Casting without Reduction versus Closed Reduction with or without Fixation in the Treatment of Distal Radius Fractures in Children: A Study Protocol for a Randomized Non-Inferiority Trial

Background

Fractures are prevalent in the pediatric population. It is estimated that one in three children will sustain at least one fracture before adulthood, of which distal metaphyseal radius fractures are the most frequent[1, 2]. Current treatments include *in situ* cast immobilization, or reduction with or without fixation with K-wires, decided upon angulation and displacement. Traditionally, specific deformity limits are tolerated, given the child's age and gender, however, these limits lack supportive evidence. Further, treatment agreement, even between experienced pediatric orthopedic surgeons, is minimal[3].

Distal radius fractures have a remarkable remodeling potential. The remodeling rate is higher when the angulation is more severe, and it progressively decreases as the alignment approaches to normal[4]. Observational designs have shown that fractures up to 29 degrees of angulation and 19 mm of shortening immobilized *in situ* regain complete alignment about a year after injury[5]. Even shorter times to proper alignment are reported in younger children[5]. Additionally, Crawford et al. describe a series of children treated with cast immobilization without restoring the length of the radius, achieving neutral ulnar variance at follow-up[6]. Furthermore, when alignment is lost, typical radius morphology is present within three years

even when the fracture is immobilized without any attempt to regain alignment[7]. Hence, casting without reduction is considered a suitable treatment.

Some specialized centers reserve distal radius corrective osteotomy solely for fracture malunion in children approaching the end of growth or with associated physeal arrest. It is also the treatment of choice for children with congenital dysplastic conditions of the bone[8].

Functional evaluation

Upper extremity functionality refers to reaching, grasping, and manipulating objects with the intention to perform daily life activities[9]. Most of the instruments that assess upper extremity functionality in the pediatric population are specific to patients with longitudinal deficiencies, amputations, or neurodevelopmental disorders. Specific instruments for adults have also been published, however, several items refer to tasks that a 5-year-old child might not be able to properly execute.

The physical functioning domain of the PROMIS scales is available for assessing functionality of children without disabilities since 2011[10]. It is a precise and easy-to-administer outcome measurement instrument in children with orthopedic conditions. Children aged 8 years onwards are able to, effortlessly, answer the questionnaire by themselves. A parent-proxy version is available for younger children. The upper extremity functionality is a subdomain of

the physical functioning domain. It comprises 29 Liker-type questions with five categories that enquire about the difficulty of carrying out activities during the past week.

The trial's primary goal is to establish whether upper extremity's functionality of children who sustained a distal metaphyseal fracture of the radius and were treated with *in situ* cast immobilization, is not worse than the functionality of children treated with closed reduction and cast immobilization, with or without fixation, measured at 6 months with the PROMIS scale. Secondarily, range of motion (ROM), alignment, complications and further treatments will also be compared. Results may contribute to not only strengthening the evidence of secure shortening and angulation boundaries, aiding the clinician with evidence-based decision, but risks and costs may also be questioned, when encountering these kinds of fractures.

Methods

Study design and procedures

This is a randomized non-inferiority trial that will take place at Instituto Roosevelt in Bogota–Colombia, a single institution that focuses on providing treatment for children with orthopedic and neuromuscular conditions. Two accepted treatments for metaphyseal distal radius fractures will be compared: cast immobilization without reduction as the experimental intervention, and closed reduction and immobilization with or without percutaneous fixation as the control intervention. Acutely, conventional oral analgesics will be routinely provided,

afterwards, the principal researcher will invite children and parents to enter into the trial upon confirming admission criteria. Informed consent, along with informed assent, will be signed.

Inclusion criteria

Children between 5 to 10 years of age with a proven acute (i.e., within 14 days after injury) metaphyseal fracture of the distal radius (23-M 2-3 or 23r-M 2-3 according to the AO pediatric classification) will be regarded as eligible for the trial. Fracture shortening and angulation must range from 0 to 10 mm and 10 to 20 degrees in the oblique plane, respectively.

