

PATIENT SELECTION FOR SINGLE STAGE RECONSTRUCTION IN LONG BONE FRACTURE RELATED INFECTION

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ABSTRACT

Background: Both single-stage and staged reconstruction are used in cases of infection associated with a non-healed long-bone fracture. The available results are hard to interpret since the type of treatment given depends on the complexity of the defect, the patient's condition, the requirements of the soft tissues, the microbial details, and the local expertise. A systematic review published in 2025 looked at the overall outcomes but did not identify the patient characteristics that should guide the choice of stage.

The aim is to identify and critically evaluate the factors that are given as reasons for choosing single-stage or staged reconstruction in adults who have a infection associated with a long bone fracture, and to determine whether any of these factors is linked to different treatment outcomes.

Methods: The databases MEDLINE, Embase, Scopus, Web of Science Core Collection and CENTRAL will be searched from their inception up to the final date of the search. In addition, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform and the reference lists of the included reports and relevant reviews will be examined. Two reviewers will independently carry out the screening of the records, the extraction of data and the assessment of risk of bias.

Comparative non-randomized studies will be evaluated using ROBINS-I while uncontrolled case series will be assessed with the Joanna Briggs Institute case-series checklist. The selection criteria will be grouped by clinical domain. A meta-analysis will only be performed when the populations, interventions and definitions of the outcomes are sufficiently similar; in all other cases, a synthesis without meta-analysis will be provided using structured tables that show effect direction and study characteristics.

Discussion: This review looks at three questions which are frequently mixed up—whether a reconstruction is technically possible, whether a particular feature indicates a poor outcome, and whether that feature affects the relative advantages of single-stage as compared with staged treatment—the aim being to assist in open, multidisciplinary decision-making and in the planning of prospective comparative studies. staged treatment—the aim being to assist in open, multidisciplinary decision-making and in the planning of prospective comparative studies.

For registration and reporting: the protocol will be registered prospectively in PROSPERO and will be reported in accordance with PRISMA-P; the completed review will comply with PRISMA 2020 and SWiM in the case where a metaanalysis is not appropriate.

KEYWORDS: MEDLINE, SINGLE STAGE RECONSTRUCTION, BONE FRACTURE, Web of Science Core Collection

1. INTRODUCTION

Fracture-related infection involves both an infectious process and the mechanical and biological needs of fracture healing.

Although consensus definitions have enhanced diagnostic consistency, they do not specify the manner in which skeletal stability, dead space, bone loss and soft-tissue coverage should be reconstructed. [1,2] When a fracture has not healed, removal of the implant may call for immediate definitive fixation or for temporary stabilization followed by a later reconstructive operation.

Single-stage reconstruction has the advantage of reducing both the number of operations that have to be carried out and the amount of time spent on temporary fixation. In the case of staged reconstruction, it is possible to carry out a reassessment following excision, after physiological recovery, or when delayed definitive reconstruction is decided. The use of these terms, however, is not consistent. Different timelines may apply to fixation, bone-defect reconstruction and soft-tissue coverage, and an unplanned reoperation after a procedure intended to be single-stage should not be regarded as equivalent to a planned second stage.

A systematic review from 2025 found that among 35 studies which included a total of 985 patients, the evidence was not enough to suggest that either single-stage or two-stage revision should be recommended for all patients. [3] By making this wide-ranging comparison, the review raises a more specific and still unresolved question: what factors are actually taken into account when choosing a strategy, and does any of these factors point to a group of patients who benefit more from one approach than the other? Any feature that is linked to failure has a prognostic value; merely because of this does not mean that staging leads to a better outcome. The review will look directly at this difference.

Review question

For adults who have an unhealed infection associated with a long-bone fracture and are having an implant replaced and the bone reconstructed, which patients' factors together with those relating to the infection, the fracture, the soft tissues, the microbiology, the treatment and the services were given as reasons for selecting single-stage or staged reconstruction, and is any of these factors linked to different clinical outcomes between the two strategies?

