E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.01.670

Research Article

Comparative Effectiveness of Systemic, Local, and Combined Antibiotic Therapy on Anatomical Outcomes after Chronic Osteomyelitis Surgery

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Received: 08.03.2026, Revised: 02.06.2026, Accepted: 13.06.2026

ABSTRACT

Background: Chronic osteomyelitis is a long term bone infection which can lead to repeated infections, bone destruction, non-union and permanent deformity. The characteristics of the microbes and how the antibiotic was given could affect the recovery from infection and structural after surgery.

Objective: To determine the influence of microbial profile and antibiotic delivery method on anatomical bone deformity following surgery for chronic osteomyelitis.

Methods: This was a prospective comparative study carried out in Rawal Institute of Health Sciences, Islamabad, between June 2025 and December 2025. Consecutive non-probability sampling was used to recruit 93 adult patients undergoing surgery for chronic osteomyelitis. Bone and deep tissue specimens were collected for culture and antimicrobial susceptibility test. Patients were classified as systemic antibiotics alone, local antibiotics alone or systemic and local antibiotics. The main outcome was anatomical bone deformity at surgery including angular deformity, limb shortening, malalignment, malunion, non-union and rotational deformity. Appropriate statistical tests and multivariable logistic regression were used to evaluate associations.

Results: The mean age of the participants was 41.8 ± 13.6 years, and 64.5% were male. Cultures were positive in 83.9% of cases, with *Staphylococcus aureus* being the most frequently isolated organism. Anatomical bone deformity occurred in 29 patients, giving an overall rate of 31.2%. Deformity was significantly more frequent in patients with polymicrobial infection, multidrug-resistant organisms, segmental bone defects and recurrent osteomyelitis. The deformity rate was 46.2% among patients receiving systemic antibiotics alone, 27.8% among those receiving local antibiotics and 16.7% among those receiving combined therapy. Multivariable analysis identified multidrug-resistant infection, polymicrobial infection, segmental bone loss and recurrence as independent predictors of deformity, while combined systemic and local antibiotic therapy was associated with reduced odds of deformity.

Conclusion: Microbial resistance, polymicrobial infection, bone loss and recurrent disease substantially increase the risk of anatomical deformity after chronic osteomyelitis surgery. Combined systemic and local antibiotic delivery may improve anatomical outcomes when used alongside adequate surgical debridement and reconstruction.

Keywords: Chronic Osteomyelitis, Microbial Profile, Local Antibiotics, Systemic Antibiotics, Anatomical Deformity, Bone Infection, Multidrug Resistance.

INTRODUCTION

Chronic osteomyelitis is a prolonged infection that is difficult to treat and includes recurrent infections, necrotic bone and impaired vascularity. It typically occurs following open fractures, orthopaedic surgery, post-operative infection or untreated acute osteomyelitis, and may result from infection of the implant. The

disease can persist for many months or years and can lead to the development of draining sinuses, sequestrum, soft tissue damage, pathological fractures and progressive bone destruction. Despite the progress in the surgical and antimicrobial treatment, chronic osteomyelitis remains a high burden disease on both the patient and the health care system [1-3].

The management of chronic osteomyelitis requires removal of infected and non-viable tissue, identification of the causative organism, administration of effective antibiotics and restoration of skeletal stability. Surgical debridement is necessary because necrotic bone does not supply adequate blood flow to allow for systemic antibiotics to reach adequate concentrations at the site of infection. However, large amounts of debridement will create a segmental bone defect which will affect the function of the affected limb and lead to a risk of shortening, angulation, malalignment, malunion and non-union. So treatment should be successful not only in curing the infection, but also in restoring or rebuilding normal anatomical alignment and function [4-7].

The microbial flora of chronic OM may play a crucial role in response to therapy. One of the reasons for Staphylococcus aureus being commonly detected is its tendency to attach to bones and implants and develop protective biofilms. Pseudomonas aeruginosa, Escherichia coli, Klebsiella species and Proteus species, which are gram-negative organisms, are also seen, especially in post-traumatic and postoperative infections. Poly-microbial growth and the presence of multidrug-resistant organisms may add to the difficulty of treatment options due to the limited antibiotic options, as well as the possibility of chronic infection and continued bone and soft-tissue destruction. Multiple deep tissue or bone samples are essential for microbiological diagnosis, for appropriate culture directed therapy [8, 9].

