joint Surg Am. 2010;92:2785-2791.
19. O'Driscoll S, Lawton R, Smith A. The "moving valgus stress test" for medial collateral ligament tears of the elbow. Am J Sports Med. 2005;33(2):231-239.
20. Flynn T. User's 220 guide to the musculoskeletal examination: Fundamentals for the evidence-based clinician. Buckner, Kentucky: Evidence in Motion. 2008.
21. Bell-Krotoski J. “Pocket filaments” and specifications for the semmes-weinstein monofilaments. J Hand Ther. 1990;3(1):26-31.
22. Beaton D, Wright J, Katz J. Development of the Quick-DASH: comparison of three item-reduction approaches, J Bone Joint Surg Am. 2005;87:1038-46.

23. Varni J, Seid M, Rode C. The PedsQL: Measurement model for the pediatric quality of life inventory. Med Care 1999;37(2):126-39.

24. Morrey B. The Elbow and Its Disorders. Philadelphia: WB Saunders; 1993.

25. Kazmers N, Qiu Y, Yoo M, Stephens A, Tyser A, Zhang Y. The Minimal Clinically Important Difference of the PROMIS and QuickDASH Instruments in a Nonshoulder Hand and Upper Extremity Patient Population. J Hand Surg Am. 2020;45(5):399-407.e6.

26. Aasheim T, Finsen V. The DASH and the QuickDASH instruments. Normative values in the general population in Norway. J Hand Surg Eur Vol. 2014;39(2):140–144.

27. International Committee of Medical Journal Editors. Defining the Role of Authors and Contributors. http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html.