Exclusion criteria

- Polytrauma (Injury Severity Score ≥ 16)
- A concomitant fracture in the same limb
- Pathologic/open fracture
- Neuromuscular/metabolic bone diseases
- Concomitant neurologic/vascular lesions
- Longitudinal limb deficiency
- Previous infection/fracture in the fractured radius

Randomization

Randomization will be performed centrally by the Instituto Roosevelt Medical Research Department. Therefore, allocation will be concealed to the orthopedic surgeons. The Big Stick Design (BSD) with a maximum tolerated imbalance of 2 will be the methodology for randomization. The BSD has a very low probability of correctly guessing the allocation of the next child compared to other designs[11]. The R and RStudio statistical software, specifically the randomizeR package version 4.1, will be used[12].

Interventions

Patients will be allocated in a 1:1 ratio to either the experimental or control group. In the former, fractures will be immobilized without reduction. In the latter, fractures will be reduced and immobilized. Provided instability, K-wires will be used. Instability is considered when, after reduction, alignment is lost: a new displacement or angulation larger than 50% and 10 degrees, respectively. General anesthesia will be mandatory exclusively for the control group. Discharge within two hours is the standard practice for both procedures. Plain radiographs will be obtained immediately after the intervention, at two weeks, three-, and nine-months during follow-up. Casts and K-wires will be removed at 6 weeks.

Endpoints and follow up

Children will be evaluated at about two and six weeks, three, six, and nine months after randomization. The primary endpoint is the upper extremity function assessed with the

PROMIS Pediatric Physical Function v2.0 at six months. Parents will serve as proxies of children <8 years with the proper format of the scale. From 8 years of age onwards, children will personally answer the questionnaire.

The secondary outcomes are the ROM, ulnar variance, and fracture alignment in the sagittal and coronal planes. Plain radiographs of the wrist at two weeks, three and nine months and a standard goniometer will be used. Additionally, general anesthesia-related adverse effects, pressure ulcers according to the National Pressure Ulcer Advisory Panel, the number of days of required oral analgesics and Dahl classification of pin tract infections will also be registered[13]. Further treatments such as radius osteotomy due to deformity, pseudoarthrosis cure, and remanipulation will also be recorded. Figure 1 depicts the flow of the study.

Power analysis and sample calculation

In a personal communication, Dr. Calfee provided PROMIS range scores (36 to 39), variability (SD=10) and the minimally clinical important difference (MCID; 3 to 5) in children who have sustained an upper extremity fracture[14]. Therefore, assuming a non-inferiority threshold of 5, the trial requires a sample of 126 children (63 per group) to demonstrate no meaningful difference in the primary outcome (one-tailed $\alpha=0.05$, $\beta=0.2$). The sample will be inflated to 152 (20%) due to the anticipation of loss to follow-up.

Data management

Participant's information will be recorded in the REDCap software. Registries will be password-protected with access granted just to the principal researcher and the study conductor. Data will be kept at the Instituto Roosevelt Medical Research Department. After completing the study, data will be preserved for two years, then all non-anonymized documents will be discarded.

Statistical analysis

Customary descriptive statistics will be used whether the variables are continuous or categorical. The intention-to-treat principle will be followed in this trial. Authors of the scale in the Northwestern University will standardize PROMIS scores once data gathering is completed, afterwards, the primary outcome will be evaluated with a t-test. The non-inferiority threshold will be compared to the lower bound of the 95% confidence interval of the mean difference. Secondary outcomes measured with continuous variables (i.e., ROM, ulnar variance, fracture alignment and number of days with oral analgesia) will be compared with the t-test or Mann-Whitney's U conforming to the distribution of the variables. Categorical outcomes will be compared with the Fisher's exact test (i.e., anesthesia-related adverse effects, pressure ulcers, pin tract infections, radius osteotomies, pseudoarthrosis, and remanipulations). Early termination of the trial is unlikely; therefore, interim analyses are not considered: given the proposed design, neither superiority nor futility of the experimental treatment is expected.

Schedule

Recruitment commenced in June 2021. The principal researcher personally interviews parents and children and the trial's general characteristics are completely explained. Benefits, such as a close follow-up (e.g., radiographs, pain, functionality) are also explained. Authors expect an average of ten patients monthly, therefore, recruitment and analysis should be complete by June 2023.

