Outcomes of external versus internal fixation for traumatic lower limb fractures in low- and middle-income countries

a systematic review and meta-analysis protocol

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Aims

Lower limb fractures are common in low- and middle-income countries (LMICs) and represent a significant burden to the existing orthopaedic surgical infrastructure. In high income country (HIC) settings, internal fixation is the standard of care due to its superior outcomes. In LMICs, external fixation is often the surgical treatment of choice due to limited supplies, cost considerations, and its perceived lower complication rate. The aim of this systematic review protocol is identifying differences in rates of infection, nonunion, and malunion of extra-articular femoral and tibial shaft fractures in LMICs treated with either internal or external fixation.

Methods

This systematic review protocol describes a broad search of multiple databases to identify eligible papers. Studies must be published after 2000, include at least five patients, patients must be aged > 16 years or treated as skeletally mature, and the paper must describe a fracture of interest and at least one of our primary outcomes of interest. We did not place restrictions on language or journal. All abstracts and full texts will be screened and extracted by two independent reviewers. Risk of bias and quality of evidence will be analyzed using standardized appraisal tools. A random-effects meta-analysis followed by a subgroup analysis will be performed, given the anticipated heterogeneity among studies, if sufficient data are available.

Conclusion

The lack of easily accessible LMIC outcome data, combined with international clinical guidelines that are often developed by HIC surgeons for use in HIC environments, makes the clinical decision-making process infinitely more difficult for surgeons in LMICs. This protocol will guide research on surgical management, outcomes, and complications of lower

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limb shaft fractures in LMICs, and can help guide policy development for better surgical intervention delivery and improve global surgical care.

Take home message

- This study will provide a comprehensive overview of the clinical outcomes of surgically treated extra-articular tibia and femur fractures in low- and middle-income countries (LMICs).
- This data will guide the development of LMIC-specific clinical guidelines and health policy development.

Introduction

Traumatic femoral and tibial fractures are among the most common fractures in low- and middle-income countries (LMICs).[1-3] External fixationand internal fixation, using intramedullary nails or plates, are two common options for surgical management of these fractures.[4–6] Nonoperative treatment such as traction is sometimes still used with variable levels of success, sometimes leading to disability and increased economic burden for the patient and community.[7,8]

The clinical need to increase access to surgical treatments instead of nonoperative treatments for lower limb fractures is clear; less so, however, is the best approach to expand services. While early treatment with internal fixation is generally recognized in high-income countries (HICs) as the chosen management, even for open fractures, in more resource-limited areas, external fixation is sometimes used exclusively for open fractures because of cost, availability of equipment and supplies, and concerns about outcomes.[5,9–12] However, a systematic review of open and closed tibia and femur fractures across LMICs has not yet been conducted, and this broader study could describe more generalizable data on the outcomes of external and internal fixation for all fractures.[13]

This study is a systematic review of the evidence on external and internal fixation outcomes in management of femoral and tibial extra-articular fractures in LMICs. Eligible papers are those that quantify and compare the outcomes of external fixation with internal fixation for management of extra-articular femoral and tibial traumatic fractures in LMICs. Specifically, this study examines infection, malunion, and nonunion as primary endpoints, and length of hospital stay and cost of care as secondary endpoints. It is expected that the evidence from this review will inform decision-making regarding the management of extra-articular femoral and tibial fractures.

Methods

Study registration

This systematic review and meta-analysis will be performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines.[14] The protocol for this review has been registered before data extraction began on PROSPERO (CRD42024568786). MP is the guarantor of this protocol.

Research questions

Our research question was developed using the population, intervention, comparator, outcome (PICO) system.[15]

Primary research question: in adult patients with lower limb extra-articular shaft fractures in LMICs, what is the difference between internal fixation with plating or intramedullary nailing, compared with external fixation in terms of infection, nonunion, and malunion rates, from 2000 to 2024?

Secondary research question: in adult patients with lower limb extra-articular shaft fractures in LMICs, what is the difference between internal fixation with plating or intramedullary nailing, compared with external fixation in terms of length of hospital stay, cost of care, time to intervention, and postoperative quality of life from 2000 to 2024?