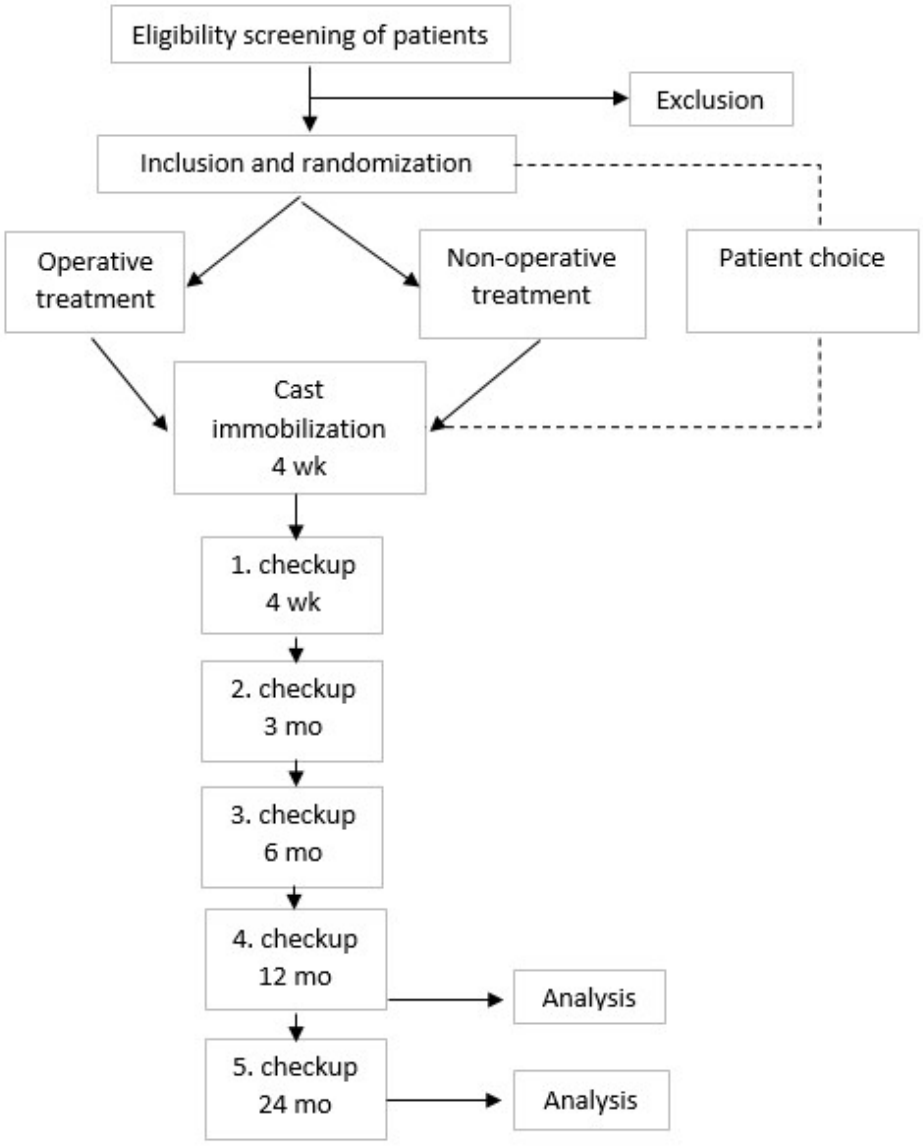

Figure 1

132x161mm (96 x 96 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym page 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry page 3, 5
	2b	All items from the World Health Organization Trial Registration Data Set NA
Protocol version	3	Date and version identifier page 1
Funding	4	Sources and types of financial, material, and other support page 15
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors page 1, 15
	5b	Name and contact information for the trial sponsor page 7
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) page 7
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention page 2, 5-6, 11-12
	6b	Explanation for choice of comparators page 10-12
Objectives	7	Specific objectives or hypotheses page 6, 12

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) page 7
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained page 7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) page 7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered page 9-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) page 14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended page 10-12
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) page 14 (figure1, table1)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations page 11-12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size page 11-12
Methods: Assignment of interventions (for controlled trials)		
Allocation:		

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions page 8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned page8 (sealed envelopes)
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions page 8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how page 8,10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial NA
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol page 8-10
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols (see informed consent)
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol (see informed consent)
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol page 11-12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) page 11-12

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) NA
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed page 7
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial page 14
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct page 14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor page 7
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval page 14
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) page 7
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) page 14
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial page 10-11 (see table1 and figure1, see informed consent)
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site page 15
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators page 10

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation page 14 and informed consent
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions page 12,13 and informed consent
	31b	Authorship eligibility guidelines and any intended use of professional writers page 14
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code page 12,13 and informed consent
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates (see informed consent)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Cast immobilization in situ versus open reduction and internal fixation of displaced medial epicondyle fractures in children between 7 and 16 years old. A study protocol for a randomized controlled trial

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Cast immobilization in situ versus open reduction and internal fixation of displaced medial epicondyle fractures in children between 7 and 16 years old. A study protocol for a randomized controlled trial

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First version of protocol.

ABSTRACT

Introduction

Medial epicondyle fracture of the humerus is a common injury in childhood. There is uniform agreement that minimally displaced fractures (dislocation ≤ 2mm) can be treated non-operatively with immobilization. Open fractures, fractures with joint incarceration or ulnar nerve dysfunction require surgery. There is no common consensus in treatment of closed medial epicondyle fractures with >2mm dislocation without joint incarceration or ulnar nerve dysfunction. We hypothesize that there is no difference of treatment outcomes between nonoperative and operative treatment.

Methods and analysis

This is a multicenter, controlled, prospective, randomized non-inferiority study comparing operative treatment to non-operative treatment of >2mm dislocated pediatric medial epicondyle fractures without joint incarceration or ulnar nerve dysfunction. A total of 120 patients will be randomized in 1:1 ratio to either operative or non-operative treatment. The study will have a parallel non-randomized patient preference arm. Operative treatment will be open reduction and internal fixation. Non-operative treatment will be upper limb immobilization in long arm cast for 4 weeks. Data will be collected at baseline and at each follow-up up to 2 years. Quick-DASH is used as primary outcome measure. Secondary outcomes are patient reported pain, differences in range of motion, PedsQL, Cosmetic VAS and Mayo Elbow Performance Score.

