RESEARCH PAPER

Recurrence and Treatment Failure in Chronic Osteomyelitis: Clinical, Microbiological, and Anatomical Predictors - A Systematic Review

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Abstract

Background: Chronic osteomyelitis remains prone to persistence and recurrence despite advances in surgical debridement, antimicrobial treatment, local antibiotic delivery, bone reconstruction, and soft-tissue coverage. Failure is rarely explained by a single factor. Host vulnerability, repeated previous treatment, microbial phenotype, bone loss, vascular compromise, and the feasibility of achieving complete source control interact to determine long-term outcome.

Objective: To systematically evaluate clinical, microbiological, and anatomical predictors of persistent infection, recurrence, reoperation, reconstructive failure, and amputation in adults treated for chronic osteomyelitis.

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 reference-list and citation searching. Eligible primary studies evaluated adults with chronic appendicular osteomyelitis, post-traumatic osteomyelitis, implant-associated infection, infected nonunion, or chronic limb osteomyelitis and reported treatment failure or recurrence in relation to identifiable predictors. Search identified 3,214 records. After removal of 706 duplicates, 2,508 records underwent title and abstract screening. Full texts of 259 reports were assessed, and 22 studies were retained for qualitative synthesis. Meta-analysis was not undertaken because of substantial heterogeneity in disease definition, reconstruction technique, microbiology, follow-up, and definitions of failure.

Results: Recurrence ranged from approximately 6% in standardized specialist-center single-stage cohorts to 45.5% in a 2026 multicenter cohort involving staged management of large bone defects. In a 424-patient induced-membrane cohort, recurrence occurred in 12.26%; at least three previous operations, post-traumatic etiology, and internal fixation during the first stage independently increased recurrence risk. In a 314-patient limb osteomyelitis cohort, recurrence was 16.9%, with segmental bone defects, smoking, and Gram-negative bacilli independently associated with recurrence. Post-traumatic tibial osteomyelitis treated with bone transport showed an 11.4% recurrence/reinfection rate; Pseudomonas aeruginosa, exposed bone, and more than three previous operations were independent predictors. Vascular compromise increased recurrence odds approximately fivefold in a 120-patient reconstructive cohort. Microbiologically, P. aeruginosa, Gram-negative bacilli, polymicrobial growth, ESBL-producing Enterobacteriaceae, and multidrug resistance were associated with unfavorable outcomes. MRSA primarily increased persistent infection rather than subsequent recurrence, with an adjusted odds ratio of 2.26 for persistence among 482 patients with S. aureus osteomyelitis. Large defects increased treatment complexity substantially; however, standardized reconstruction could mitigate anatomical risk.

Conclusion: Recurrence in chronic osteomyelitis is best predicted by the accumulation of risk across three domains: compromised host and treatment history, difficult microbiology, and anatomical/reconstructive complexity. Smoking, vascular compromise, repeated previous operations, exposed bone, post-traumatic disease, segmental defects, internal fixation in active infection, Gram-negative organisms, P. aeruginosa, and polymicrobial or resistant infection identify higher-risk patients. Anatomical severity is not synonymous with inevitable failure when complete source control and appropriate reconstruction are achievable. Multidimensional preoperative risk assessment should therefore guide debridement, microbiological sampling, reconstruction, antimicrobial planning, and duration of follow-up.

Keywords: chronic osteomyelitis; recurrence; treatment failure; post-traumatic osteomyelitis; Pseudomonas aeruginosa; Gram-negative bacilli; MRSA; bone defect; smoking; vascular compromise; systematic review

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Introduction

Chronic osteomyelitis is a persistent infection of bone and surrounding tissues characterized by microbial biofilm, necrotic or avascular bone, sequestration, chronic inflammation, sinus formation, and variable destruction of the bone and soft-tissue envelope.

Treatment can require repeated operations over months or years. Definitive management commonly incorporates radical removal of infected and necrotic tissue, multiple deep microbiological samples, targeted antimicrobial therapy, management of bone and soft-tissue dead space, stable skeletal fixation, and reconstruction of both bone and soft tissue when required.

Even after apparently successful treatment, recurrent infection remains an important problem. Recurrence is particularly difficult to evaluate because published studies frequently use different terminology. Some define failure as persistent drainage or positive cultures after initial treatment. Others define recurrence as a new clinical episode after a period of infection-free survival. Still others combine persistent infection, reoperation, reinfection, amputation, or nonunion into a composite treatment-failure endpoint.