Systemic antibiotics are also of value, but may be less effective in poorly vascularized and/or necrotic bone. Local antibiotic delivery systems have been developed to ensure high level of antibiotic concentrations at the infection site with minimal systemic exposure. Antibiotic loaded cement beads, spacers and antibiotic coated intramedullary devices are common locally available delivery systems. Dead space management following debridement may also be helped by local antibiotics. Systemic and local therapy may be helpful to obtain residual bacteria at the surgical site as well as systemic coverage of surrounding tissues and potential systemic spread [10-12].

Despite the increasing use of local antibiotic carriers, evidence regarding their effect on postoperative anatomical deformity remains limited. Most previous studies have focused primarily on infection eradication, recurrence or bone union, with less attention given to structural complications such as angular deformity, limb shortening, malalignment and segmental bone loss. The present study was therefore conducted to evaluate the influence of microbial profile and antibiotic delivery method on anatomical bone deformity following surgery for chronic osteomyelitis. It also aimed to identify microbial and clinical factors independently associated with poor anatomical outcomes.

METHODOLOGY

This prospective comparative study was conducted at the Department of Orthopaedic Surgery, Rawal Institute of Health Sciences, Islamabad, from June 2025 to December 2025. The study was designed to assess the influence of microbial characteristics and antibiotic delivery methods on the development of anatomical bone deformity following surgery for chronic osteomyelitis. A total of 93 patients meeting the eligibility criteria were enrolled through consecutive non-probability sampling. Patients of either sex, aged 18 years or above, with clinically and radiologically confirmed chronic osteomyelitis requiring operative management were included. Chronic osteomyelitis was defined by a persistent bone infection of at least six weeks' duration, supported by clinical findings such as a discharging sinus, local pain, swelling or previous recurrent infection, together with radiological or intraoperative evidence of sequestrum, involucrum or infected necrotic bone. Patients with acute osteomyelitis, malignant bone disease, active skeletal tuberculosis, congenital bone deformity, incomplete clinical records or follow-up shorter than three months were excluded.

On admission, detailed demographic and clinical data was collected using a structured data

collection form. The following parameters were recorded: age, sex, BMI, smoking status, diabetes mellitus, anaemia, duration of infection, anatomical site, affected side, cause of osteomyelitis, previous surgery, presence of a draining sinus, soft-tissue defect, pathological fracture and segmental bone loss. The osteomyelitis was defined as occurring in tibia, femur, humerus, radius or ulna, foot, or other bones. The presumed cause was classified as: post-traumatic, postoperative or haematogenous. Baseline tests were complete blood count, erythrocyte sedimentation rate, C-reactive protein, blood glucose and renal and liver function tests. Plain radiographs were done in the anteroposterior and lateral views and computed tomography or magnetic resonance imaging was used if needed to determine the amount of sequestration, the amount of destruction of the cortex, the involvement of the medulla and the extension of soft-tissue.

All patients were debrided under suitable anaesthetic. The surgery involved removal of the sinus tract, the removal of any dead soft tissue and the removal of any dead bone until healthy bleeding margins were reached, known as sequestrectomy and resection. To the extent possible, multiple deep tissue/bone specimens were obtained prior to antibiotic therapy. Aerobic and anaerobic culture and antimicrobial susceptibility testing was performed on at least three different specimens. No superficial swab cultures were done to determine causative organism. Infections were classified as culture positive or culture negative, monomicrobial or polymicrobial, Gram-positive or Gram-negative, and drug-sensitive or multidrug resistant. Typical microbiological procedures were followed for identification of the isolated organisms and their antimicrobial susceptibility was determined by the laboratory protocol. Multidrug resistance was considered as non-susceptibility to 3 or more antimicrobial agents in the 3 relevant classes of antibiotics.

Patients were divided based on the method of antibiotic delivery after surgical debridement. The 1st group of children were treated with systemic antibiotics; the 2nd group with local; and the 3rd group with both. Systemic treatment was used in a non-systematic manner and was later adjusted based on the results of sensitivity and culture. Intravenous therapy was then followed by oral antibiotic therapy when clinically indicated and length of therapy depended on infection type, infectious organism and response to therapy. Local antibiotic delivery consisted of antibiotic loaded polymethylmethacrylate (PMMA) cement beads, cement spacers, or antibiotic coated intramedullary devices. The local delivery antibiotic type and dose were chosen based on culture sensitivity and compatibility with the local antibiotic treatment regime and carrier. When needed, stabilization using external or internal fixation, bone grafting and soft-tissue flap reconstruction were performed. Standard wound care, Analgesia, Physiotherapy and nutritional support were provided to all patients.

