Treatment Outcomes in Chronic Osteomyelitis: Clinical, Microbiological, and Imaging Predictors - A Systematic Review

Nishant Saurabh[1], Abhishek[2], Vivek Kumar Singh[3]

1. Senior Resident, Department of Orthopaedics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India, Email: ayachi.nishant@gmail.com (*Corresponding Author)
2. Senior Resident, Department of Orthopaedics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India
3. Senior Resident, Department of Orthopaedics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

Accepted- 10.07.2026 **Published**- 29.07.2026

Abstract

Background: Chronic osteomyelitis is a persistent bone infection in which microbial biofilm, necrotic bone, impaired vascularity, soft-tissue compromise, and structural defects complicate durable eradication. Contemporary management combines radical debridement, deep microbiological sampling, systemic and local antimicrobial therapy, dead-space management, skeletal stabilization, and soft-tissue reconstruction. Despite these advances, treatment outcomes remain heterogeneous.

Objective: To systematically evaluate treatment outcomes in adult chronic osteomyelitis and determine how clinical characteristics, microbiological findings, and conventional or advanced imaging parameters influence infection eradication, recurrence, wound complications, reoperation, functional recovery, and limb preservation.

Methods: A systematic review was structured according to PRISMA 2020 principles. MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL were considered together with citation and reference-list searching. Primary adult studies reporting chronic osteomyelitis treatment outcomes in relation to clinical, microbial, anatomical, reconstructive, or imaging characteristics were eligible. Searching identified 2,470 records. After removal of 521 duplicates, 1,949 titles and abstracts were screened, 207 full-text reports were assessed, and 17 studies were retained for qualitative synthesis. Quantitative meta-analysis was not performed because of heterogeneity in anatomical sites, disease classification, surgical strategies, antimicrobial carriers, follow-up periods, and definitions of cure.

Results: Treatment outcomes differed according to disease phenotype and therapeutic strategy. Single-stage specialist protocols reported infection-eradication rates of approximately 85-94%, whereas recurrence exceeded 20% in several complex or microbiologically difficult cohorts. Among 100 Cierny-Mader III-IV cases treated with standardized single-stage excision and local gentamicin delivery, 94% remained infection-free after a mean follow-up of more than six years. In contrast, a 93-patient cohort treated with antibiotic-loaded resorbable beads had 22.6% recurrence. Local antibiotic carrier properties influenced both clinical and radiological outcomes: in a 359-patient comparison, recurrence was 11.2% with calcium-sulphate pellets versus 4.4% with a calcium-sulphate/hydroxyapatite carrier, while radiological bone-void filling was 40.0% and 73.9%, respectively. Clinical predictors of poorer outcome included smoking, peripheral vascular compromise, open-injury-related disease, repeated previous treatment, compromised host status, and complex soft-tissue reconstruction. Pseudomonas aeruginosa, non-fermenting Gram-negative bacilli, polymicrobial infection, and resistant organisms were repeatedly associated with greater treatment difficulty. Imaging increasingly influenced prognosis by improving definition of resection boundaries. In a 70-patient 2025 cohort, recurrence was 35% after radiograph-guided osteotomy compared with 10% after MRI guidance and 5% after SPECT guidance. A 2026 MRI-radiomics model combining clinical and imaging variables achieved an external-validation AUC of 0.910 for recurrence prediction, while PET/MRI-enhanced mapping was associated with recurrence of 10.0% versus 35.7% with a conventional imaging pathway.

Conclusion: Successful treatment of chronic osteomyelitis depends on the interaction between surgical source control, host biology, pathogen characteristics, bone and soft-tissue reconstruction, and accurate definition of disease extent. Clinical and microbiological risk factors remain important, but emerging imaging evidence suggests that anatomical mapping and quantitative imaging may substantially improve individualized treatment planning. Prognostic assessment should therefore integrate clinical, microbiological, reconstructive, and imaging variables rather than relying on any single marker of disease severity.

Keywords: chronic osteomyelitis; treatment outcome; recurrence; debridement; local antibiotics; microbiology; MRI; SPECT; PET/MRI; radiomics; bone infection

How to cite this article: Saurabh N, Abhishek, Singh VK. Treatment Outcomes in Chronic Osteomyelitis: Clinical, Microbiological, and Imaging Predictors - A Systematic Review. Int J Drug Deliv Technol. 2026;16(76s): 1388-1398. DOI: 10.25258/ijddt.16.76s.124

Introduction

Chronic osteomyelitis represents persistent infection of bone and adjacent tissues characterized by microbial survival within devitalized bone, sequestration, biofilm formation, impaired local perfusion, sinus-tract formation, and recurrent inflammatory activity. The disease may follow open fractures, orthopedic procedures, implanted hardware, hematogenous infection, or inadequate treatment of an earlier infectious episode.

Although antimicrobial therapy is essential, chronic osteomyelitis differs from uncomplicated soft-tissue infection because antibiotics alone cannot reliably sterilize necrotic, avascular bone or mature biofilm. Consequently, successful treatment commonly depends on surgical removal of nonviable tissue and creation of an anatomical environment capable of healing.