The biology of recurrence is also heterogeneous. Residual infected sequestra may result in true relapse. A previously contaminated limb may develop reinfection with a different organism. Implants can support persistent biofilm. Large debridement defects can become mechanically unstable or poorly vascularized. Soft-tissue breakdown can expose bone to renewed contamination.

Large observational cohorts illustrate this complexity. A Brazilian cohort of 192 treated patients with chronic post-traumatic osteomyelitis reported treatment failure in 20%. Advanced age, intraoperative transfusion, and Pseudomonas aeruginosa independently predicted failure.

A later cohort of 424 patients treated using an induced-membrane strategy demonstrated recurrence in 12.26%, with repeated previous operations, post-traumatic disease, and internal fixation during the first stage emerging as independent predictors.

Microbiology provides another prognostic dimension. Staphylococcus aureus remains a major pathogen, but methicillin resistance appears to influence persistent infection more strongly than late recurrence. Gram-negative organisms, particularly P. aeruginosa, are more consistently associated with unfavorable outcomes.

Anatomical complexity is similarly difficult to interpret in isolation. Segmental bone defects strongly increase recurrence in some treatment settings. Large staged defects may be associated with high reinfection and revision rates. Yet specialist-center experience demonstrates that even diffuse Cierny-Mader disease can achieve excellent infection control when debridement and reconstruction are performed systematically.

The present systematic review focuses specifically on recurrence and treatment failure and evaluates how clinical, microbiological, and anatomical factors interact to influence long-term outcome.

Aim and Objectives

The primary aim was to systematically identify predictors of treatment failure and recurrence among adults with chronic osteomyelitis.

- Persistent infection following initial treatment.
- Recurrence after a period of apparent cure.
- Reinfection.
- Repeat surgical debridement.
- Amputation.
- Nonunion and reconstructive failure.
- Host and treatment-history factors.
- Microbiological predictors.
- Anatomical predictors of adverse outcome.
- Distinguishing biological risk from source-control difficulty.

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 adult patients with chronic long-bone osteomyelitis, chronic post-traumatic osteomyelitis, postoperative chronic osteomyelitis, implant-associated chronic bone infection, infected nonunion, or complex chronic appendicular osteomyelitis requiring reconstructive surgery. Studies focused primarily on pediatric disease, vertebral osteomyelitis, acute hematogenous osteomyelitis, chronic nonbacterial osteomyelitis, or diabetic-foot infection without separately identifiable chronic bone outcomes were excluded.

Outcomes

Primary outcomes were persistent infection, recurrence, reinfection, and treatment failure. Secondary outcomes included repeat debridement, revision reconstruction, nonunion, amputation, and failure to achieve an infection-free reconstructed limb.

Outcome Definitions

Persistent infection was defined as failure to achieve initial eradication after definitive treatment. Recurrence was defined as renewed infection following an interval in which infection was considered clinically controlled. Reinfection referred to a subsequent episode involving a newly identified microbiological phenotype where clearly reported. Treatment failure represented a broader composite outcome that could include persistent infection, recurrence, unplanned reoperation for infection, or amputation.

Information Sources

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

Search Strategy

Search terms included combinations of chronic osteomyelitis, post-traumatic osteomyelitis, limb osteomyelitis, infected nonunion, recurrence, reinfection, persistent infection, treatment failure, risk factors, predictors, Pseudomonas, MRSA, polymicrobial, bone exposure, segmental defect, internal fixation, vascular compromise, and Cierny-Mader.

Study Selection

Records were combined and duplicates removed. Titles and abstracts were screened for adult chronic osteomyelitis studies. Potentially relevant reports underwent full-text review. Reports were excluded when the infection was acute or anatomically non-comparable, no treatment-failure

endpoint was reported, no prognostic factor could be extracted, follow-up was inadequate, or the cohort substantially duplicated another included study.

Data Extraction

Data extracted from eligible studies included study design, sample size, infection site, etiology, previous surgery, host comorbidity, smoking, vascular status, bone exposure, soft-tissue status, Cierny-Mader stage, bone-defect dimensions, reconstructive strategy, microbiology, antimicrobial resistance, treatment approach, follow-up duration, recurrence, persistent infection, reoperation, amputation, and adjusted predictors where available.