All patients were followed clinically and by serial radiographs postoperatively. Primary outcome was the presence of anatomical bone deformity at follow-up (angular deformity, malalignment, rotational deformity, limb shortening, joint contracture, malunion, non-union or persistent of segmental bone loss). Angular deformity was assessed on follow-up radiographs in degrees, and length discrepancy in centimetres. Secondary endpoints were eradication of the infection, recurrence, healing of wounds, reoperation and need for corrective surgery. IBM SPSS Statistics was used for analysing the data. The continuous variables were presented as Mean±SD, the categorical variables were presented as frequency and percentages. The chi-square test or Fisher's exact test was used to examine associations between categorical variables, while an independent-samples t-test was used for normally distributed continuous variables. Variables with clinical significance or p value < 0.20 in univariable analysis were used in a multivariable binary logistic regression model to identify variables that were independent predictors of anatomical deformity. Odds ratios with 95% confidence intervals were calculated and p values <0.05 were regarded as significant.

RESULTS

Ninety-three patients who had undergone surgery for chronic osteomyelitis were included in the study. The mean age of the subjects was 41.8 ± 13.6 years (range 18-72 years). The majority of patients in this case study were male (64.5%). The tibia was the most common bone involved, followed by the femur. The most common cause of infection was post-traumatic

osteomyelitis. In 29 patients (31.2%) there was an anatomical deformity in follow-up.

Table 1. Demographic and Clinical Characteristics of the Study Participants

Variable	Frequency (%) or Mean ± SD
Total patients	93
Age, years	41.8 ± 13.6
Age ≤40 years	43 (46.2)
Age >40 years	50 (53.8)
Male	60 (64.5)
Female	33 (35.5)
Diabetes mellitus	24 (25.8)
Smoking history	31 (33.3)
Anaemia	27 (29.0)
Previous osteomyelitis surgery	39 (41.9)
Draining sinus at presentation	58 (62.4)
Mean duration of infection, months	14.7 ± 8.9
Anatomical bone deformity	29 (31.2)
No anatomical bone deformity	64 (68.8)

In 39 patients (41.9%), the tibia was the site of osteomyelitis, while 24 patients (25.8%) had osteomyelitis in the femur. Other bones involved in the disease were the humerus, radius or ulna and foot bones. Over half of the patients had a post-traumatic infection. Patients who developed anatomical deformity had a longer mean duration of infection than those without deformity.

Table 2. Clinical Characteristics of Chronic Osteomyelitis

Clinical variable	Frequency (%)
Anatomical site	
Tibia	39 (41.9)
Femur	24 (25.8)
Humerus	11 (11.8)
Radius/ulna	8 (8.6)
Foot or other bones	11 (11.8)
Cause of osteomyelitis	
Post-traumatic	50 (53.8)
Postoperative	29 (31.2)
Haematogenous	14 (15.1)
Presence of sequestrum	54 (58.1)
Soft-tissue defect	32 (34.4)
Pathological fracture	11 (11.8)
Segmental bone defect	26 (28.0)
Infection recurrence	20 (21.5)

Microbiological culture were positive in 78 patients (83.9%) and negative in 15 patients (16.1%). Polymicrobial infection was not as common as monomicrobial infection. Staphylococcus aureus was the most common organism isolated followed by Pseudomonas aeruginosa. Approximately 25% of culture-positive patients had multidrug-resistant organisms.

Table 3. Microbiological Profile of Chronic Osteomyelitis

Microbiological variable	Frequency (%)
Culture-positive infection	78 (83.9)

Culture-negative infection	15 (16.1)
Monomicrobial infection	61 (65.6)
Polymicrobial infection	17 (18.3)
Gram-positive organisms	44 (47.3)
Gram-negative organisms	34 (36.6)
Multidrug-resistant infection	23 (24.7)
Staphylococcus aureus	27 (29.0)
Methicillin-resistant *S. aureus*	11 (11.8)
Pseudomonas aeruginosa	16 (17.2)
Escherichia coli	9 (9.7)
Klebsiella species	7 (7.5)
Proteus species	5 (5.4)
Other organisms	11 (11.8)

As for antibiotic therapy, 39 patients were treated with systemic antibiotics, 18 with local antibiotic delivery and 36 with both systemic and local antibiotic therapy. The most frequently used local delivery system was the antibiotic loaded cement beads. Patients who received only systemic antibiotics had the highest and patients who received combined therapy had the lowest incidence of postoperative deformity.