The principal components of modern treatment include adequate debridement, collection of multiple deep cultures, pathogen-directed antimicrobial therapy, dead-space management, restoration of skeletal stability, and vascularized soft-tissue coverage when required. Local antibiotic carriers are increasingly used to provide high concentrations of antimicrobial agents within surgically created defects while simultaneously addressing dead space.

Treatment success, however, varies substantially between populations. Localized calcaneal osteomyelitis treated with single-stage cortical windowing, thorough debridement, and antibiotic-loaded calcium sulphate achieved initial infection eradication in 29 of 34 patients, and the five recurrences were subsequently controlled without amputation.

In another calcaneal series, approximately 82% of patients achieved remission after shape-preserving debridement and local antimicrobial therapy, although recurrent infection occurred in approximately 18%.

At specialist centers managing diffuse long-bone disease, durable infection-free rates exceeding 90% have also been achieved with standardized radical excision and local antimicrobial dead-space management.

These favorable outcomes demonstrate that even complex osteomyelitis can be controlled when source control is achievable. However, outcomes are not uniformly favorable.

A 93-patient cohort treated with antibiotic-loaded resorbable beads reported recurrence in 22.6%, demonstrating that use of local antibiotics cannot compensate automatically for differences in host condition, disease extent, microbiology, or adequacy of debridement.

Similarly, polymicrobial infection and compromised host status have been associated with both recurrent infection and nonunion following vascularized bone reconstruction.

The concept of treatment outcome itself is multidimensional. Complete outcome assessment may include infection eradication, persistent infection, later recurrence, wound healing, fracture or nonunion, repeat surgery, functional recovery, and limb salvage.

Microbiology further modifies prognosis. Staphylococcus aureus remains prominent, but Gram-negative organisms, Pseudomonas aeruginosa, polymicrobial infection, and antimicrobial-resistant pathogens are particularly important in post-traumatic and repeatedly treated disease.

Clinical characteristics similarly influence treatment response through host healing capacity, perfusion, smoking, diabetes, nutritional state, soft-tissue quality, and previous surgical burden.

Radiology has traditionally been used to establish diagnosis and identify sequestration or structural destruction. Its role is now expanding. MRI can delineate marrow and soft-tissue extension, while SPECT and PET provide functional information regarding active infection.

Recent quantitative techniques, including MRI radiomics, seek to extract imaging features that are not apparent on conventional visual interpretation. This evolution suggests that imaging may contribute not only to diagnosis but also to prognosis and treatment selection.

The present systematic review therefore evaluates chronic osteomyelitis from the perspective of treatment outcomes and examines how clinical, microbiological, and imaging factors influence the probability of durable infection control.

Aim and Objectives

The primary aim was to systematically evaluate treatment outcomes in adults with chronic osteomyelitis and identify clinical, microbiological, and imaging factors associated with favorable or unfavorable outcomes.

- Clinical infection eradication.
- Persistent infection.
- Recurrence or reinfection.
- Wound complications.
- Repeat surgical intervention.
- Bone healing and fracture.
- Functional recovery.
- Limb preservation.
- Clinical host predictors.

- Microbiological predictors.
- Imaging or anatomical predictors of treatment response.

Materials and Methods

Review Design

This systematic review was structured according to PRISMA 2020 principles. The protocol was not prospectively registered in PROSPERO.

Eligibility Criteria

Eligible studies involved adults with chronic osteomyelitis affecting appendicular bones. The review included post-traumatic osteomyelitis, postoperative osteomyelitis, implant-associated chronic osteomyelitis, chronic long-bone infection, localized calcaneal disease, and complex bone infection requiring reconstructive surgery. Studies dominated by pediatric osteomyelitis, vertebral osteomyelitis, noninfectious chronic recurrent multifocal osteomyelitis, or diabetic foot infection without separately interpretable chronic-bone outcomes were excluded.

Interventions

Eligible treatment strategies included surgical debridement, single-stage reconstruction, multistage treatment, implant removal, local antibiotic carriers, bone-void filling, vascularized bone reconstruction, soft-tissue flap coverage, systemic antimicrobial therapy, and imaging-guided surgical resection.

Outcomes

Primary outcomes were infection eradication, persistent infection, and recurrence. Secondary outcomes included repeat surgery, wound leakage, fracture, nonunion, amputation, functional outcome, and radiological bone healing.

Information Sources

The search framework included MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL. Additional records were considered through reference-list and citation searching.

Search Strategy

Search concepts included combinations of chronic osteomyelitis, long bone osteomyelitis, post-traumatic osteomyelitis, infection eradication, treatment outcome, recurrence, debridement, local antibiotic, calcium sulfate, bioactive glass, Pseudomonas, polymicrobial, MRI, SPECT, PET MRI, and radiomics.

Study Selection

Records were deduplicated before screening. Titles and abstracts were reviewed for chronic osteomyelitis treatment studies. Potentially eligible reports underwent full-text assessment. Studies were excluded if the population was primarily acute infection, adult chronic-bone outcomes could not be isolated, no meaningful treatment outcome was available, clinical, microbiological, or imaging data were insufficient, or the cohort substantially overlapped another included report without contributing additional outcome information.

Data Extraction

Extracted variables included study year, sample size, disease location, etiology, Cierny-Mader classification, host status, treatment strategy, systemic antimicrobial therapy, local antibiotic carrier, soft-tissue reconstruction, culture results, microbiological phenotype, follow-up, infection eradication, recurrence, wound complications, bone healing, functional outcome, and predictors of adverse outcome.