Risk-of-Bias Considerations

Interpretation focused on clarity of the chronic osteomyelitis definition, completeness of follow-up, definition of treatment failure, microbiological sampling methodology, standardization of surgery, and adjustment for confounding variables. Given the observational nature of the evidence and substantial variation between cohorts, a single pooled risk-of-bias score was not used for data synthesis.

Data Synthesis

A structured narrative synthesis was undertaken. Meta-analysis was not performed because studies differed substantially in etiology, anatomical site, disease severity, reconstructive method, microbiology, follow-up, and definitions of recurrence or failure.

Predictor Classification

Clinical Predictors

Age; Smoking; Vascular compromise; Systemic host status; Previous failed surgery; Number of previous operations; Intraoperative transfusion; Post-traumatic etiology; Open-injury-related infection.

Microbiological Predictors

Pseudomonas aeruginosa; Other Gram-negative bacilli; MRSA; Polymicrobial infection; ESBL-producing Enterobacteriaceae; Multidrug-resistant organisms; Culture-negative disease.

Anatomical and Reconstructive Predictors

Tibial involvement; Exposed bone; Sinus formation; Segmental defect; Critical-sized bone defect; Diffuse corticomedullary disease; Internal fixation in active infection; Nonunion; Soft-tissue defects; Need for flap reconstruction; Large reconstruction volume.

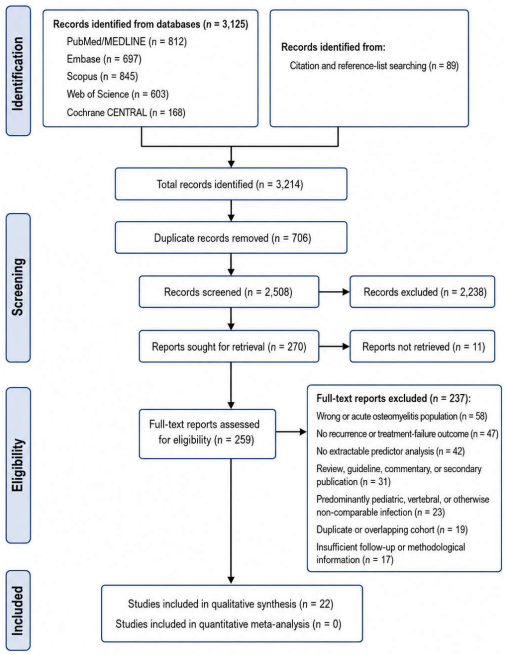
PRISMA 2020 Study Selection

The search identified 3,125 records from databases: PubMed/MEDLINE 812, Embase 697, Scopus 845, Web of Science 603, and Cochrane CENTRAL 168. An additional 89 records were identified through citation and reference-list searching.

Total records identified: 3,214. Duplicate records removed: 706. Records screened: 2,508. Records excluded after title and abstract screening: 2,238. Reports sought for retrieval: 270. Reports not retrieved: 11. Full-text reports assessed for eligibility: 259.

A total of 237 reports were excluded: wrong or acute osteomyelitis population (58), no recurrence or treatment-failure outcome (47), no extractable predictor analysis (42), review/guideline/commentary or secondary publication (31), predominantly pediatric, vertebral, or otherwise non-comparable infection (23), duplicate or overlapping cohort (19), and insufficient follow-up or methodological information (17). Twenty-two studies were included in qualitative synthesis and none in quantitative meta-analysis.

Figure 1. PRISMA 2020 flow diagram of study identification and selection



Results

Characteristics of Included Studies

Twenty-two primary studies contributed to the synthesis. Cohort sizes ranged from 14 patients undergoing vascularized bone reconstruction to more than 480 patients with organism-specific extremity osteomyelitis. The evidence covered post-traumatic chronic osteomyelitis, large bone-defect reconstruction, specialist-center single-stage treatment, and microbiologically difficult chronic infection

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Table 1. Included Studies and Major Predictors of Recurrence or Failure