Table 4. Antibiotic Delivery Methods and Surgical Treatment

Treatment variable	**Frequency (%)**
Systemic antibiotics only	39 (41.9)
Local antibiotics only	18 (19.4)
Combined systemic and local antibiotics	36 (38.7)
Culture-directed antibiotic therapy	68 (73.1)
Empirical antibiotic therapy	25 (26.9)
Antibiotic-loaded cement beads	27 (29.0)
Antibiotic cement spacer	15 (16.1)
Antibiotic-coated intramedullary nail	12 (12.9)
Surgical debridement	93 (100.0)
Sequestrectomy	54 (58.1)
Bone grafting	25 (26.9)
External fixation	23 (24.7)
Soft-tissue flap reconstruction	18 (19.4)

Of these 29 patients who developed anatomical deformity, the most typical pattern was an angular deformity. Shortening and malalignment of the limbs were also very common. There were 12 patients with malunion and 10 with non-union. An additional corrective surgical procedure was needed in nine patients.

Table 5. Patterns of Postoperative Anatomical Bone Deformity

Deformity outcome	**Frequency (%)**
Any anatomical deformity	29 (31.2)
Angular deformity	12 (12.9)
Limb shortening	8 (8.6)
Malalignment	7 (7.5)
Rotational deformity	4 (4.3)
Joint contracture	6 (6.5)
Malunion	12 (12.9)
Non-union	10 (10.8)
Corrective surgery required	9 (9.7)

Amongst the polymicrobial and monomicrobial infected patients, anatomical deformity occurred significantly more often in the polymicrobial infected patients. Patients with MDR had similarly a significantly higher deformity rate compared to DROs. There was also a higher percentage of deformity for Gram-negative infections than for Gram-positive infections.

Table 6. Association between Microbial Profile and Anatomical Bone Deformity

Microbial factor	Deformity present n (%)	Deformity absent n (%)	p-value
Gram-positive infection	10 (22.7)	34 (77.3)	0.041
Gram-negative infection	15 (44.1)	19 (55.9)	
Monomicrobial infection	14 (23.0)	47 (77.0)	0.012
Polymicrobial infection	9 (52.9)	8 (47.1)	
Drug-sensitive organisms	12 (21.8)	43 (78.2)	0.003
Multidrug-resistant organisms	11 (47.8)	12 (52.2)	
Culture-negative infection	3 (20.0)	12 (80.0)	0.302
Culture-positive infection	26 (33.3)	52 (66.7)	

Anatomical outcome was also significantly related to the method of antibiotic administration. Local therapy yielded a deformity rate of 5/18 (27.8%) whereas combined therapy yielded a deformity rate of 6/36 (16.7%) and systemic antibiotics alone yielded a deformity rate of 18/39 (46.2%). There was a significant difference between the three treatment groups.

Table 7: Association between Antibiotic Delivery Method and Anatomical Bone Deformity

Antibiotic delivery method	Deformity present n (%)	Deformity absent n (%)	p-value
Systemic antibiotics only	18 (46.2)	21 (53.8)	0.011
Local antibiotics only	5 (27.8)	13 (72.2)	
Combined systemic and local antibiotics	6 (16.7)	30 (83.3)	

Deformity was a much more common finding when patients were affected by a recurrence than when they were not. Segmental bone defects, soft-tissue defects and repeated surgery and infection for >12 months were also significantly associated with anatomical deformity.

Table 8. Clinical Factors Associated with Anatomical Bone Deformity

Clinical factor	Deformity present n (%)	Deformity absent n (%)	p-value
Infection duration >12 months	21 (44.7)	26 (55.3)	0.004
Infection duration ≤12 months	8 (17.4)	38 (82.6)	
Segmental bone defect present	15 (57.7)	11 (42.3)	<0.001
Segmental bone defect absent	14 (20.9)	53 (79.1)	
Soft-tissue defect present	15 (46.9)	17 (53.1)	0.018
Soft-tissue defect absent	14 (23.0)	47 (77.0)	
Infection recurrence present	13 (65.0)	7 (35.0)	<0.001
No infection recurrence	16 (21.9)	57 (78.1)	
More than one surgery	18 (46.2)	21 (53.8)	0.009
One surgical procedure	11 (20.4)	43 (79.6)	

Multivariate logistic regression revealed that multidrug-resistant infection, polymicrobial infection, and segmental bone defect and recurrence of osteomyelitis were independent predictors of postoperative deformy. Combined systemic and local antibiotic delivery, on the

other hand, was linked to reduced risk of deformity.