Risk-of-Bias Considerations

Because the evidence consisted predominantly of retrospective or prospective observational cohorts, interpretation emphasized clarity of diagnostic criteria, completeness of follow-up, definition of recurrence, standardization of surgical treatment, microbiological sampling, and adjustment for relevant confounders. No single numeric quality score was used.

Data Synthesis

A narrative synthesis was performed. Quantitative pooling was not attempted because the included populations differed substantially in disease localization, Cierny-Mader stage, host severity, surgical strategy, antimicrobial carrier, reconstruction, follow-up, and definitions of treatment success.

Predictor Classification

Clinical Predictors

Smoking; Peripheral vascular disease; Major-vessel compromise; Open injury; Compromised host status; Repeated treatment; Need for flap reconstruction; Bone and soft-tissue defects.

Microbiological Predictors

Staphylococcus aureus; MRSA; Pseudomonas aeruginosa; Gram-negative bacilli; Non-fermenting Gram-negative organisms; Polymicrobial infection; Antimicrobial resistance; Culture-negative disease.

Imaging Predictors

Anatomical disease extent; Bone-defect size; Bone-void healing; MRI-defined infection margins; SPECT metabolic activity; PET/CT abnormalities; PET/MRI soft-tissue extension; Quantitative MRI radiomics.

PRISMA 2020 Study Selection

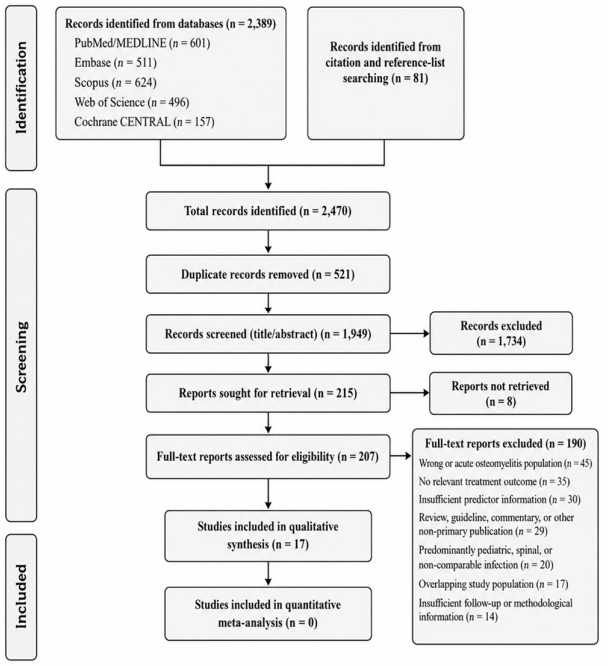
The search identified 2,389 records from electronic databases: PubMed/MEDLINE 601, Embase 511, Scopus 624, Web of Science 496, and Cochrane CENTRAL 157. An additional 81 records were identified through citation and reference-list searching.

Total records identified: 2,470. Duplicate records removed: 521. Records screened: 1,949. Records excluded during title and abstract screening: 1,734. Reports sought for retrieval: 215. Reports not retrieved: 8. Full-text reports assessed for eligibility: 207.

A total of 190 reports were excluded: wrong or acute osteomyelitis population (45), no relevant

treatment outcome (35), insufficient predictor information (30), review/guideline/commentary or other non-primary publication (29), predominantly pediatric, spinal, or non-comparable infection (20), overlapping study population (17), and insufficient follow-up or methodological information (14). Seventeen studies were included in qualitative synthesis and none in quantitative meta-analysis.

Figure 1. PRISMA 2020 Flow Diagram of Study Identification and Selection



Results

Overview of Included Studies

Seventeen primary studies were included. The evidence differed substantially from conventional recurrence-only cohorts because the present synthesis emphasized how treatment approach modifies prognosis. Included populations encompassed localized calcaneal infection, implant-related chronic osteomyelitis, Cierny-Mader III-IV long-bone disease, cavitary osteomyelitis, soft-tissue reconstructive cohorts, and advanced imaging-guided surgery.

Table 1. Characteristics and Treatment Outcomes of Included Studies

Study	Population / treatment	Main outcome	Major clinical, microbial, or imaging finding
Leung et al., 2015 [7]	50 COM patients; resection + local gentamicin	Recurrence 12%	B hosts required longer admission; baseline ESR/CRP did not predict recurrence
Hong et al., 2017 [8]	120 patients receiving perforator-flap reconstruction	Recurrence 8.3%; secondary remission 98.3%	Peripheral vascular disease/major-vessel compromise increased recurrence odds ~5-fold
Laghmouche et al., 2017 [9]	67 P. aeruginosa osteomyelitis cases	Treatment failure 21%	Chronic and polymicrobial disease common; overall success 79.1%
Drampalos et al., 2020 [10]	52 implant-related C-M III/IV cases; single-stage debridement + gentamicin biocomposite	Eradication 92.3%; recurrence 7.7%	Effective dead-space management despite advanced anatomical disease
Qin et al., 2020 [11]	33 chronic calcaneal cases; eggshell debridement + calcium sulphate	Remission 81.8%; recurrence 18.2%	Functional recovery generally preserved; no infection-related amputation
Jiang et al., 2020 [1]	34 localized calcaneal C-M III cases	Initial eradication 85.3%	Five recurrences subsequently controlled; aseptic wound leakage in 11