Ethics and dissemination

Ethical approval has been obtained from Helsinki University Hospital (HUS) ethical board HUS/1443/2019. Each study center has obtained their own permission for the study. A written

authorization from legal guardian will be acquired and the child will be informed about the trial. Results of the trial will be disseminated as published articles in peer-reviewed journals.

Trial registration

The trial has been registered at clinicaltrials.gov with registration number NCT04531085.

STRENGTHs AND LIMITATIONS OF THIS STUDY

Strengths:

This study is the first RCT to examine the treatment and outcome of dislocated medial epicondyle fractures.

This is a multicenter study with all five university hospitals in Finland participating.

The trial has a blinded outcome assessor independent of treating and recruiting surgeons.

Limitations:

Primary outcome measure (Quick DASH) is not validated for use in children.

Treating surgeon is not blinded to the allocated treatment.

INTRODUCTION

The incidence of medial epicondyle fractures of the humerus in children and adolescents is ≥3:100000 and account for approximately 12-20% of all pediatric elbow fractures [1,2] 30-50% of these fractures are associated with elbow dislocation and 5-18% are incarcerated [3,4]. Dysfunction of ulnar nerve has been reported in 10-16% of cases[3].

Minimally displaced (≤ 2mm) fractures without incarceration or ulnar nerve dysfunction are treated non-operatively [5-10]. There is no common consensus between pediatric surgeons how to treat medial epicondyle fractures with > 2 mm dislocation[11-12]. It has been suggested that incarcerated fractures and fractures with elbow dislocation should be treated operatively, and that competitive athletes should be treated operatively with lower threshold than children and adolescents without sporting activities[13].

Grahn et al (2020)[1] conducted a controlled treatment trial based on prospectively collected data from ≤ 16 years old patients with more than 2 mm displaced non-incarcerated medial epicondyle fractures with a minimum follow-up of 1 year. Partial avulsion fractures were excluded, 41 were treated non-operatively and 40 operatively. They found that neither the degree of primary fracture displacement with or without concomitant elbow dislocation nor the choice of treatment (ORIF or long arm cast) affected outcome. Normal elbow function was restored in 74/81 patients. All but one primarily non-operatively treated patients had returned to the same or higher level of sport as pre-injury, whereas six surgically treated patients had down-graded their sporting activities. Pain at medial humeral epicondyle either with direct contact or under load was reported by four non-operatively and by six operatively treated children with normal sensation and elbow stability (1). In a systematic review of the literature regarding treatment of medial epicondyle fractures Kamath et al (2009)[14] found operative treatment to be superior to conservative in terms of bony union. However, the review did not show differences in terms of pain or patient reported outcome measures between the two treatment modalities. According to the study of Lawrence et al. (2013)[15] there was no difference in outcome assessed by QuickDASH and

elbow range of motion at 2 years from injury in 6 non-operatively and 14 operatively treated athletes. Axibal et al. (2018)[16] showed similar results with no difference in the objective outcome in less than one year follow-up between 22 operated patients matched to 22 non-operated patients.

In light of current findings we applied for ethical review board approval to conduct a randomized non-inferiority trial with the hypothesis being that conservatively treated medial epicondyle fractures fare as well as operatively treated.

METHODS AND ANALYSIS

Study design:

The study is designed as a multicenter parallel-group non-inferiority randomized controlled trial (RCT) that complies with the CONSORT guidelines (Figure 1). A patient preference arm will be available. Patient recruitment will be done at all university hospital areas of Finland (Helsinki, Kuopio, Oulu, Tampere, Turku). The study is coordinated by Helsinki University Central Hospital, Children's Hospital pediatric orthopedic unit (HUS New Chlidren's Hospital, Stenbäckinkatu 9 C, 00029 HUS, Finland). Trial data analysts and person performing the recruitment will be unaware of the assigned treatment. The study is overseen by an external study monitor according to trial data monitoring protocol provided by HUCH Clinical Research Institute (Clinical Research Institute HUCH Ltd. P.O Box 700, FI-00029 HUS, Helsinki, Finland, https://hyksinstituutti.fi/services/monitoring-services/?lang=en). The trial is registered at clinicaltrials.gov with trial registration number: NCT04531085. Any changes in study protocol will be uploaded to the trial registry.

