Internal fixation versus casting of displaced tibial shaft fractures in children and dolescents: a study protocol of a randomized controlled trial

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Introduction

Tibial shaft fracture is a common fracture in the pediatric and adolescent population. Displaced tibial shaft fractures have traditionally been treated with closed reduction and cast immobilization. Amount of surgically treated fractures have increased notably especially since flexible intramedullary nails have gained increasing popularity. The outcomes of both conservative and operative treatment are not clear and to date there is no randomized prospective trial comparing different methods of treatment.

Methods and analysis

We will conduct a multicenter, randomized non-inferiority trial comparing closed reduction and cast immobilization to intramedullary nailing in 6-15 year old children and adolescents with displaced tibial shaft fractures (AO-pediatric classification 42-D/4.1-5.2, w/o fibular fracture) and open proximal tibial physis. A total of 60 patients will be randomly assigned 1:1 ratio to closed reduction and cast immobilization or internal fixation with flexible intramedullary nails. We will follow the patients 10 years and

compare results at baseline and each follow up. The primary outcome will be radiographic union at good alignment at one year. The secondary outcomes include PedsQL (*Pediatric Quality of Life Inventory),* number of re-interventions, length of hospital stay, complications, and volume of injured extremity compared with uninjured leg. Patients unwilling for randomization will be asked to participate in a paraller prospective cohort. Our null hypothesis is that intramedullary nailing is non inferior to conservative treatment.

Ethics and dissemination

We have received ethical board approval (Dnro: ETMK105/1801/2017) and permission to conduct the study at each study center. Informed consent is obtained from one parent and all patients 12 years or above. Results will be disseminated in peer-review publications.

Registration

The trial will be registered a clinicaltrials.gov.

Introduction

Tibial shaft fracture is the third most common pediatric long bone fracture and most common long bone shaft fracture accounting for 2% of all fractures and 35-40% of tibial fractures[1,2] . The overall reported incidence is 2.8/10.000 person-years.[2]

There is common consensus that minimally displaced tibial shaft fractures especially in small children should be treated non-invasively with cast immobilization. On the other hand it is generally accepted that open fractures, fractures with compartment syndrome and fractures associated with polytrauma need surgical intervention[1,3,4].

Traditionally also closed, displaced tibial shaft fractures have been treated non-operatively with closed reduction and cast immobilization with good short and long term results[3,4,4,5]. However, recent studies show that the amount of these fractures treated surgically, especially with flexible intramedullary nails, has increased significantly from as low as 4,5% to 30-60%,[6,7] which reflects the overall trend of increasing rate of operative treatment of fractures in pediatric and adolescent population[8].

Data supporting this change in practice are sparse and studies concerning this subject show controversial results. Cast treatment is still related to very few complications, but on the other hand requires often additional measures such as wedging, re- casting and in many cases up to three months long immobilization[3,4,9]. Failure rates of non-operative treatment vary from 3% to 40%[3,4,9] . Surgical treatment with flexible intramedullary nails has been demonstrated to be a safe, effective method with skeletally immature individuals regardless of age and weight[10]. Flexible nails has multitude advantages over other fixation techniques and they allow early mobilization and weight bearing compared to non-operative treatment[11]. However it is associated with other problems like compartment syndrome and need of hardware removal[11–13]

Malunion of tibial fracture may increase risk of pain and osteoarthritis, limits normal function and may cause cosmetic disability[14,15], although correlation to the amount of malunion is unclear[16] Acceptable alignment in adults has traditionally been defined as ≤ 5° of coronal or sagittal angulation, < 50 % displacement and 10 to 15 mm of shortening and no rotation.[17] Similar criteria are applied to over 8-year old children,[3,18] whereas criteria for children younger than 8-year old have been defined as ≤ 10° of coronal or sagittal

angulation,< 100 % displacement and 10 to 15 mm of shortening. However there are no published studies in this age group about correlation of malunion with outcome of the treatment.

To this date there is no randomized controlled study comparing non-operative and surgical treatment of tibial fracture in children and adolescent. Our null hypothesis is that intramedullary nailing of displaced tibial shaft fractures in 7-15 year old skeletally immature pediatric and adolescent patients is superior to cast immobilization in maintaining correct alignment during fracture healing and in restoring of normal functions of the injured limb.