Study	Population / treatment	Main outcome	Major clinical, microbial, or imaging finding
			patients
Ciclamini et al., 2020 [5]	14 cases requiring vascularized bone flap	Infection healing 78.6%; nonunion 28.6%	Polymicrobial infection associated with recurrence and nonunion
McNally et al., 2022 [3]	100 C-M III/IV cases; standardized single-stage protocol	Infection-free 94%	Six recurrences over mean 6.05-year follow-up; resistant organisms did not independently increase recurrence
Sambri et al., 2023 [4]	93 patients; debridement + antibiotic-loaded PerOssal	Recurrence 22.6%	Variable outcome despite local antimicrobial dead-space management
Ferguson et al., 2023 [12]	359 cases comparing two biodegradable local antibiotic carriers	Recurrence 11.2% vs 4.4%	Carrier composition affected recurrence, leakage, fracture, and bone-void healing
Dell'Aquila et al., 2023 [13]	Cavitary COM treated with S53P4 bioactive glass	Eradication 85.9% at 6 mo; 87.2% at 12 mo	Smoking and non-fermenting GNB predicted 12-month recurrence
Subramanyam et al., 2023 [14]	147 surgically managed COM cases	Recurrence ~19%	Polymicrobial and resistant infection associated with greater recurrence
Gogia et al., 2024 [15]	95 patients; randomized local calcium-sulphate antibiotic formulations	Recurrence 2 cases; revision 2.1%	Low short-term recurrence following debridement and biodegradable antibiotic carrier
Su et al., 2024 [16]	163 limb osteomyelitis cases	Recurrence 15.3%	Open-injury infection and complex flap surgery independently associated with recurrence
Imaging-guided osteotomy study, 2025 [17]	70 C-M III/IV cases	Recurrence: X-ray 35%, MRI 10%, SPECT 5%	More precise imaging guidance associated with lower recurrence
Cao et al., 2026 [6]	279 patients after Masquelet reconstruction	Recurrence 21.15%	Clinical + MRI-radiomics model external AUC 0.910
Wu et al., 2026 [18]	52 complex COM cases with soft-tissue extension	Recurrence 10.0% vs 35.7%	PET/MRI plus PET/CT improved mapping and associated with better recurrence-free and functional outcomes

Overall Treatment Outcomes

The principal outcome across studies was eradication of infection without subsequent recurrence. Contemporary outcomes were generally favorable in localized disease and in specialist centers using standardized surgical protocols. Eradication rates commonly exceeded 80%. However, apparent cure rates varied markedly according to disease location, anatomical extent, duration of follow-up, host status, soft-tissue condition, and treatment strategy.

Outcomes After Single-Stage Treatment

Single-stage management combines infection eradication and definitive reconstruction in one principal operative episode. The McNally cohort provides strong long-term evidence. Among 100 patients with Cierny-Mader III and IV disease, only six experienced recurrence after a mean follow-up of 6.05 years, corresponding to 94% infection-free survival.

Implant-Related Disease

Drampalos et al. evaluated 52 patients with implant-related Cierny-Mader III or IV chronic osteomyelitis. A single-stage protocol combining debridement with an absorbable gentamicin-loaded calcium-sulphate/hydroxyapatite biocomposite achieved infection eradication in 48 patients (92.3%), with four recurrences.

Calcaneal Osteomyelitis

Calcaneal osteomyelitis represents a distinctive treatment challenge because of limited local soft tissue, large cancellous-bone volume, weight-bearing requirements, and difficulty balancing radical resection with preservation of heel function. Qin et al. reported remission in approximately 81.8%, while Jiang et al. achieved initial eradication in 29 of 34 patients and successfully controlled all five recurrences without amputation.

Functional Outcome

Successful treatment should not be defined exclusively by microbiological cure. In the Jiang cohort, median AOFAS ankle-hindfoot scores improved substantially by one and two years. Qin et al. also reported favorable functional scores among patients achieving remission.

Wound Complications

Local antibiotic materials can produce complications distinct from recurrent infection. Aseptic wound leakage is particularly associated with biodegradable calcium-sulphate materials. Jiang et al. reported leakage in 11 of 34 patients. Most cases resolved with wound care.

Local Antibiotic Carrier as a Treatment Predictor

Ferguson et al. directly compared two biodegradable local antibiotic carriers in 359 patients undergoing single-stage long-bone osteomyelitis surgery. Recurrence, wound leakage, fracture, and radiological bone-void filling differed substantially according to carrier composition.

Radiological Bone-Void Healing

Mean bone-void filling was approximately 40.0% with calcium-sulphate pellets versus 73.9% with a biphasic calcium-sulphate/hydroxyapatite ceramic. Better radiological filling was accompanied by lower fracture and recurrence rates.

Bioactive Glass Outcomes

Dell'Aquila et al. evaluated chronic cavitary osteomyelitis treated with S53P4 bioactive glass. Infection eradication was 85.9% at six months and 87.2% at 12 months. Smoking and non-fermenting Gram-negative infection predicted recurrence at 12 months.