Patient recruitment:

All patients with a medial epicondyle fracture referred to the aforementioned hospitals will be screened for eligibility by a specialist of either hand surgery, pediatric surgery, pediatric orthopedics or orthopedics. If inclusion criteria are met, written consent is asked from the guardian. Patients and parents are given a written informed consent regarding the trial. The patient version is age adjusted for easier understanding according to the Finnish Investigators Network for Pediatric Medicines (www.finpedmed.fi)

Inclusion criteria

Patients aged 7-16 years presenting with a ≥ 2mm displaced non-incarcerated medial epicondyle fracture with or without concomitant elbow dislocation and normal ulnar nerve function.

Exclusion criteria

Pathological fracture, open fracture, systemic bone disease, concomitant fracture or injury of the same upper limb requiring operative intervention, other disease preventing participation in full follow-up regime and range of motion exercises.

Randomization

After agreeing to participation in the trial patients are randomized according to a computer generated randomization list[17] to either operative or non-operative treatment. Randomization ratio is 1:1, block size 10. Prior to recruitment assigned arm of the RCT trial has been placed in sealed envelops. Each study center receives a set of 10 consecutive envelopes at a time. Allocation sequence is kept at the main study center (HUS, New Children's hospital) where it is unavailable to recruiting physicians. Patient allocation in the trial is determined as the patient opens the assigned envelope.

Patient's choice arm

Patients who meet inclusion criteria, but refuse participation in the randomized trial are offered to choose treatment method (operative or non-operative) and continue in a prospective parallel patient preference arm that otherwise follow the same treatment and FU protocol as the RCT.

Baseline

Standard anterior-posterior and lateral radiographs of the elbow will be obtained after closed reduction of the possible elbow dislocation. All participants in either the RCT or patient's choice arm undergo cone-beam or normal computer tomography (CT) before treatment initiation. Initial fracture dislocation will be calculated from the CT scans in three planes (anterior-posterior, cranial-caudal and medial-lateral) and both radiographs (anterior-posterior and lateral) using the method described by Edmonds et al (2010)[18]. Date of injury, method of injury, patient's age at time of injury, sex, injured side, dominant hand and main sport or musical instrument as well as level will be documented. Motor and sensory function as well as range of motion of both upper limbs will be assessed. Carrying angle (degrees) and valgus stress test will be assessed if possible for both limbs.

Intervention

Non-operative treatment means upper limb immobilization with forearm in neutral pro-supination with a long arm cast for 4 weeks. Treatment is started after baseline examination.

Operative treatment is scheduled after baseline examination and is to be done within 7 days from injury. During sedation both elbows are stress tested using the valgus stress test, any instability is documented, carrying angle of both elbows are measured. Procedure of preference is open reduction and internal fixation (ORIF) with cannulated non-resolvable 4.0 mm screw with or without washer. If the fracture fragment is too small or fragmented for screw fixation 1.6 mm – 1.8 mm Kirshner-wires and/or bone anchor are used. After fracture fixation the injured side is again stress tested. Radiographs (anterior-posterior and lateral) documenting the fixation are taken. Long arm cast with forearm in neutral pro-supination is applied for 4 weeks. Time from injury to surgery, fixation method, length of surgery (min)

and surgeon's level of training (consultant, registrar) will be documented. Hardware is not routinely removed.

All patients will receive a written exercise plan explaining the active and passive ROM exercises that are to be performed at a minimum three times per day from cast removal. Physiotherapy will be offered if guardians and/or patients feel that no progress in ROM after 2 weeks of home exercises.