Eligibility criteria

To capture as much of the available evidence in literature as possible from a wide variety of countries and settings, the study type eligibility criteria have intentionally been kept very broad. The year 2000 was chosen as a cut-off because of the rapid expansion of health investments in LMICs since 2000 due to the Millennium Development Goals and subsequent Sustainable Development Goals frameworks.[16] We assumed that the practice of orthopaedic care may have been significantly altered in LMICs because of this increased attention for health over the past two decades compared to the 1980s and 1990s, and that including older evidence may not be relevant.

Study type eligibility criteria

The eligibility criteria is any study containing original research reporting on primary data and including at least five eligible patients with the same bone affected and same treatment group, and reporting on at least one surgical intervention and one outcome of interest: randomized controlled trials; cohort studies; case-control studies; published abstracts; editorials, letters to the editor, short reports, and conference proceedings; university theses and dissertations; and clinical trial data published in a clinical trial registry that have not yet been published as a scientific article elsewhere. There are no limitations on language or journal title.

The following study types will be excluded to avoid duplication of data in the paper: scoping and systematic reviews; reports published by governing bodies reporting on data from the scientific literature; abstracts and conference proceedings reporting on earlier versions of a dataset that has been published as a full paper afterwards.; Studies published before the year 2000; articles reporting on fractures due to other reasons than trauma, such as osteoporosis, fragility fractures secondary to bone malignancies, or constitutional bone diseases;. and studies reporting on the prevalence of surgical intervention types without reporting on outcomes, will be excluded as well.

Articles reporting on patient subsets that were selected based on a specific patient demographic or outcome, other than the demographics described here or outcomes of interest, were excluded. Case reports were excluded given that data from such reports are not generalizable or representative of a regional practice or country.

Study population eligibility criteria

Any study reporting on an extra-articular tibia fracture or an extra-articular femur fracture at least 5 cm below the lesser trochanter, sustained after 1 January 2000, with patients aged ≥ 16 years who were treated in an LMIC as defined by the World Bank, will be eligible.[17] This includes both open and closed fractures.

Cohorts that span an inclusion period including 1/1/2000 are also eligible. Cohorts whose inclusion criteria span an age range including age 16 years are also eligible if the population aged below 16 years were considered skeletally mature by the authors or an adult surgical fixation technique was deemed clinically appropriate.

Study intervention eligibility criteria

Any study reporting on the population of interest that was treated with either an external fixator, any type of intramedullary nail, or any type of plate.

Studies reporting on a combination of interventions are excluded, except for studies reporting on open fractures treated with an external fixator and a second-stage conversion to a plate or an intramedullary nail, as this can be considered standard of care.[9]

Study outcomes eligibility criteria

Any study reporting on the population of interest that was treated with one of the interventions of interest, and reports on any of the following primary outcomes, will be eligible: postoperative infection rates; malunion rates; and nonunion rates.

Primary outcome measures

To assure internal consistency in the collected primary outcome data, the data will not be categorized according to the descriptions in the origin paper. Data will be recategorized, if necessary, based on the definitions below.

Postoperative infection

Multiple diagnostic criteria for postoperative infections have been described in the literature, but none have been universally accepted.[18] For this review, we will consider an infection to be present if the infection required antibiotic treatment, and if the description in the origin paper meets any of the criteria below:

- A surgical site infection that developed within 28 days of surgical fixation; with at least one of the following clinical signs present: redness, swelling, purulence, fistula, or sinus connected with the fracture site.
- Sustained elevated ESR/CRP combined with an elevated total leucocyte count or elevated polymorphonuclear (PMN) count beyond seven days postoperatively.
- Positive blood culture that cannot be explained by any other patient complaints.
- A positive gram-stain, direct microscopic exam, histopathological exam, or a leucocyte count of > 50,000/mm^3 on a tissue or fluid sample taken from the wound or fracture site.
- A radiological exam showing clear evidence of bone sequestration, volucrum formation, chronic osteomyelitis, subperiosteal or subcutaneous abscess formation, or a fistula.

Infections will be further classified as superficial, deep, or osteomyelitis, if these data are available, using the following criteria:

Superficial infection: if the infection is described as only limited to skin and subcutaneous tissue with no signs of deep tissue infection; or if the infection is identified as a pin site infection or cellulitis.