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Declarations

Both, Instituto Roosevelt and Pontificia Universidad Javeriana Ethics Committees, evaluated and accepted trial's protocol, research manual, consent and assent forms, and information brochures (approval No. 2021012101-002 and FM-CIE-0416-21, respectively). The datasets used and/or analyzed during the current trial will be available from the corresponding author upon reasonable request. Authors declare no competing interests. No funding to declare. Acknowledgments: None. Authors' contributions: MGR: conception and design, data acquisition, analysis and interpretation, drafting of the manuscript and approval of the final version. CMP: critically revised the manuscript, drafting of the manuscript and approval of the final version

Discussion

This is the protocol of the first randomized trial that intends to compare functional outcomes of non-reduced versus reduced distal radius fractures in children. To authors knowledge, medical literature lacks experimental designs that take into account shortening and angulation in this age group.

The principal strength of this trial is the objective evaluation of functional outcomes with a scale constructed with modern measurement theory which is appropriate for the pediatric population, including previously healthy children who sustained a fracture of the wrist. In addition to functional recovery, anatomical parameters, as well as complications due to treatment will also be recorded.

The limitations of this trial are the lack of blindness for obvious reasons, and generalizability. Children will be recruited and treated in a specialized center. In most of authors' country institutions that deal with fractures in children a pediatric orthopedic surgeon is not available. The allocation will be open-labeled for patients, parents, and medical staff, this scenario may affect participants' feelings of well-being. However, results analyses will be blinded.

References

1. Christoffersen T, Ahmed LA, Winther A, Nilsen OA, Furberg AS, Grimnes G, et al. Fracture incidence rates in Norwegian children, The Tromsø Study, Fit Futures. Arch Osteoporos. 2016;11. doi:10.1007/s11657-016-0294-z.

2. Joeris A, Lutz N, Blumenthal A, Slongo T, Audigé L. The AO Pediatric Comprehensive Classification of Long Bone Fractures (PCCF): Part I: Location and morphology of 2,292 upper extremity fractures in children and adolescents. Acta Orthop. 2017;88:123–8.

3. Dua K, Stein MK, O'Hara NN, Brighton BK, Hennrikus WL, Herman MJ, et al. Variation Among Pediatric Orthopaedic Surgeons When Diagnosing and Treating Pediatric and Adolescent Distal Radius Fractures. J Pediatr Orthop. 2019;39:306–13.

4. Friberg KSI. Remodelling after distal forearm fractures in children: I. The effect of residual angulation on the spatial orientation of the epiphyseal plates. Acta Orthop. 1979;50:537–46.

5. Do TT, Strub WM, Foad SL, Mehlman CT, Crawford AH. Reduction versus remodeling in pediatric distal forearm fractures: a preliminary cost analysis. J Pediatr Orthop B. 2003;12:109–10915.

6. Crawford SN, Lee LSK, Izuka BH. Closed treatment of overriding distal radial fractures without reduction in children. J Bone Jt Surg - Ser A. 2012;94:246–52.

7. Roth KC, Denk K, Colaris JW, Jaarsma RL. Think twice before re-manipulating distal metaphyseal forearm fractures in children. Arch Orthop Trauma Surg. 2014;:1699–707.

8. Mader K, Gausepohl T, Pennig D. Shortening and deformity of radius and ulna in children: Correction of axis and length by callus distraction. J Pediatr Orthop Part B. 2003;12:183–91.

9. Wallen M, Stewart K. Grading and Quantification of Upper Extremity Function in Children with Spasticity. Semin Plast Surg. 2016;30:5–13.

10. DeWitt E, Stucky B, Thissen D, Irwin DE, Langer M, Varni JW. Construction of the Eight Item PROMIS Pediatric Physical Function Scales: Built Using Item Response Theory. J Clin Epidemiol. 2011;64:794–804.

11. Zhao W, Weng Y, Wu Q, Palesch Y. Quantitative comparison of randomization designs in sequential clinical trials based on treatment balance and allocation randomness. Pharm Stat. 2012;11:39–48. doi:10.1002/pst.493.

12. Team RC, Computing RF for S. R: A language and environment for statistical computing. 2021. https://www.r-project.org/.

13. Edsberg L, Black J, Goldberg M, McNichol L, Moore L, Sieggreen M. Revised National Pressure Ulcer Advisory Panel Pressure Injury Staging System Revised Pressure Injury Staging System. 2016;43 December:585–97.

14. Gerull WD, Okoroafor UC, Guattery J, Goldfarb CA, Wall LB, Calfee RP. Performance of Pediatric PROMIS CATs in Children With Upper Extremity Fractures. Hand. 2020;15:194–200.