Table 9. Multivariable Logistic Regression for Predictors of Anatomical Bone Deformity

Predictor	Adjusted odds ratio	95% confidence interval	p-value
Multidrug-resistant infection	3.18	1.22–8.29	0.018
Polymicrobial infection	2.91	1.04–8.13	0.042
Segmental bone defect	4.26	1.57–11.56	0.004
Infection recurrence	5.08	1.71–15.10	0.003
Infection duration >12 months	2.44	0.94–6.33	0.067
Combined systemic and local antibiotics	0.31	0.11–0.88	0.028
Diabetes mellitus	1.62	0.58–4.52	0.357
Previous osteomyelitis surgery	1.73	0.68–4.40	0.251

Overall, anatomical bone deformity occurred in nearly one-third of patients after chronic osteomyelitis surgery. Resistant and polymicrobial infections, recurrent osteomyelitis and segmental bone loss were the strongest factors associated with poor anatomical outcomes. Patients treated with combined systemic and local antibiotic therapy demonstrated a significantly lower frequency of deformity than those treated with systemic antibiotics alone.

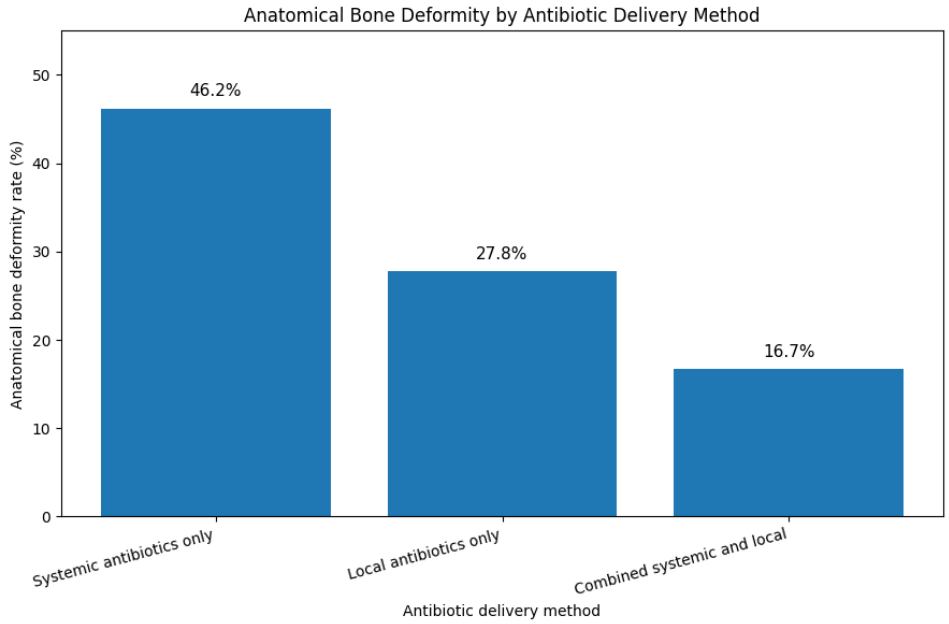

Figure 1. Anatomical bone deformity rates according to antibiotic delivery method.

The deformity rate was highest among patients receiving systemic antibiotics alone (46.2%), followed by local antibiotics alone (27.8%), while the lowest rate was observed with combined systemic and local antibiotic therapy (16.7%).

DISCUSSION

The present study examined the relationship between microbial characteristics, antibiotic delivery methods and anatomical bone deformity following surgery for chronic osteomyelitis. Anatomical deformity developed in 31.2% of patients, demonstrating that structural complications remain common despite surgical debridement and antimicrobial treatment. Angular deformity was the most frequently observed abnormality, followed by limb shortening, malalignment, malunion and non-union. These outcomes may result from

prolonged infection, destruction of cortical and cancellous bone, loss of mechanical stability, impaired blood supply and extensive removal of non-viable bone during debridement. Chronic osteomyelitis is particularly difficult to treat because necrotic bone and poorly vascularized tissue reduce antibiotic penetration and provide an environment in which bacterial biofilms can persist. Consequently, successful management requires not only infection eradication but also preservation or reconstruction of bone alignment, stability and length. Current evidence supports a comprehensive treatment strategy involving radical debridement, dead-space management, culture-directed antibiotics, skeletal stabilization and appropriate soft-tissue coverage [13-15].