Deep infection: an infection developed within one year at the fracture site, including infections of the bone and deep purulent collections and abscesses; if the infection is diagnosed on deep tissue sampling; or if the patient develops a fistula to the fracture site.

Osteomyelitis: a radiological exam showing clear evidence of any of the following: bone sequestration; volucrum formation; chronic osteomyelitis; subperiosteal or subcutaneous abscess formation; or a fistula.

Malunion

A fracture will be considered to have healed as a malunion if a deformity is present in the sagittal, axial, or coronal planes: varus/valgus angulation, procurvatum/recurvatum or a limb shortening; or a rotation deformity is described in the origin paper. The following cut-off values will be used for the purposes of this review: varus-valgus angulation > 5°; recurvatum or procurvatum > 5°; internal rotation > 15°; external rotation > 20°; and limb shortening > 1 cm.

Nonunion

A non-consolidated fracture will be considered a nonunion, if the description in the origin paper meets any of the following criteria at nine months postoperatively: there is palpable mobility or pain at the fracture site; an inability to bear weight on the treated limb; radiological examination confirms the absence of bridging calluses in three out of four cortices in minimum two different directions; and serial radiographs show persistent fracture lines and/or no signs of healing.[19]

Search strategies

Studies discussing fixation of femoral and tibial traumatic fractures in LMICs were identified by searching MEDLINE/PubMed, Embase, Global Health, and Global Index Medicus[20] on 27 June 2022. The content of local journal and article databases such as PakMediNet or African Journals Online, is often covered by the latter two databases we searched. We therefore believe that our search strategy offers a pragmatic balance between the number of databases searched and the reach of our search outside of the established journals. Controlled subject vocabulary terms (i.e. MeSH, Emtree, CAB Thesaurus) were included when available and appropriate. The search strategies were designed and carried out by a health sciences librarian (CM). Publication date was limited to 2000 onward, based on fixation technique of interest. No language limit was applied. The searches will be run again in all databases in 2024 to capture additional papers published after 2022.

We searched the Pan African Clinical Trial Registry, EU Clinical Trials Register, ISRCTN registry, clinicaltrials.gov, and the WHO: International Clinical Trials Registry Platform (ICTRP), for completed trials with available data that have not yet been published in the scientific literature.

Table I. Data extraction variables.

Study variables
General information
Study ID
Title
First author
Year of publication
Publication type
Name of journal
Funding sources
Conflicts of interest of study authors
Characteristics of included studies
Study start date
Study end date
Retrospective/prospective study
Study design
Country in which the study was conducted
Country income level
Primary/secondary/tertiary hospital
Single vs multiple sites included in study
Name of database, if database study
Sample size of total study
Sample size of included patients in final analysis (for studies also reporting on other fractures)
Participant characteristics
Age of participants
Sex of participants
Mechanism of injury
Were patients with comorbidities included?
Were patients with pre-existing bone conditions included?
Fracture characteristics
Fracture site (femur/tibia)
Fracture location (proximal/mid-shaft/distal)
AO Classification, if included
Wound type
Soft-tissue injury type, if included
Gustilo Anderson Classification, if included
Any associated injuries
Intervention
Surgical intervention
Type of surgical fixation and name of specific implant, if included
Surgical approach (open/minimally invasive)
Intraoperative complications, if reported
Blood transfusion, if reported
Was initial intervention delayed?
Time to first intervention
Time to second intervention, if applicable
Postoperative care protocol, if documented
Primary outcomes
Nonunion rate
Time to union
Malunion rate
Type of malunion (rotation/shortening/angulation)
Gross infection rate
Infection rate per infection subtype (superficial/deep/osteomyelitis)
Intervention comparison (external vs internal fixation)
Statistical analysis comparing intervention subgroups, if reported
Statistical tests used
Statistical outcome measures and results reported
Secondary outcomes
Length of hospital stay
Duration of follow-up
Cost of care
Additional information
HRQoL assessment scores, if reported
Time to HRQoL assessment
Statistical test/technique/results used for comparison of HRQoL scores
Number of postoperative deaths

(*Continued*)

(*Continued*)

HRQoL, health-related quality of life.

The exact search strategies for all databases can be found in the Supplementary Material.