Study	Population	Failure/recurrence outcome	Major predictor findings
Tice et al., 2003	454 osteomyelitis patients	Recurrence ~30%	P. aeruginosa associated with substantially greater recurrence
Kinik & Karaduman, 2008	26 Cierny-Mader III patients	3 initial recurrences	Recurrent cases attributed principally to inadequate debridement
Leung et al., 2015	50 chronic osteomyelitis patients	Recurrence 12%	B-host status prolonged admission but did not independently predict recurrence
Hong et al., 2017	120 patients requiring perforator-flap coverage	Recurrence 8.3%	Peripheral vascular disease/major vessel compromise increased recurrence odds ~5-fold
Jorge et al., 2017	192 treated post-traumatic cases	Failure 20%	Age 61-80 yr HR 6.09; >80 yr HR 9.98; transfusion HR 2.24; P. aeruginosa HR 2.70
Laghmouche et al., 2017	67 pseudomonal osteomyelitis cases	Failure 21%	Chronic and polymicrobial disease common; organism required intensive source control
Wang et al., 2020	424 extremity cases treated by induced-membrane technique	Recurrence 12.26%	>=3 previous operations OR 2.30; post-traumatic disease OR 5.53; first-stage internal fixation OR 5.28
Drampalos et al., 2020	52 implant-related C-M III/IV cases	Recurrence 7.7%	High anatomical complexity controlled with standardized debridement and dead-space management
Ciclamini et al., 2020	14 vascularized bone-flap reconstructions	Infection recurrence 21.4%	Polymicrobial infection associated with recurrence and nonunion
Yalikun et al., 2021	149 post-traumatic tibial cases	Recurrence/reinfection 11.4%	P. aeruginosa OR 6.06; bone exposure OR 7.41; >3 previous operations OR 1.75
McNally et al., 2022	100 C-M III/IV cases	Recurrence 6%	Host class, etiology, organism, and gentamicin resistance not independently associated with recurrence under standardized source control
Subramanyam et al., 2023	147 chronic osteomyelitis patients	Recurrence 19%	Polymicrobial growth and ESBL/MDR organisms increased recurrence
Wu et al., 2023 - ALCS cohort	314 limb cases	Recurrence 16.9%	Segmental defect OR 5.25; smoking OR 3.00; Gram-negative infection OR 2.38
Wu et al., 2023 - S. aureus cohort	482 cases	Persistence 13.7%; recurrence 8.5%	MRSA increased persistent infection OR 2.26 but did not significantly increase later recurrence
Dell'Aquila et al., 2023	92 patients at 6 mo; 78 at 12 mo	Recurrence after bioactive glass	Smoking PR 4.0 and non-fermenting GNB PR 3.87 at 12 months
Su et al., 2024	163 limb osteomyelitis patients	Recurrence 15.3%	Open-injury disease and complex flap-associated cases had markedly higher recurrence
Tsang et al., 2024	83 C-M IV cases	Recurrence 4/83 overall	Critical defect prolonged union but did not independently worsen infection eradication using standardized

Study	Population	Failure/recurrence outcome	Major predictor findings
			reconstruction
Imaging-guided osteotomy cohort, 2025	70 C-M III/IV cases	Recurrence varied by margin strategy	Importance of accurate anatomical delineation of infected bone
Armbruster et al., 2026	101 staged large-defect osteomyelitis/nonunion cases	Reinfection 45.5%; revision 58.4%	Larger defects and larger implanted biocomposite volumes predicted failure
Cao et al., 2026	279 Masquelet-treated patients	Recurrence 21.15%	Age, previous surgery, infection duration, and imaging-derived features contributed to recurrence model
Wu et al., 2026	52 complex bone-soft-tissue infections	Recurrence differed by preoperative mapping	Greater anatomical definition associated with reduced recurrence
Contemporary orthoplastic cohorts	Chronic bone infection with soft-tissue reconstruction	Infection resolution >90% in selected cohorts	Anatomical risk can be modified by coordinated source control and reconstruction

Recurrence Patterns

Recurrence rates varied considerably. Low recurrence was reported in selected standardized single-stage cohorts. Higher recurrence occurred in post-traumatic disease, large defects, patients requiring multiple previous operations, poorly vascularized limbs, and microbiologically difficult infection. These differences support the interpretation that recurrence should be viewed as a risk accumulation phenomenon.