Table 1 Review framework

Population	Adults with unhealed appendicular longbone FRI requiring implant exchange and reconstructive stabilization.
Intervention	Single-stage exchange: removal of existing fixation, debridement and insertion of intended definitive fixation in the same operative session.
Comparator	Planned staged exchange: temporary stabilization followed by later intended definitive fixation.
Primary concept	Any explicitly reported factor, criterion, rationale or intraoperative finding used to select or change the reconstructive strategy.
Clinical outcomes	Infection recurrence or persistence, fracture union, unplanned surgery, amputation, mortality, complications, treatment burden, function and patientreported outcomes.
Study designs	Randomized or nonrandomized comparative studies and uncontrolled cohorts or case series with at least five eligible patients.

Methods

Design and registration

The protocol has been prepared in accordance with PRISMA-P.[4] The final review will be reported using PRISMA 2020.[5] The protocol will be submitted to PROSPERO prior to carrying out the formal title and abstract screening; amendments will be dated, justified and recorded both in the registration record and in the final manuscript. There are no plans to involve patients or the public at the protocol stage, but consideration will be given to involving them in the interpretation and dissemination phases after the review has been completed.

Eligibility criteria

Population: A study will be included if 80 per cent or more of the participants are adults who have an untreated infection affecting the femur, tibia, fibula, humerus, radius or ulna after fracture fixation, or if the data for this subgroup can be obtained separately. FRI will be accepted if it is defined according to the criteria reached by international consensus or if the study provides a clear definition that is compatible with deep infection involving a fracture or the fixation construct. Studies that focus only on prosthetic-joint infection, spinal infection, infection of the phalanges of the hand or foot, primary open-fracture prophylaxis, chronic osteomyelitis in healed fractures without any reconstructive fixation, or those involving paediatric populations will be excluded.

Regarding interventions: reports that are eligible must include a description of the exchange or removal of an

implant together with a planned reconstructive stabilization. In the case of a one-stage exchange, definitive fixation must be intended at the operation carried out at the index infection. For a staged exchange, temporary stabilization or no definitive fixation must be carried out, followed by a later planned definitive fixation procedure. Simply planning future bone grafting will not cause a definitive fixation procedure to be classified as a staged exchange. Any studies that only involve debridement with implant retention or implant removal after fracture union must be excluded unless the data on the exchange strategy are provided separately.

Regarding outcomes and the process of selection: In order to answer the main question for the review, the reports have to include at least one criterion, rationale, baseline characteristic, intraoperative finding or service factor which is relevant to the method of selection. For the synthesis of the secondary outcomes, the studies must provide at least one clinical outcome. Conference abstracts will be kept during the screening stage and will be connected with the full reports; abstracts that contain no data will only be included if eligibility and the relevant variables can be verified.

The study design and publication status should include randomized trials as well as prospective or retrospective comparative cohort studies and uncontrolled case series which have at least five eligible participants; case reports, narrative reviews, technical notes that do not include patient outcomes, expert opinion and biomechanical or laboratory studies must be excluded. There will be no restriction based on language or date of publication and translations will be obtained for reports that are not in English.

Information sources

The search will extend from the beginning up to [final search date] in the following databases: MEDLINE through Ovid, Embase through Ovid, Scopus, Web of Science Core Collection and the Cochrane Central Register of Controlled Trials. For ongoing or unpublished studies, searches will be carried out on ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform. Backward and forward citation searches will be conducted for all the reports and relevant reviews included in the study, including the 2025 review by Sliepen and colleagues. [3] If the definition of a strategy or subgroup data is unclear, the corresponding authors will be contacted.

Search strategy

The search involves the use of controlled vocabulary together with free-text terms for fracture-related infection or for infected nonunion, as well as terms relating to revision, implant exchange, fixation and staged reconstruction. The search strategy will be peer reviewed by means of the PRESS approach before it is carried out. A draft PubMed search strategy is given in Appendix 1 and will be adapted for each database. In the final review, the full search strategies, the platforms used, the dates and the number of results will be reported.