Selection of sources of evidence

Abstract and full-text screening will be performed in Covidence Systematic Review Software.[21] Each article will be screened by two independent reviewers sourced from a pool of eight reviewers consisting of medical students and recent medical graduates (HS, MRA, PFO, SRB, A. Shah). Conflicts will be resolved by a third reviewer who is a senior resident in orthopaedics or a fully licensed orthopaedic surgeon (MP). Articles in a language other than English will be translated to English using DeepL translator (DeepL, Germany)[22] or Google Translate (Google, USA).[23] Articles for which a full-text cannot be obtained through any of the authors' university libraries will be automatically excluded. All reasons for exclusion will be recorded in Covidence and the result of the screening process will be visualized in a PRISMA flowchart.

Data extraction

Data extraction will be performed in Covidence by two independent extractors sourced from a pool of three extractors. Conflicts will be resolved by the first author (MP). Data will be collected on study characteristics; the clinical setting where the study was done; population, intervention, and at least one of the primary outcomes; and secondary outcomes where available. A full list of the variables can be found in Table I.

Risk of bias

The Johanna Briggs Institute (JBI) Critical Appraisal Tools[24] will be used to assess the risk of biases, which shall be reported as low-risk, moderate-risk, or high-risk of biases depending on the number of domains in which the article in question fails to meet the minimum standard.[24] The following domains will be used in assessing risk (where applicable for the specific study design): confounding, randomization process biases, participant selection bias, classification bias, deviation bias, bias from missing data, outcome measurement bias, and bias in the selection of reported results. All included studies will be independently scored by the two reviewers who are doing the data extraction for that respective paper, using the JBI tool applicable to the respective study design of the included study, and a discussion will facilitate consensus on the bias risk levels. Publication bias will be assessed using funnel plots and statistical tests (e.g. Egger's test).

Quality of evidence

We will assess the methodological quality of included studies using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Framework.[25] The quality of evidence will be classified as high, moderate, low, or very low. Whenever there are apparent differences in intervention methods, performance, and detection, biases will not be considered when assessing study quality. Studies will be classified into high quality when selection bias is graded as low risk, while others are graded as low or unclear. Studies will be considered low quality when selection bias is assessed as high risk, and moderate quality will be regarded as not meeting the above criteria. We will use these assessments to evaluate the evidence's overall strength and identify potential limitations of the findings.

Statistical analysis

The specific type of statistical analysis performed will depend on the nature of the data collected. The findings of the study will be reported through the following measures:

Descriptive statistics

For continuous (quantitative) variables, including age and cost of care, the mean (SD) will be reported. For categorical (qualitative) variables, including sex and type of fracture frequency, the number (%) will be reported. We will present the median and IQR in case of skewed data. All the outcome measures will also be summarized with adjusted relative risk or odds ratios (ORs), 95% CIs, and p-values from two-sided tests.

Data will be reported for the total cohort of patients included in the review and for 12 different subgroups. The subgroups by grouping patients with the same fracture location (tibia vs femur), the same fracture type (open vs closed), and the same surgical treatment (plate vs intramedullary nail vs external fixator) together.

Inferential statistics

Comparison of baseline characteristics and study outcomes between treatment groups will be made for normally distributed continuous variables using *t*-tests when there are only two groups, while analysis of variance (ANOVA) will be used for more than two groups. For non-normally distributed continuous outcome variables, the Mann-Whitney U test will be performed for two groups, and the Kruskal-Wallis test will be conducted for three or more groups. For categorical outcome variables, Pearson's chi-squared test ($\chi 2$) will be performed, and in case of a small sample size (expected cell frequencies < 5), Fisher's exact test will be used. All p-values will be two-tailed, with the significance level at 5%.

We will reduce heterogeneity (variation) among studies using subgroup analysis and matching papers based on the same country; and sharing a similar method of patient recruitment and sample size. For papers with no match, we would match that paper with the most similar country based on population demographics or study patient recruitment type. A two-way sensitivity analysis will be carried out for the primary outcomes to explore and compare both external fixator and intramedullary nailing/plating under different scenarios, and to assess the robustness of the results.