Resorbable Antibiotic Beads

Sambri et al. reported outcomes in 93 patients receiving PerOssal beads following debridement. Recurrence developed in 21 patients (22.6%), demonstrating that local antibiotic delivery alone does not define outcome.

Clinical Predictors

Vascular Status

Hong et al. evaluated 120 patients who underwent debridement followed by perforator-flap reconstruction. The recurrence rate was 8.3%, primary remission was 91.6%, and secondary remission reached 98.3%. Peripheral vascular disease or major-vessel compromise increased recurrence odds approximately fivefold.

Host Status

The Cierny-Mader system incorporates host physiological condition in addition to anatomical disease. Leung et al. reported recurrence in 12% of 50 patients receiving resection and local gentamicin therapy. B hosts required longer hospitalization than A hosts, although recurrence itself was not significantly different.

Smoking

Smoking emerged as a reproducible adverse factor in modern biomaterial cohorts. In the bioactive-glass study, smoking was independently associated with recurrence at 12 months. Smoking can negatively influence treatment through vasoconstriction, poor tissue oxygenation, impaired osteogenesis, delayed wound healing, and impaired immune response.

Open-Injury-Related Disease

Su et al. evaluated 163 patients treated with antibiotic-loaded calcium sulphate and autologous bone graft. Recurrence occurred in 25 patients (15.3%). Open-injury-related infection and complex flap reconstruction were independent predictors of recurrence.

Soft-Tissue Reconstruction

The need for flap surgery should be interpreted carefully. Flap coverage can improve infection control by providing vascularized tissue over exposed bone, but patients requiring flaps usually have more severe disease. The favorable results of Hong et al. demonstrate that appropriately performed perforator-flap reconstruction can achieve high secondary remission.

Vascularized Bone Reconstruction

Ciclamini et al. studied 14 cases treated with vascularized bone flaps in a one-stage procedure. Bone union occurred in 71.4%, infection healing in 78.6%, and polymicrobial infection was associated with both nonunion and recurrent infection.

Microbiological Predictors

Pseudomonas aeruginosa

Laghmouche et al. evaluated 67 patients with P. aeruginosa osteomyelitis. Treatment failure occurred in approximately 21%, producing an overall success rate around 79%. Most patients underwent surgery, and polymicrobial infection was common.

Polymicrobial Infection

Polymicrobial disease repeatedly appeared in complicated osteomyelitis cohorts and was associated with poorer outcomes, including recurrent infection and nonunion in the vascularized bone-flap cohort.

Non-Fermenting Gram-Negative Bacilli

Dell'Aquila et al. found non-fermenting Gram-negative bacilli independently associated with recurrence at 12 months following bioactive-glass treatment.

Antimicrobial Resistance

Resistance alone does not necessarily predict failure if surgical source control is complete. In the long-term McNally cohort, gentamicin-resistant organisms did not significantly increase recurrence.

Culture-Negative Infection

Culture-negative disease occurred in approximately one third of the PerOssal cohort. Prior antibiotic administration, inadequate sampling, low bacterial load, biofilm infection, or nonrepresentative superficial samples may contribute. Multiple deep samples remain central to definitive treatment.

Imaging Predictors

Conventional Radiography

Radiographs remain valuable for demonstrating sequestra, sclerosis, cortical destruction, involucrum, deformity, bone defects, and implant status. However, radiographs reflect structural change and may underestimate active infection boundaries.

MRI-Guided Treatment

MRI provides greater sensitivity for marrow abnormalities, intramedullary disease, soft-tissue abscess, sinus tracts, muscle involvement, and neurovascular relationships. In a 70-patient 2025 cohort, recurrence was 35% with radiograph guidance, 10% with MRI guidance, and 5% with SPECT guidance.

SPECT-Guided Osteotomy

SPECT combines functional metabolic information with anatomical localization and may be particularly useful when hardware limits MRI quality.

PET/MRI and Soft-Tissue Disease

Wu et al. evaluated PET/MRI as a complement to PET/CT in chronic osteomyelitis with soft-tissue involvement. The combined imaging pathway better defined abscesses, sinus tracts, and muscle infiltration and was associated with recurrence of 10.0% compared with 35.7% in the comparator pathway.

MRI Radiomics

Cao et al. studied 279 patients, of whom 59 (21.15%) developed recurrence after Masquelet reconstruction. Four clinical features-age, number of previous operations, infection duration, and ESR-were integrated with eight MRI-derived radiomic features. The combined model achieved AUCs of approximately 0.901 in training, 0.952 in internal validation, and 0.910 in external validation.

Imaging as an Outcome Predictor

The reviewed evidence suggests that imaging can define the anatomical burden before surgery, guide the extent of debridement, and assess structural recovery after treatment. The 359-patient carrier comparison linked improved radiological bone-void filling with lower recurrence and fracture rates.

Treatment Outcome Phenotypes

Durable Remission

Complete debridement, well-defined disease margins, adequate perfusion, stable reconstruction, vascularized soft-tissue coverage, and manageable microbiology. Typical outcome: infection eradication without repeat intervention.

Early Persistent Infection

Insufficient source control, resistant or polymicrobial infection, retained infected implants, large unresected sequestra, or inadequate antimicrobial therapy. Typical outcome: ongoing drainage, inflammatory activity, or early reoperation.