Clinical Predictors

Previous Operations

Repeated previous surgery was one of the most consistent clinical predictors. In the 424-patient induced-membrane cohort, having undergone three or more previous operations independently increased recurrence risk (OR 2.30). Repeated procedures can create soft-tissue scarring, vascular damage, bone loss, residual biofilm, implant exposure, and increasingly complex reconstructive requirements.

Post-Traumatic Etiology

In the induced-membrane cohort, post-traumatic osteomyelitis had a substantially greater recurrence risk than hematogenous disease (OR 5.53). Post-traumatic disease combines initial contamination, devitalized bone, open soft-tissue injury, implants, scarred tissue, and repeated surgical intervention.

Age and Physiological Reserve

Age was an important predictor in the Brazilian post-traumatic cohort. Age 61-80 years was associated with HR 6.09 and age above 80 years with HR 9.98 compared with younger adults. Age likely represents interaction with vascular disease, frailty, poor nutrition, renal impairment, diabetes, and diminished wound-healing capacity.

Smoking

Smoking is among the most consistently modifiable factors. Wu et al. reported an independent threefold increase in recurrence (OR 3.00). Dell'Aquila et al. similarly found smoking associated with approximately fourfold greater recurrence risk at 12 months.

Vascular Compromise

Hong et al. studied 120 patients undergoing debridement and perforator-flap reconstruction. Peripheral vascular disease or major vessel compromise increased recurrence odds approximately 5.1-fold. Vascular compromise is particularly important because antimicrobial delivery, soft-tissue healing, bone regeneration, flap survival, and immune function all depend on blood supply.

Intraoperative Transfusion

The Brazilian cohort identified intraoperative transfusion as an independent predictor (HR 2.24). This association may be a surrogate for greater operative blood loss, more radical surgery, advanced anatomical disease, or reduced physiological reserve.

Microbiological Predictors

Pseudomonas aeruginosa

P. aeruginosa was one of the most reproducible adverse microbial predictors. In the Brazilian cohort HR was 2.70 for treatment failure; in the 149-patient bone-transport cohort OR was 6.06 for recurrence or reinfection. In the induced-membrane cohort, recurrence among patients with P. aeruginosa isolated at the initial stage was approximately 28%.

Gram-Negative Bacilli

Gram-negative infection more broadly was independently associated with recurrence. In the 314-patient limb cohort, the OR was 2.38 compared with S. aureus infection. Non-fermenting Gram-negative bacilli also increased recurrence in the bioactive-glass cohort.

MRSA and Persistent Infection

Among 482 patients with S. aureus extremity osteomyelitis, MRSA independently increased the likelihood of persistent infection (OR 2.26) but did not significantly increase recurrence after initial infection eradication. This suggests methicillin resistance may primarily affect early eradication rather than late relapse.

Polymicrobial Infection

Polymicrobial infection repeatedly marked difficult disease. It was associated with recurrence in a 147-patient cohort and with both recurrent infection and nonunion following vascularized bone reconstruction. It may indicate greater original contamination, chronic sinus tracts, repeated surgery, large tissue defects, and previous healthcare exposure.

ESBL and Multidrug-Resistant Organisms

ESBL-producing Enterobacteriaceae and multidrug-resistant infection were adverse prognostic features in contemporary cohorts. Resistance can contribute through delayed effective treatment, reduced availability of oral antibiotics, greater treatment toxicity, and increased healthcare exposure.

Culture Concordance and Reinfection

Only limited concordance has been reported between organisms cultured at the index procedure and organisms identified at recurrence. This suggests that some apparent recurrences may represent reinfection rather than persistence and reinforces the importance of obtaining fresh deep cultures whenever chronic osteomyelitis reappears.

Anatomical Predictors

Bone Exposure

Bone exposure was one of the strongest predictors identified in post-traumatic tibial osteomyelitis (OR 7.41). Exposed bone implies loss of the biological soft-tissue envelope, reduced vascular support, ongoing environmental contamination, poor wound healing, and increased need for flap coverage.

Tibial Osteomyelitis

The tibia is disproportionately represented in recurrent post-traumatic osteomyelitis because of limited anteromedial soft-tissue coverage, a high frequency of open fractures, vascular injury after severe trauma, and frequent need for complex reconstruction.