Methods and analysis

Study design

This is a pragmatic, parallel group (1:1) multi-center, randomized controlled, non-inferiority trial. The study is based on a prospective inception cohort design. The study is coordinated by Helsinki University Central Hospital, Children's Hospital unit for pediatric orthopedics. Recruitment of patients is done at all five Finnish university hospitals (Helsinki, Tampere, Turku, Oulu and Kuopio University Hospitals) and three central hospitals (Satakunta, Lappi and Kanta-Häme) in Finland with catchment area of 900 000 million children aged less than 16 years of age). The trial will be registered at clinicaltrials.gov. Any changes in study protocol will be uploaded to the trial registry.

Patients recruitment

A specialist of either pediatric surgery, pediatric orthopedics or orthopedics will screen all patients for inclusion criteria and eligibility. If the criteria are met written consent is obtained from one guardian and patients over 12 years. Patients and parents are given a written informed consent regarding the trial. The patient version is age adjusted for easier understanding

Eligibility criteria

We will include 6 to 15-year old children with open tibial physis capable of communicating in Finnish or Swedish with displaced tibial shaft fracture (AO-pediatric classification 42-D/4.1-5.2, w/o fibular fracture) that requires manipulation to restore correct displacement and alignment. The criteria of unacceptable alignment and need for manipulation are coronal angulation over 5 degrees, sagittal angulation over 10 degrees, over 50% cortical overlap and over 1 cm shortening.

We will exclude patients with open fracture, compartment syndrome, neurovascular deficit, pathological fracture, systemic disease affecting bone structure and quality and associated injuries preventing either casting or intramedullary nailing.

Randomization

All included patients will receive temporary long leg cast after admission to the hospital. Randomization is done while patient is under general anesthesia in the operating theater with the treating surgeon opening the assigned envelop.

Assigned allocation is sealed in individual coded envelopes.

Preferred treatment cohort

Patients meeting inclusion criteria but unwilling to participate in the RCT are asked to join "preferred treatment cohort". Usually, the unwillingness to participate in the RCT is due to a preference for one of the treatment modalities. The patients will receive the usual treatment of their choice after information of both methods is given. This cohort will continue through the trial in a prospective parallel "observational cohort" and follow the same treatment and follow up protocol as the randomized patients. Analysis of the outcome will be done separately from the randomized group and the results will be compared with the results of the RCT.

Baseline

Fracture displacement is calculated by experienced pediatric radiologist and pediatric orthopedic surgeon unrelated to the trial from the lateral and AP radiographs of the injured leg. Date of injury, method of injury, patients' age at the time of injury, sex, injured side, time from injury to intervention, length of procedure, blood loss in the surgery group, surgeon's level of training (consultant, registrar) and AO-classification of the fracture are documented.

Intervention

Cast group:

Fracture is reduced under general anesthesia. Long leg circular cast (synthetic, plaster cast or combination according to surgeons' preference), is applied from toes to upper thigh. After casting the alignment is documented with standard AP and lateral radiographs. If

adequate alignment cannot be achieved after two attempts of casting, patient is transferred to intramedullary nailing group and operative treatment is performed under same anesthesia with same principles as in intramedullary nailing group.

Cast immobilization with long cast and partial weight bearing is continued for six weeks or until callus of three cortexes can be seen in radiographs. Cast wedging in outpatient clinic is performed during follow up if alignment is lost between 10 to 14 days. If alignment cannot be restored by wedging patient is recommended to transfer intramedullary nailing group. The criteria for unacceptable alignment are coronal angulation over 5 degrees, sagittal angulation over 10 degrees, over 50% cortical overlap and over 1 cm shortening.

Intramedullary nailing (IN) group

Patients will have prophylactic antibiotic (*cefuroxime* 15mg/kg or *clindamycin* 2mg/kg) 30-60 minutes before surgery. Two flexible intramedullary nails (FIN) is used to support reduction. If adequate closed reduction to allow nail pass across the fracture site is not achieved in 30 minutes, open reduction is applied. No cast is applied in IN group. With flexible intramedullary nails mobilization of knee and ankle joints is allowed immediately post operatively and partial weight bearing is allowed after six weeks or when callus of three cortexes can be seen.