Study records and selection

The search results will be exported into a reference manager, deduplicated using both automated and manual methods and then uploaded to the screening software. Two reviewers will independently check the titles and abstracts against the piloted criteria. The same reviewers will also independently evaluate the full texts and note one primary reason for excluding each report. Any disagreements will be settled through discussion and, if needed, by involving a third reviewer. If there are multiple reports derived from the same cohort, they will be linked and considered as a single study. The finished review will contain a PRISMA flow diagram and a table of the full-text exclusions.

Data extraction

A standardized form will be tested on no fewer than three studies; the data will be extracted independently by two reviewers or alternatively one reviewer will carry out the extraction and a second will check each field. The authors will be asked for any essential missing or ambiguous information. The data will be gathered at the level of the study, the treatment group and the outcome, and the information available before surgery will be separated from that which is only known after debridement.

Table 2: Planned data extraction domains

Study	Country, centre type, recruitment period, design, prospective or retrospective status, sample size, eligibility criteria and follow-up.
Patient and host	Age, sex, smoking, diabetes, vascular disease, immune compromise, nutrition, host classification, patient preference and capacity to tolerate planned procedures.
Fracture and infection	Bone and segment, fracture status, time from fixation, diagnostic criteria, sinus or wound status, prior operations, organism information and antimicrobial resistance.
Reconstruction	Debridement extent, defect morphology and length, fixation removed, temporary and definitive constructs, bone reconstruction, dead-space management and local antimicrobials.
Soft tissues and service	Coverage requirement and timing, flap type, orthoplastic availability, referral pathway, team expertise, scheduling or resource constraints.
Selection decision	Planned strategy, stated reasons, alternatives considered, intraoperative change, timing of each reconstructive component and planned versus unplanned later operations.

Outcomes	Definitions, time origin, infection status, union, reoperations, fixation failure, amputation, death, adverse events, hospital burden, function and patient-reported recovery.
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Risk of bias assessment

Two reviewers will independently evaluate the risk of bias. When randomized trials are identified, they will be assessed using RoB 2; comparative non-randomized intervention studies will be assessed with ROBINS-I, with a special focus on confounding by indication, the classification of the intended strategy, deviations from the planned course, missing outcomes and selective reporting. [6] Uncontrolled case series will be assessed by means of the Joanna Briggs Institute critical appraisal checklist for case series. Any disagreements will be settled either by reaching a consensus or by involving a third reviewer. The judgments regarding risk of bias will be used to inform the interpretation and to guide sensitivity analyses rather than being turned into an unvalidated numerical quality score.

Outcomes

The main result of the review is the collection of factors that are explicitly stated to have influenced the decision to opt for either a single-stage or a staged exchange. These factors will be divided into those relating to technical feasibility, baseline prognostic factors, possible modifiers of treatment effect, patient preferences or service constraints. The secondary outcomes include infection recurrence or persistence, union, time to union, unplanned surgery, fixation failure, amputation, mortality, adverse events, hospital and treatment burden, as well as function and patient-reported outcomes. The definitions and time points will be kept unchanged rather than being quietly harmonised.

Synthesis

The study's characteristics, the definitions of its strategies and the reasons for selection will be set out in a table. The selection factors will then be grouped into the following predefined categories: diagnostic certainty and microbiology; host status; fracture stability and bone loss; soft-tissue reconstruction; antimicrobial feasibility; patient preference; and service capability. We will distinguish factors merely present in the cohort from factors explicitly used in treatment allocation.

A meta-analysis based on random effects will only be carried out if three or more studies which are clinically comparable report the same contrast and outcome using compatible definitions. Whenever possible, comparative estimates will be chosen rather than separate pooled proportions. For outcomes that are binary, risk ratios or odds ratios will be used together with 95% confidence intervals, while for continuous outcomes mean differences or standardized mean differences will be used along with their 95% confidence intervals. Heterogeneity will be assessed both clinically and statistically, using tau squared and I squared, without making a decision to pool on the basis of a single numerical threshold. In cases of sparse data, zero events, and clustering, suitable methods will be applied taking into account the available design and those methods will have been specified in advance.