Segmental Bone Defects

Segmental bone loss was a powerful independent predictor in the 314-patient cohort (OR 5.25; 95% CI 1.80-15.26). Large defects create dead space, instability, reduced vascularity, a need for staged reconstruction, and increased treatment duration.

Large Defects and Staged Reconstruction

A 2026 multicenter cohort involving 101 patients with large bone defects reported treatment success of 30.7%, revision of 58.4%, and reinfection of 45.5%. Larger bone defects and larger volumes of implanted material significantly increased failure risk.

Critical Bone Defects

Critical defects substantially prolong reconstruction but do not inevitably reduce infection eradication when standardized treatment is used. In a Cierny-Mader type-IV cohort, critical bone defects prolonged union but did not significantly worsen infection eradication.

Internal Fixation During Active Infection

Internal fixation during the first stage of induced-membrane treatment independently increased recurrence risk (OR 5.28). Stable fixation can be essential, but hardware placed within incompletely eradicated infection can provide a surface for biofilm persistence.

Sinus Tracts

Chronic sinus formation reflects communication between infected bone and the external environment and may indicate persistent sequestration, mixed microbial colonization, soft-tissue failure, or uncontrolled dead space.

Soft-Tissue Reconstruction

The need for flap reconstruction is frequently associated with severe underlying disease. Flap requirement is better considered a marker of anatomical complexity than a cause of recurrence, because well-performed vascularized coverage can substantially improve final infection control.

Cierny-Mader Classification

The Cierny-Mader system remains useful for planning treatment burden but should not be interpreted deterministically. Specialist-center evidence shows high infection-free rates even among Cierny-Mader III-IV patients when debridement and reconstruction are standardized.

Persistence Versus Recurrence

Predictors differ according to the phase of treatment. Early persistence is particularly associated with MRSA, incomplete debridement, retained infected implants, inadequate antimicrobial coverage, and severe active infection. Later recurrence is more consistently associated with smoking, vascular compromise, bone exposure, large defects, post-traumatic disease, previous failed operations, and Gram-negative infection.

Timing of Recurrence

Recurrence can occur long after apparent cure. Long-term specialist-center data include recurrences during the first and second years and as late as 4.5 years

after treatment. One-year follow-up may therefore underestimate long-term recurrence.

Interaction Between Predictor Domains

The strongest risk likely occurs when adverse factors cluster. A smoker with poor limb perfusion, post-traumatic tibial infection, several previous operations, exposed bone, a segmental defect, and polymicrobial Gram-negative infection has several independent mechanisms promoting failure. Risk assessment should therefore focus on combinations of predictors, not isolated variables.

Domain	Lower-risk features	Higher-risk features
Host	Non-smoker, good perfusion, physiologically fit	Smoking, vascular compromise, frailty
Treatment history	First definitive procedure	Multiple previous failed operations
Etiology	Hematogenous/localized	Post-traumatic/open-injury infection
Soft tissue	Intact vascularized envelope	Exposed bone, sinus, flap requirement
Microbiology	Single susceptible Gram-positive organism	Pseudomonas, GNB, polymicrobial, MDR/ESBL
Anatomy	Localized disease without segmental defect	Tibial disease, diffuse corticomedullary involvement, segmental defect
Fixation/reconstruction	Stable reconstructable defect with adequate source control	Large staged reconstruction or fixation in inadequately controlled infection
Source control	Complete debridement achievable	Residual sequestration or uncertain margins

Treatment as a Modifier of Prognosis

Risk factors do not determine outcome independently of treatment. Some predictors identify patients requiring more treatment rather than patients in whom treatment is unlikely to succeed. Standardized debridement, appropriate stabilization, local and systemic antimicrobial treatment, dead-space management, and vascularized reconstruction can substantially modify high-risk anatomy and microbiology.

Table 2. Integrated Recurrence-Risk Framework

Discussion

This systematic review demonstrates that recurrence and treatment failure in chronic osteomyelitis reflect the cumulative effect of host and treatment history, microbial phenotype, and anatomical/reconstructive complexity. The most consistent clinical predictors included repeated previous operations, post-traumatic etiology, smoking, vascular compromise, advanced age in selected cohorts, and intraoperative transfusion. The strongest microbiological signals included Pseudomonas aeruginosa, other Gram-negative bacilli, polymicrobial infection, ESBL-producing organisms, and multidrug resistance. Anatomical predictors included bone exposure, segmental defects, tibial location, large reconstruction defects, soft-tissue compromise, and fixation within an incompletely controlled infection.