Blinding

This trial tests a clinical intervention that is not suitable for protection against treatment bias. Recruiter will be blinded. Consultant on duty at will perform randomization and allocation. Non-operative treatment will be started immediately after recruitment. ORIF will be performed by surgeon on duty. Surgeon is not blinded. Trial data is collected at each appointment at the outpatient clinic by a physician not related to the trial. Statistician analyzing trial data is blinded to treatment group.

Outcome measure

Follow-up is set at 1, 3, 6, 12 and 24 months from initiation of treatment with the option of ending the FU at 12 months if patients is pain free with full ROM in relation to uninjured side. Elbow standard radiograph (anterior-posterior and lateral) are taken at each appointment from 3 months on until bone union is achieved or trial ends (Table 1).

Table 1, data collection time points

	Baseline	Treament Day 0	1. Checkup 4 wk	2. Checkup 3 mo	3. Checkup 6 mo	4. Checkup 12 mo	5. Checkup 24 mo
Diagnosis, eliqibility	x						
Randomisation	x						

Surgery or non-operative treatment		x					
Physical examination	x		x	x	x	x	x
Questionnaires			x	x	x	x	x
Computer tomography	x						
Standard radiograph	x		x	x	x	x	x

Patients will be examined at the pediatric orthopedic outpatient clinic. Upon each appointment active and passive ROM of both upper limbs (elbow extension-flexion, pro-supination, wrist extension-flexion) as well as carrying angle are measured using a goniometer. Stability of both elbows are assessed using the moving valgus test[19] and the valgus stress test[20]. Distal sensation is examined by Semmes-Weinstein monofilaments[21]. Signs of cold intolerance will be assessed. Grip strength is measured with a dynamometer.

Patients and guardians are requested to answer the following patient reported outcome measures at each appointment; QuickDASH©[22], Pediatric Quality of Life Inventory™ (PedsQL), PedsQL Pediatric Pain Questionnaire[23], cosmetic visual analoque scale (VAS 0-100) and Mayo elbow performance score (MEPS)[24].

Time of returning to main sport or music and its level will be documented (weeks). Any adverse effects (wound infection, nerve damage) are documented as well as hardware problems and possible hardware removal as well as conversion of treatment during FU (cast to ORIF or ligament reconstruction).

Allthough QuickDash is not validated for use in under 18 year olds it was selected as it has been used in the literature in evaluating results of fracture healing in adolecents, and it is available in both national languages (Finnish and Swedish)[25,26].

Primary outcome

Statistically significant difference in QuickDASH score is 6.8[25-26] at 12 months FU.

Secondary outcome

Difference in active ROM in comparison to uninjured arm, PedsQL, PEDS QL Pain module, Cosmetic VAS, MEPS, need for additional procedures.

Sample size

Based on the results of Nikolas et al (2020)[25] and Aasheim et al (2014)[26] we assume clinically significant difference between the groups to be 6,8 and the standard deviation of the QuickDASH score to be 10 points. With 0,05 significance level and 80% power a non-inferiority comparison would require 27 patients per group. Allowing a 20% dropout rate the required sample would be 30 patients per group. For subgroup analysis (less than 12 years vs. 12 years and over) 30 patients per age group needs to be collected. Assuming 50-50 split in the patients between the age groups the sample size would be 60 per ORIF and non-operated equaling a total of 120 patients.

Statistical analysis

Data will be analyzed by using the Wilcoxon rank-sum test in Python 3.8. (Python Software Foundation, Wilmington, Delaware, U.S.A). Our null hypothesis is that there is no difference in outcome between non-operative versus ORIF. Level of significance is set at $p < 0.05$.

Both treatment groups will be internally analyzed for differences in primary outcome regarding age (less than 12 years vs. 12 years and over) at time of injury and amount of initial fracture displacement (mm). Depending on group size, patient choice arm can be merged for analysis to same RCT group.

Patient and Public Involvement

Patients, caregivers or public were neither involved in the development of the research questions nor the planning of the study design. They are neither involved in the recruitment nor conduct of the study. Results of the study are published only in peer-reviewed journals, no other information of the results of the study are provided to the patients or caregivers. Patients or caregivers will not take part in assessment regarding possible burden of the interventions of this study.