Follow up protocol and data collection

Both groups will participate the same follow-up protocol: Patients are examined at the outpatient clinic scheduled at 10-14 days, 6 weeks and at 3, 12 and 24 months and 10 years. Alignment and consolidation is documented during each visit with standard lateral

and AP radiographs. At 12 months follow up a CT scout is performed to find possible length discrepancy and to compare alignment to uninjured leg. At each appointment a specific follow up form is filled and patients and guardians are requested to answer Pediatric Quality of Life Inventory (PedsQL)[19,20] and Cosmetic visual analogue scale (VAS 0-100). The volume of uninjured and injured leg are determined by measuring circumference of leg at its thickest point.

Any adverse effects including wound necrosis, infections, skin problems related to casting, time needed for casting before radiographic and clinical consolidation of fracture, nerve or tendon injuries, delayed union, malunion, non-union, hardware problems, possible need for hardware removal and need for crossover from cast group to IN group will be recorded.

Outcome

Primary outcome

Primary outcome is radiographic union in good alignment at one-year follow-up measured in anteroposterior (AP) and lateral radiographs. The criteria for malunion are the same as those for acceptable alignment of the primary tibial fracture. Tibial length discrepancy will be measured from CT scout compared with uninjured tibia. An X-ray of the affected leg will be taken at each follow up and CT scout at 1 year follow up.

Two pediatric orthopedic surgeons and one pediatric radiologist, all blinded to clinical data, will read radiographs. Measurements will be recorded as an average of the three separate measurements performed.

Secondary outcomes

Pediatric Quality of Life Inventory (PedsQL) and visual analogy scale (VAS) at six weeks, one year and two year follow up, number of re-interventions during two year follow up, length of hospital stay, complications and volume of injured extremity compared with uninjured leg.

Statistical power calculation and analysis

Analysis will be by intention to treat based on children who will reach two-year follow-up. In case of significant cross-over a per protocol analysis will be added. A difference of 20% between the rates of malunion was set to represent a clinically significant difference between the two treatment methods. With the assumption of satisfactory union rates of 75% in the cast group and 95% in the intramedullary nailing group and type I error of 0.05 and a type II error of 0.2, 30 patients will be needed in each group. The sample size will be increased by 10% to allow for drop-outs.

After the final data set is formed from the primary data, data set access will be limited to the statistician and the authors of the final publication. The codes of the RCT arms will be known only to the research assistants until the blinded data interpretation has taken place.

Patient and public involvement

Patients, guardians or any third party were not involved in the development of this study design. Results of this study will be published only in peer-reviewed journals and no information besides that is given to the patients or guardians.

Ethics and dissemination

A joint ethical committee evaluation was obtained (approval number Dnro: ETMK105/1801/2017) for the study from the Ethical Committee of the Hospital for Southwest Finland. The separate permission to conduct the trial will be applied at each study center. The study is run by Helsinki University Hospital, New Children´s Hospital department of Pediatric Orthopedics and Traumatology. All patients 12 years or above and their guardians sign a written Informed consent before randomization.

We will obtain all research data during the standard orthopedic care of these children. Both participant data forms and electronic databases will be maintained in secure storage at the coordinating center for 10 years after completion of study. 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 participation. The Finnish Patient Insurance Centre will provide compensation for treatment injuries. The findings of this study will be disseminated through peer-reviewed publications and conference presentations.

Discussion

In this protocol manuscript we describe an RCT that aims to assess if surgical treatment with intramedullary nailing is superior to conservative treatment with closed reduction and casting in skeletally immature patients with tibial shaft fractures. To our knowledge, there is no RCT comparing effectiveness of these treatment modalities. We chose intramedullary nailing as the surgical method since it is the generally accepted, safe and

effective treatment method suitable for all skeletally immature patients with tibial shaft fracture. We chose union and correct alignment as primary outcome since in lower extremities malalignment changes the mechanical axis of the limb resulting increased risk of long term adverse effects like osteoarthritis and pain that might not emerge during adolescence.

After completion, trial will provide valuable evidence of the treatment of tibial shaft fractures in pediatric populations.

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