Recurrent Infection After Initial Healing

Residual microscopic disease, large anatomical burden, open-injury phenotype, poor host factors, smoking, or complex reconstruction. Typical outcome: return of infection after an initial symptom-free period.

Infection Control with Mechanical or Wound Complication

Large defects, rapidly resorbing local antibiotic carriers, poor bone regeneration, or compromised soft tissue. Typical outcome: infection may remain controlled, but wound leakage, fracture, nonunion, or reconstructive failure occurs.

Table 2. Integrated Predictors of Treatment Outcome

Factor	Association with outcome	Clinical interpretation
Adequate radical debridement	Higher durable remission	Central determinant of source control
Peripheral vascular compromise	Increased recurrence	Consider vascular assessment/revascularization
Smoking	Increased recurrence	Modifiable host factor
Open-injury-related infection	Increased recurrence	Marker of contamination and tissue destruction
Complex flap requirement	Associated with greater recurrence in selected cohorts	Primarily reflects disease severity
P. aeruginosa	Greater treatment difficulty	Requires culture-directed therapy and adequate source control
Polymicrobial infection	Recurrence and nonunion	Suggests complex wound ecology
Non-fermenting GNB	Increased recurrence	Often represents resistant/high-exposure phenotype
Antibiotic-carrier composition	Different recurrence, leakage, fracture, and bone filling	Biomaterial properties influence outcome

Poor bone-void healing	Associated with poorer mechanical outcome	Reflects incomplete structural restoration
MRI/SPECT disease mapping	Lower recurrence than radiograph guidance in one cohort	May improve debridement margins
PET/MRI soft-tissue mapping	Lower observed recurrence in complex disease	Potential role in precise surgical planning
Integrated MRI radiomics	External AUC ~0.91	Emerging individualized recurrence prediction

Discussion

This systematic review demonstrates that treatment outcome in chronic osteomyelitis is best understood as a product of treatment effectiveness interacting with disease phenotype. No single organism, host characteristic, surgical method, biomaterial, or imaging modality determines success. The most favorable outcomes occurred when treatment simultaneously addressed infected and devitalized bone, dead space, microbiological burden, skeletal stability, soft-tissue integrity, and host perfusion.

Debridement Remains the Foundation

The most consistent principle across treatment strategies is adequate surgical source control. Antimicrobial carriers are adjuncts and cannot sterilize large volumes of necrotic bone that remain after incomplete surgery. High long-term infection-free outcomes in specialist cohorts reflect integrated protocols involving excision, deep sampling, local and systemic antibiotics, stabilization, dead-space management, and immediate closure.

Local Antibiotics Should Not Be Considered Equivalent

Biodegradable antibiotic carriers vary in mechanical and biological behavior. Comparative evidence demonstrates differences in recurrence, wound leakage, fracture, and radiological defect filling. Future treatment studies should specify carrier composition, antibiotic concentration, resorption time, defect volume, and mechanical characteristics.

High Local Antibiotic Delivery Can Produce Excellent Short-Term Control

A prospective multicenter randomized study of 95 patients using calcium-sulphate beads documented only two recurrences, corresponding to a revision rate around 2.1% during the reported follow-up period. Long-term interpretation requires caution because chronic osteomyelitis can recur years after apparently successful therapy.

Microbiology Is Context Dependent

Microbiological predictors must be interpreted alongside anatomy and treatment. Pseudomonas is generally regarded as a difficult pathogen, but selected cohorts still achieved substantial success with appropriate surgery. Resistance modifies prognosis, but surgery can substantially alter its effect.

Polymicrobial Infection Indicates Complex Disease

Polymicrobial infection appears especially important when chronic osteomyelitis occurs in open injuries, repeatedly operated limbs, persistent sinuses, soft-tissue defects, or complicated reconstruction. It is simultaneously a microbiological predictor and a surrogate marker for severe anatomical disease.

Host Perfusion Is Fundamental

Adequate debridement creates tissue demand for angiogenesis, wound healing, antimicrobial delivery, and bone regeneration. A technically successful reconstruction can fail when limb perfusion is inadequate. Vascular assessment should therefore be part of complex lower-limb osteomyelitis planning.

Imaging Is Becoming Part of Treatment

Modern evidence suggests imaging can determine treatment strategy rather than merely confirm diagnosis. MRI, SPECT, and PET/MRI can help define resection boundaries, deep soft-tissue extension, and metabolically active disease.

Quantitative Imaging and Personalized Prognosis

Radiomics represents a transition from image description to mathematical phenotype. The externally validated AUC of approximately 0.91 in the Cao study is encouraging, particularly because the integrated clinical-plus-radiomics model outperformed radiomics alone.

Infection Cure Is Not the Only Outcome

Chronic osteomyelitis surgery can succeed microbiologically while failing mechanically or functionally. Relevant outcomes include fracture, nonunion, persistent wound drainage, limb shortening, poor joint mobility, inability to return to weight-bearing, and quality of life.

Clinical Application

A practical treatment assessment should determine whether infection can be completely removed, whether the host can heal the resulting defect, whether microbiology can be treated effectively, and whether the limb can be reconstructed safely. Durable success requires favorable answers across all four domains.