Meta-analysis

If a sufficient amount of data is available to perform the meta-analysis, a random-effects meta-analysis followed by a subgroup analysis will be performed, given the anticipated heterogeneity among studies. When studies report the same outcome, we pool the results using a random-effects model. For continuous variables, weighted mean differences (WMDs) will use the inverse variance method, and for categorical variables, risk ratio (RR) or OR with a 95% CI will be calculated using the Mantel-Haenszel analysis method with two-sided p-values for each outcome. In studies in which clustering effects are not considered, we will adjust the SDs by the design effect, using intraclass coefficients if given in papers or external estimates obtained from similar studies.

Heterogeneity among the results will be assessed using a chi-squared test and the I^2 statistic. An I^2 value > 50% will reflect 'substantial heterogeneity'. We will conduct sensitivity analyses by sequentially excluding individual studies to investigate possible sources of heterogeneity, emphasizing study quality, socioeconomic, demographic, and treatment factors. Statistical significance will be indicated by a p-value < 0.05. The meta-analysis results will be summarized appropriately, focusing on the study's outcome measures.

Team diversity statement and development of recommendations

After the statistical analysis of the available data, the team aims to use the results to develop general and region-/country-specific clinical and policy recommendations for the surgical management of lower limb extra-articular fractures. The senior research team consists of four fully licensed orthopaedic surgeons: two LMIC-trained and -based (MP, KJA-H), and two HIC-trained and -based with extensive experience in LMICs (A. Saeed, EM); one HIC-trained and

-based plastic surgeon with extensive experience in LMICs (DSC); and a HIC-based librarian (CM). The junior research team consists of ten HIC-based medical students and recent medical graduates with diverse backgrounds in terms language, citizenship, country where medical training was obtained, and international work experience (HS, MRA, PFO, SRB, A. Shah); one LMIC-based medical student; and a LMIC-based biostatistics student (SJ). We aim to leverage this diversity in experience and perspective to develop culturally and context-sensitive recommendations, and to facilitate the dissemination of results outside of HIC academic institutions.

Discussion and dissemination of results

Clinical decision-making is a complex process during which the clinician should ideally take into consideration: the patient characteristics and their preferences, knowledge of the natural history of the disease process, available resources, their own skillset, and the economic impact for the patient and the wider community when choosing one treatment over another. The lack of easily accessible LMIC outcome data combined with international clinical guidelines that are often developed by HIC surgeons for use in HIC environments makes the clinical decision-making process infinitely more difficult for surgeons in LMICs. With this review we aim to consolidate the available data on some of the most commonly seen fractures in LMICs, and provide guidance, developed by a diverse team and based on LMIC experiences and data. We hope for this review to confirm that difficult trade-offs that need to be made in LMICs concerning cost, infection risks, and the impact of postoperative complications are made diligently and offer the best available care for the affected patients within the known constraints.

It is quite feasible that results will show that in environments in which high sterility levels might be harder to maintain, equipment and supplies might be difficult to obtain, or cost of internal fixation could be prohibitive, and that external fixation is the superior choice for management of extra-articular femoral and tibial fractures. While internal fixation might provide greater patient satisfaction, fewer infections, and malunion, earlier weightbearing, shorter hospitalization, and perhaps other benefits in HICs, this may not be true at all in LMICs. Additionally, it is understandable that although trying to achieve one standard for such management could be desirable, this may prove difficult in resource-constrained settings with high variability in resources available across hospitals and countries. Consequently, it might be wise to emphasize the need for an improved overall surgical health system rather than simply trying to advocate for a move to internal fixation as the gold standard as quickly as possible because of results from HICs.

The results of this review will be particularly pertinent as a first step for quantifying the outcomes of external and internal fixation across LMICs in a uniform way, and identifying best practices and remaining quality and safety gaps in these settings. Sub-group analysis will allow us to develop specific recommendations for open fractures as they remain a major burden on the health system and require a specific approach. Consequently, an examination of existent data as is being done in this review is the best method of providing some level of guidance to the practitioner and to the global health policymaker.

Social media

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Supplementary material

Search strategies for all databases.

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Data sharing

There is no primary data used in this research protocol. The data collected as part of the systematic review is all publicly available data from published sources. A compiled dataset is available from the corresponding author upon reasonable request.

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Ethical review statement

This study did not recruit human subjects, and was not subject to an Institutional Review Board. Consent for publication was obtained from all authors and collaborators on this protocol.

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