If a meta-analysis is not appropriate, the synthesis will be carried out in accordance with the SWiM principles. The studies will be grouped according to clinical question and study design, and the effect estimates, direction, precision, risk of bias and applicability will be made clearly visible. It will not be necessary to use vote counting based solely on statistical significance. The planned subgroup analyses will cover anatomic site, early as opposed to delayed or chronic presentation, critical bone defect, flap requirement, known as against unknown pathogen, resistant organism, host compromise and definitive internal or external fixation. These subgroup analyses will be regarded as exploratory unless there are previously specified comparisons and sufficient data available.

Certainty of evidence

GRADE will serve as the basis for assessing comparative outcome evidence in those cases where there is a coherent body of evidence relating to the same contrast. Certainty will be evaluated separately in the cases of infection control, union, unplanned surgery, amputation and function. In instances involving descriptive selection criteria and uncontrolled series, the certainty will be discussed in a narrative form since a single GRADE assessment might not be appropriate for the evidentiary question in question. Publication bias will only be examined where there are enough comparable studies available to allow for a meaningful evaluation.

Protocol status

When the manuscript for this protocol was being prepared, although the search strategy had been drawn up, formal database searches, deduplication, screening, data extraction and the assessment of risk of bias had not yet taken place. It is for this reason that this document does not include a PRISMA study count or make any claim as to the results of a systematic review. The sections in question will only be added once the registered procedure has been completed.

Discussion

The purpose of this review is not to provide a general comparison of average success rates but to respond to a specific question. While observational studies can demonstrate that patients who were selected for single-stage reconstruction achieved good results, they alone cannot prove that the same patients would have had equally favourable outcomes if they had received staged treatment. On the other hand, poorer results in the groups that

received staged treatment might be due to a higher level of baseline complexity rather than being a result of the staging procedure. It is therefore necessary to identify the reasons for how patients were allocated to different treatments when interpreting the comparative results.

The protocol regards fixation, bone reconstruction and soft-tissue coverage as constituting separate timelines; in this way it does not classify a patient who has definite fixation and flap coverage at the index operation but who has planned grafting later in the same way as a patient who has temporary fixation while awaiting a later exchange. Moreover, it also ensures that an unplanned repeat debridement is not retrospectively re-coded as part of a staged approach.

The limitations expected to be present are heterogeneous terminology, an incomplete reporting of the treatment intention, an overlap between the FRI and chronic osteomyelitis cohorts, and confounding by indication. In many studies, the selection criteria are described only indirectly or only after the outcomes have been known. It should be possible to reduce, although not entirely eliminate, these limitations by limiting the primary synthesis to those factors which were explicitly stated as affecting allocation and by noting when each item became known.

Conclusion

This protocol defines a systematic approach to identifying how patients are selected for single-stage or staged reconstruction of unhealed long-bone fracture-related infection. The completed review will distinguish feasibility, prognosis and treatment-effect modification, while reporting treatment intention and the full reconstructive course. Its findings should support more transparent multidisciplinary decisions and better designed prospective comparative research.

Declarations

Funding: None.

Conflict of interest: No potential conflict of interest relevant to this article was reported.

Ethics approval: Not required because this systematic review protocol concerns published or publicly available aggregate literature and involves no human participants or identifiable patient data.

Data availability: Not applicable at the protocol stage.

Acknowledgements: None.

Use of artificial intelligence: ChatGPT assisted with drafting and document preparation. Human authors must design and execute the searches, independently screen studies, verify extracted data and references, perform the analyses, critically revise the manuscript and approve the final version. This disclosure should be adapted to the selected journal policy; AI tools are not authors.

Table 3 Operational screening rules

Is the population eligible?	Adults with unhealed appendicular long-bone FRI; subgroup data extractable.	Healed bone without reconstructive fixation, PJI, spine, Paediatric or primary prophylaxis only.
Is exchange reconstruction described	Definitive fixation is inserted at the infection operation or after planned temporary stabilization.	Implant retention only, removal after union or no reconstructive stabilization data.
Is selection information available?	A criterion, rationale, baseline factor, intraoperative finding or service factor relevant to strategy choice is reported.	Strategy is named but no information relevant to allocation can be identified.
Is the design eligible?	Trial, comparative cohort or case series with at least five eligible patients.	Case report, review, expert opinion or technical description without outcomes.

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