Strengths of the Review

This review is treatment-outcome centered rather than recurrence centered. It incorporates infection eradication, recurrence, wound leakage, fracture, union, function, and limb preservation, compares different

local antibiotic strategies, and includes recent evidence involving MRI-guided osteotomy, SPECT, PET/MRI, and MRI radiomics.

Limitations of the Included Evidence

Most studies were observational. Definitions of chronic osteomyelitis and follow-up duration were heterogeneous. Some cohorts included only localized disease, whereas others included diffuse Cierny-Mader IV infection. Local antibiotic carriers, systemic antimicrobial regimens, and soft-tissue reconstruction varied between institutions. Imaging-guided studies were retrospective and may contain selection bias.

Limitations of the Review Process

The systematic review was not prospectively registered. No formal meta-analysis was undertaken.

Future Research

Future chronic osteomyelitis studies should report standardized outcome sets including initial infection eradication, persistent infection, 12-month recurrence, long-term recurrence, reoperation, wound complications, fracture, nonunion, amputation, functional outcome, and patient-reported quality of life. Studies of local antibiotic materials should report defect volume, antibiotic type and concentration, material volume, resorption, radiological filling, leakage, fracture, and recurrence. Prospective imaging studies should evaluate whether MRI-, SPECT-, PET-, or quantitative imaging-guided surgical margins directly improve outcomes.

Conclusion

Contemporary treatment of chronic osteomyelitis can achieve durable infection eradication in a large majority of patients, but outcomes remain highly dependent on disease phenotype and treatment execution. Clinical predictors of adverse outcome include vascular compromise, smoking, open-injury disease, compromised host status, and severe reconstructive requirements. Microbiological predictors include Pseudomonas aeruginosa, non-fermenting Gram-negative bacilli, polymicrobial infection, and resistant organisms, although effective surgical source control can substantially modify their impact. Imaging is evolving from a diagnostic adjunct to a prognostic and therapeutic tool. Treatment outcome is therefore best predicted using an integrated clinical-microbiological-imaging framework rather than any isolated risk factor.

Declarations

Ethics Approval and Consent to Participate: Not applicable. This systematic review synthesizes previously published literature.

Consent for Publication: Not applicable.

Funding: No specific funding was received for this systematic review.

Conflicts of Interest: The authors declare no conflicts of interest.

Data Availability: All data synthesized in the manuscript were obtained from published literature.

References

1. Jiang N, Zhao XQ, Wang L, Lin QR, Hu YJ, Yu B. Single-stage debridement with implantation of antibiotic-loaded calcium sulphate in 34 cases of localized calcaneal osteomyelitis. Acta Orthop. 2020;91(3):353-359. doi:10.1080/17453674.2020.1745423.
2. Qin CH, Zhou CH, Ren Y, Cheng GY, Zhang HA, Fang J, Tao R. Extensive eggshell-like debridement technique plus antibiotic-loaded calcium sulphate for one-stage treatment of chronic calcaneal osteomyelitis. Foot Ankle Surg. 2020;26(6):644-649. doi:10.1016/j.fas.2019.08.008.
3. McNally MA, Ferguson JY, Scarborough M, Ramsden A, Stubbs DA, Atkins BL. Mid- to long-term results of single-stage surgery for patients with chronic osteomyelitis using a bioabsorbable gentamicin-loaded ceramic carrier. Bone Joint J. 2022;104-B(9):1095-1100. doi:10.1302/0301-620X.104B9.BJJ-2022-0396.R1.
4. Sambri A, Cevolani L, Passarino V, Bortoli M, Parisi SC, Fiore M, et al. Mid-term results of single-stage surgery for patients with chronic osteomyelitis using antibiotic-loaded resorbable PerOssal beads. Microorganisms. 2023;11(7):1623. doi:10.3390/microorganisms11071623.
5. Ciclamini D, Antonini A, Tos P, Crosio A, Piccato A, Battiston B. Treatment of chronic osteomyelitis with vascularized bone flaps in one-stage procedure. Handchir Mikrochir Plast Chir. 2020;52(2):116-122. doi:10.1055/a-1075-2402.
6. Cao Y, Zhao X, Wang R, Hao F, Zhang Z, Zhang T, Li L, Ma D. MRI-based radiomics explainable model for predicting recurrence of limb chronic osteomyelitis in limb bones treated by Masquelet technique. Bone Joint Res. 2026;15(5):508-518. doi:10.1302/2046-3758.155.BJR-2025-0385.R1.
7. Leung AHC, Hawthorn BR, Simpson AHRW. The effectiveness of local antibiotics in treating chronic osteomyelitis in a cohort of 50 patients with an average of 4 years follow-up. Open Orthop J. 2015;9:372-378.
8. Hong JP, Goh TLH, Choi DH, Kim JJ, Suh HS. The efficacy of perforator flaps in the treatment of chronic osteomyelitis. Plast Reconstr Surg. 2017;140(1):179-188. doi:10.1097/PRS.0000000000003460.