ETHICS AND DISSEMINATION

There is no common consensus for dislocated (>2mm) medial epicondyle fractures. Treatment method vary by clinic and treating surgeon. Both ORIF and long arm cast are well established treatment methods for humeral medial epicondyle fractures. If at any point an imminent problem in healing is observed, warranting a change in the treatment regimen, this will be done at the discretion of the treating physician regardless of the initial treatment allocation. The participants will be treated according to our best knowledge during and after the trial. Patients will not receive any compensation for participiation. The Finnish Patient Insurance Centre will provide compensation for treatment injuries.

We have obtained national ethical approval from Helsinki University Hospital (HUS) ethical board HUS/1443/2019. A local permission to conduct the trial will be obtained by each study center (Kuopio University Hospital, Oulu University Hospital, Tampere University Hospital and Turku University Hospital). A written authorization from guardian will be acquired and child will be informed about the trial. Results of the trial will be disseminated as published articles in peer-reviewed journals. Authorship will follow the ICMJE recommendations[27].

Time schedule

Last patient FU is expected by the end of 2023 and publication by the end of 2024.

CONCLUSION

The goal of this study is to compare two well-established treatment methods of dislocated non-incarcerated humeral medial epicondyle fractures in 7-16 year old patients.

CONTRIBUTORSHIP STATEMENT

Dr. Hämäläinen, Dr. Ahonen and Dr. Grahn have conceived and designed the study, performed the analysis and written the paper. Dr. Helenius, Dr. Jalkanen, Dr. Lastikka, Dr. Nietosvaara, Dr. Salonen and Dr. Sinikumpu have participated in writing the paper.

COMPETING INTEREST STATEMENT

Dr. Helenius reports grants from Medtronic and Stryker. Dr. Helenius is consulting surgeon at Medtronic. Dr. Sinikumpu is consulting surgeon at Bioretec ltd. None of the other authors report any conflict of interest.

FUNDING

This research did not receive grants from any funding agency in the public, commercial or not-for-profit sectors. No direct or indirect funding will be acquired from industry related to this study.

DATA SHARING

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Figure 1: flowchart of the study.

REFERENCES

1. Grahn P, Hämäläinen T, Nietosvaara Y, Ahonen M. Comparison of outcome between nonoperative and operative treatment of medial epicondyle fractures Acta Orthop. 2020 Online ahead of print.
2. Flynn J, Skaggs D, Waters P. Rockwood & Wilkins` Fractures in Children, Eight edition. Wolters Kluwer 2014.
3. Louahem D, Bourelle S, Cottalorada J. Displaced medial epicondyle fractures of the humerus: surgical treatment and results. A report of 139 cases. Arch Orthop Trauma Surg. 2010;130:649-655.
4. Hyvönen H, Korhonen L, Hannonen J, Serlo W, Sinikumpu JJ. Recent trends in children's elbow dislocation with or without a concomitant fracture. BMC Musculoskelet. 2019;20:294.
5. Gottschalk H, Eisner E, Hosalkar H. Medial epicondyle fractures in the pediatric population. J Am Acad Orthop Surg 2012;20:223-232.
6. Smith F. Medial epicondyle injuries. J Am Med Assoc. 1950;142:396-402.
7. Blount W. Fractures in Children. London: Williams & Wilkins; 1955.
8. Maylahn D, Fahey J. Fractures of the elbow in children: Review of three hundred consecutive cases. J Am Med Assoc. 1958;166:220-228.
9. Bede W, Lefebvre A, Rosman M. Fractures of the medial humeral epicondyle in children. Can J Surg. 1975;18(2):137-142.
10. Tarollo L, Mugani R, Catani F. Pediatric medial epicondyle fractures with intra-articular elbow incarceration. J Orthop Trauma. 2015;16:117-123.
11. Lee H, Shen H, Lee C, Wu S. Operative treatment of displaced medial epicondyle fractures in children and adolecents. J Shoulder Elb Surg. 2005;14(2):178-85.