Previous Failed Treatment Is a Major Warning Sign

Repeated operations appear in several independent datasets and likely reflect more than simple treatment exposure. Each failed operation can lead to additional scar formation, further vascular injury, additional bone removal, greater implant exposure, and microbial selection pressure.

Anatomy Determines the Difficulty of Source Control

The largest anatomical effect estimates were observed for bone exposure and segmental defects. When debridement creates a segmental defect with associated soft-tissue loss, treatment becomes a combined infection, reconstruction, vascular, and mechanical problem.

Microbiology Cannot Be Considered in Isolation

The strong association between Pseudomonas and recurrence has been reproduced across several populations, but Pseudomonas also disproportionately occurs in contaminated trauma, previously treated wounds, and complex healthcare-associated infection. The organism may represent both a biological pathogen effect and a marker of difficult underlying anatomy.

MRSA Primarily Predicts Persistence

MRSA increased the probability that initial treatment failed to clear infection but did not significantly increase late recurrence after successful eradication. Future studies should distinguish failure to achieve cure from loss of cure after an infection-free period.

Baseline Inflammatory Markers Are Less Informative

Several cohorts found that presentation CRP, ESR, white cell count, and hemoglobin did not independently predict recurrence. These biomarkers remain useful for diagnosis and monitoring but provide less prognostic information than treatment history, microbiology, vascularity, or structural anatomy.

Clinical Implications

The evidence supports comprehensive preoperative risk assessment incorporating host status, number of previous operations, vascularity, deep microbiology, antimicrobial susceptibility, bone exposure, defect size, soft-tissue status, fixation requirements, and reconstructive feasibility.

Proposed Management Principles for High-Risk Patients

Patients with multiple recurrence predictors should be considered for treatment in experienced multidisciplinary bone-infection units. Management should emphasize aggressive but anatomically appropriate debridement, multiple deep tissue cultures, culture-directed antimicrobial therapy, vascular assessment and optimization, smoking cessation, stable skeletal reconstruction, adequate dead-space management, and early soft-tissue reconstruction.

Strengths of the Review

This review focuses specifically on recurrence and failure rather than general treatment success. It distinguishes persistent infection, recurrence, and reinfection and integrates patient, microbial, and anatomical variables across large contemporary cohorts.

Limitations of the Included Evidence

Most studies were retrospective. Definitions of recurrence varied. Some cohorts included chronic osteomyelitis together with septic nonunion. Surgical techniques and antimicrobial strategies differed, several cohorts originated from specialist referral centers, and some factors may represent disease severity rather than direct causal mechanisms.

Limitations of the Review Process

The review was not prospectively registered. No quantitative meta-analysis was performed because clinical heterogeneity would make a pooled predictor estimate difficult to interpret.

Future Research

Future prognostic studies should use standardized definitions and report persistent infection separately from recurrence. Reinfection should be distinguished from microbiologically proven relapse where possible. A minimum prognostic dataset should include age, smoking, vascular status, diabetes, nutritional status, number of previous operations, etiology, affected bone, bone exposure, defect size, soft-tissue status, deep culture microbiology, antimicrobial resistance, fixation, reconstruction, and at least two years of follow-up.

Conclusion

Recurrence and treatment failure in chronic osteomyelitis are determined by the interaction between patient vulnerability, previous treatment burden, microbiological difficulty, and anatomical complexity. Repeated previous operations, post-traumatic disease, smoking, vascular compromise, bone exposure, and segmental defects are among the most clinically important recurrence predictors. Pseudomonas aeruginosa, other Gram-negative bacilli, polymicrobial infection, ESBL-producing organisms, and multidrug resistance further increase treatment difficulty. MRSA appears particularly associated with failure of initial eradication rather than later recurrence. Large bone defects increase reconstructive burden and, in some treatment settings, reinfection and revision. However, anatomical severity does not inevitably predict failure when debridement, stabilization, antimicrobial treatment, dead-space management, and vascularized reconstruction are optimized. Clinicians should evaluate the combined recurrence phenotype of the host, organism, anatomy, and previous treatment history.

Declarations

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

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 summarized in this review were derived from published studies.

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