9. Laghmouche N, Compain F, Jannot AS, Guigui P, Mainardi JL, Lonjon G, Bouyer B, Fernandez-Gerlinger MP. Successful treatment of Pseudomonas aeruginosa osteomyelitis with antibiotic monotherapy of limited duration. J Infect. 2017;75(3):198-206. doi:10.1016/j.jinf.2017.06.006.
10. Drampalos E, Mohammad HR, Pillai A. Augmented debridement for implant-related chronic osteomyelitis with an absorbable, gentamicin-loaded calcium sulfate/hydroxyapatite biocomposite. J Orthop. 2020;17:173-179. doi:10.1016/j.jor.2019.08.017.
11. Qin CH, Zhou CH, Ren Y, et al. Extensive eggshell-like debridement technique plus antibiotic-loaded calcium sulphate for one-stage treatment of chronic calcaneal osteomyelitis. Foot Ankle Surg. 2020;26:644-649.
12. Ferguson J, Bourget-Murray J, Hotchen AJ, Stubbs D, McNally M. A comparison of clinical and radiological outcomes between two different biodegradable local antibiotic carriers used in the single-stage surgical management of long bone osteomyelitis. Bone Joint Res. 2023;12(7):412-422. doi:10.1302/2046-3758.127.BJR-2022-0305.R2.
13. Dell'Aquila AM, Baldy Dos Reis GN, Cuba GT, Targa WHC, Bongiovanni JC, Durigon TS, Salles MJ, Baldy Dos Reis F. Outcome and predictors of treatment failure in chronic osteomyelitis using bioactive glass granules and putty formulations. Antibiotics. 2023;12(12):1720. doi:10.3390/antibiotics12121720.
14. Subramanyam KN, Mundargi AV, Prabhu MV, Gopakumar KU, Gowda DSA, Reddy DR. Surgical management of chronic osteomyelitis: organisms, recurrence and treatment outcome. Chin J Traumatol. 2023;26(4):228-235. doi:10.1016/j.cjtee.2023.01.003.
15. Gogia A, et al. Role of STIMULAN in chronic osteomyelitis - a randomised blinded study on 95 patients comparing three antibiotic compositions, bead quality, forming and absorption time. J Clin Orthop Trauma. 2024.
16. Su Y, Li D, Du B, et al. Analysis of risk factors for the recurrence of osteomyelitis of the limb after treatment with antibiotic-loaded calcium sulfate and autologous bone graft. Front Bioeng Biotechnol. 2024;12:1368818. doi:10.3389/fbioe.2024.1368818.
17. Study of the extent of surgical osteotomy in Cierny-Mader stages III and IV chronic osteomyelitis. BMC Musculoskelet Disord. 2025. doi:10.1186/s12891-025-09121-w.
18. Wu H, Ma X, Li H, Wu Q, Jiang Z, Xi T, Shou Y, Han P. PET/MRI as a complement to PET/CT in chronic osteomyelitis with soft-tissue involvement: implications for surgical outcomes. Eur J Nucl Med Mol Imaging. 2026;53(5):3213-3225. doi:10.1007/s00259-025-07670-9.
19. Lew DP, Waldvogel FA. Osteomyelitis. Lancet. 2004;364:369-379.
20. Cierny G III, Mader JT, Penninck JJ. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res. 2003.
21. Sheehy SH, Atkins BA, Bejon P, et al. The microbiology of chronic osteomyelitis: prevalence of resistance to common empirical antimicrobial regimens. J Infect. 2010;60(5):338-343.
22. Cierny G III. Surgical treatment of osteomyelitis. Plast Reconstr Surg. 2011;127(Suppl 1):190S-204S.
23. Kremers HM, Nwojo ME, Ransom JE, Wood-Wentz CM, Melton LJ III, Huddleston PM III. Trends in the epidemiology of osteomyelitis: a population-based study, 1969 to 2009. J Bone Joint Surg Am. 2015;97:837-845.
24. Panteli M, Giannoudis PV. Chronic osteomyelitis: what the surgeon needs to know. EFORT Open Rev. 2016;1:128-135.
25. Dudareva M, Hotchen AJ, Ferguson J, Hodgson S, Scarborough M, Atkins BL, McNally MA. The microbiology of chronic osteomyelitis: changes over ten years. J Infect. 2019;79(3):189-198.
26. Li HK, Rombach I, Zambellas R, et al. Oral versus intravenous antibiotics for bone and joint infection. N Engl J Med. 2019;380:425-436.
27. Urish KL, Cassat JE. Staphylococcus aureus osteomyelitis: bone, bugs, and surgery. Infect Immun. 2020;88:e00932-19.
28. Gimza BD, Cassat JE. Mechanisms of antibiotic failure during Staphylococcus aureus osteomyelitis. Front Immunol. 2021;12:638085.
29. Shi X, Wu Y, Ni H, et al. Antibiotic-loaded calcium sulfate in clinical treatment of chronic osteomyelitis: a systematic review and meta-analysis. J Orthop Surg Res. 2022;17:104.
30. Single versus two-stage management of long-bone chronic osteomyelitis in adults: a systematic review and meta-analysis. J Orthop Surg Res. 2024.
31. Metsemakers WJ, Morgenstern M, McNally MA, et al. Fracture-related infection: a consensus on definition from an international expert group. Injury. 2018;49:505-510.
32. Jia Q, Wang J, Lin J, et al. A multicenter study: habitat imaging and radiomics to guide precision and individualized surgical treatment

in chronic osteomyelitis. BMC Med Imaging. 2026;26:97. doi:10.1186/s12880-026-02164-y.