12. Pezzutti D, Lin J, Singh S, Rowan M, Samora J. Pediatric medial epicondyle fracture management: A systematic review. J Pediatr Orthop. 2020;40(8):e697-e702.
13. Baety J, Kasser J. Chapter 15 in Rockwood & Wilkins`Fractures in Children 8th edition. Philadelphia, PA : Lippicott Williams & Wilkins; 2014.
14. Kamath A, Baldwin K, Horneff J, Hosalkar H. Operative versus non-operative management of pediatric medial epicondyle fractures: a systematic review. J Child Orthop. 2009;3(5):345-357.
15. Lawrence J, Patel N, Macknin J, Flynn J, Cameron D, Wolfgruber H, Ganley T. Return to competitive sports after medial epicondyle fractures in adolescent athletes: results of operative and nonoperative treatment. Am J Sports Med. 2013;41(5):1152–1157.
16. Axibal D, Carry P, Skelton A, Mayer S. No Difference in return to Sport and Other Outcomes Between Operative and Nonoperative Treatment of Medial Epicondyle Fractures in Pediatric Upper-Extremity Athletes. Clin J Sport Med. 2018; 1;10.1097/JSM.0000000000000666
17. Urbaniak, G. C., & Plous, S. Research Randomizer. 2011.
18. Edmonds E. How displaced are “nondisplaced” fractures of the medial humeral epicondyle in children? Results of a three-dimensional computer tomography analysis. J Bone Joint Surg Am. 2010;92:2785-2791.
19. O'Driscoll S, Lawton R, Smith A. The "moving valgus stress test" for medial collateral ligament tears of the elbow. Am J Sports Med. 2005;33(2):231-239.
20. Flynn T. User's 220 guide to the musculoskeletal examination: Fundamentals for the evidence-based clinician. Buckner, Kentucky: Evidence in Motion. 2008.
21. Bell-Krotoski J. “Pocket filaments” and specifications for the semmes-weinstein monofilaments. J Hand Ther. 1990;3(1):26-31.
22. Beaton D, Wright J, Katz J. Development of the Quick-DASH: comparison of three item-reduction approaches, J Bone Joint Surg Am. 2005;87:1038-46.

23. Varni J, Seid M, Rode C. The PedsQL: Measurement model for the pediatric quality of life inventory. Med Care 1999;37(2):126-39.

24. Morrey B. The Elbow and Its Disorders. Philadelphia: WB Saunders; 1993.

25. Kazmers N, Qiu Y, Yoo M, Stephens A, Tyser A, Zhang Y. The Minimal Clinically Important Difference of the PROMIS and QuickDASH Instruments in a Nonshoulder Hand and Upper Extremity Patient Population. J Hand Surg Am. 2020;45(5):399-407.e6.

26. Aasheim T, Finsen V. The DASH and the QuickDASH instruments. Normative values in the general population in Norway. J Hand Surg Eur Vol. 2014;39(2):140–144.

27. International Committee of Medical Journal Editors. Defining the Role of Authors and Contributors. http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html.

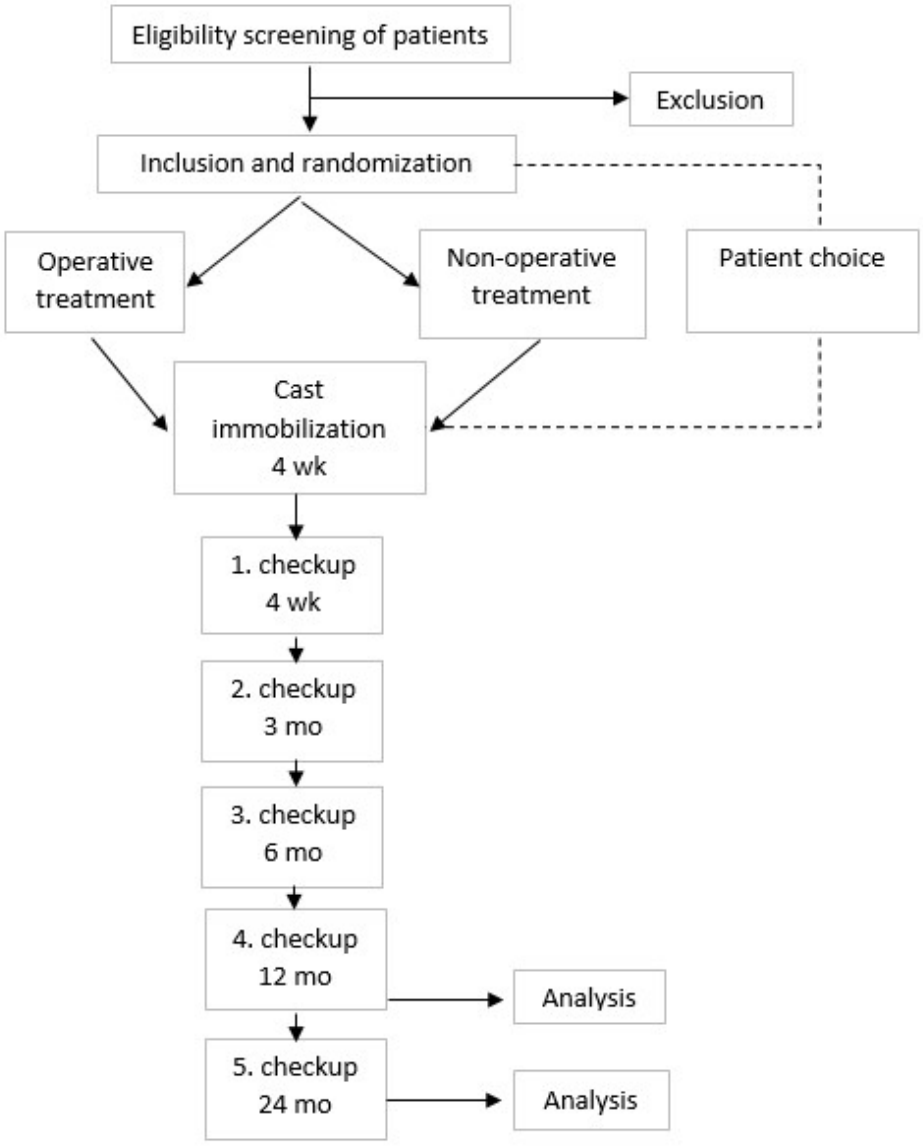

Figure 1

132x161mm (96 x 96 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym page 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry page 3, 5
	2b	All items from the World Health Organization Trial Registration Data Set NA
Protocol version	3	Date and version identifier page 1
Funding	4	Sources and types of financial, material, and other support page 15
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors page 1, 15
	5b	Name and contact information for the trial sponsor page 7
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) page 7
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention page 2, 5-6, 11-12
	6b	Explanation for choice of comparators page 10-12
Objectives	7	Specific objectives or hypotheses page 6, 12

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) page 7
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained page 7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) page 7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered page 9-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) page 14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended page 10-12
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) page 14 (figure1, table1)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations page 11-12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size page 11-12
Methods: Assignment of interventions (for controlled trials)		
Allocation:		

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions page 8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned page8 (sealed envelopes)
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions page 8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how page 8,10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial NA
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol page 8-10
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols (see informed consent)
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol (see informed consent)
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol page 11-12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) page 11-12

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) NA
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed page 7
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial page 14
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct page 14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor page 7
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval page 14
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) page 7
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) page 14
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial page 10-11 (see table1 and figure1, see informed consent)
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site page 15
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators page 10

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation page 14 and informed consent
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions page 12,13 and informed consent
	31b	Authorship eligibility guidelines and any intended use of professional writers page 14
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code page 12,13 and informed consent
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates (see informed consent)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.