Microbiological results indicated that S. aureus was the most commonly isolated bacteria followed by P. aeruginosa, E. coli, Klebsiella species and Proteus species. Clinically plausible as S. aureus has strong adherence and biofilm-forming properties, while Gram-negative organisms are usually found in post-traumatic, postoperative and hospital-associated bone infections. The culture positivity rate of 83.9% underscores the need to take more than just a few superficial wound swabs, and to sample deep tissue and bone. Anatomical deformity was significantly associated with polymicrobial and multidrug resistant infections and these were independent predictors of infection despite adjusting for other clinical factors. Polymicrobial infections can lead to more extensive tissue damage and more comprehensive coverage with antimicrobials is needed, multidrug resistance can reduce the effectiveness of antimicrobial treatment and can extend the duration of the active infection. Additionally, previous investigations have revealed altered microbial profile and the development of antimicrobial resistance in chronic OM, highlighting the importance of culture directed therapy and prudent antibiotic usage [16-18].

One of the most important findings was that the method of antibiotic delivery was strongly related to anatomic outcome. 46.2% of patients receiving systemic antibiotics alone had deformity, whereas the figures were 27.8% and 16.7% for patients receiving local antibiotics and combined systemic and local antibiotic therapy, respectively. The odds of postoperative deformity were independently associated with combined treatment in a multivariable model. The use of local antibiotic delivery systems such as antibiotic loaded cement beads, spacers and coated intramedullary devices can create a high concentration of antibiotic directly in the infected bone and surgical dead space. This technique might be particularly useful in locations that lack a good blood supply so that systemic antibiotics can rarely achieve adequate local levels. Additionally, local antibiotic carriers can help with the management of dead space and decrease the amount of bacteria that still remain after debridement. However, use of local therapy should be treated as an adjunct, not as an alternative to good debridement and appropriate systemic therapy. In the last years, some clinical studies have shown that the use of local antibiotics in the surgical treatment of osteomyelitis of the long bones leads to a lower re-debridement rate and good clinical results in terms of infection control [19].

The most powerful clinical factors predicting anatomical deformity in this study were segmental bone defects and recurrent infection. Patients with segmental bone loss had more than four times the adjusted odds of deformity, and the odds were raised by about five times for patients who had recurrence. Control of infection must include removal of infected and necrotic bone; large resections may result in structural gaps, loss of load transmission and loss of limb alignment. Without proper reconstruction and stabilization of these defects, the patient can get shortening, angulation, non-union or malunion. Recurrent infections cause continuous inflammation, tissue death, further surgery and loss of bone mass, further inhibiting bone regeneration. The correlation of soft-tissue defects with deformity further emphasizes the need to provide sufficient vascularization for the coverage since exposed bone and poorly vascularized tissue are more likely to sustain infection and a delay in healing. Today, orthopaedic debridement is also more commonly combined with reconstructive surgery like bone grafting, bone transport, local antibiotic carriers, stable fixation and flap coverage, depending on the size and location of the defect [20].

The study has several limitations that should be considered while interpreting its findings. It was performed in one institution and included relatively few patients (93) which may limit the generalizability of the results. Treatment

allocation methods were not randomized, and the fact that some infections were more severe than others, and some were more complex or involved more bone loss, may have affected treatment choice. The type of local antibiotic carrier, antimicrobial agent and duration of systemic therapy has also varied and could have influenced outcomes. Furthermore, the follow-up period could be too short to detect all late recurrences and/or progressive deformities. In spite of these drawbacks, the study brings clinically relevant findings to the forefront that the virulence of the bacteria and the type of antibiotic used affect anatomical healing post chronic osteomyelitis surgery. Larger, multi-centre, prospective studies with longer follow-up times and standardised treatment protocols are needed in the future to compare specific local delivery systems and outcomes measured by radiology, function and patient-reported measures.

CONCLUSION

Anatomical bone deformity occurred in nearly one-third of patients following surgery for chronic osteomyelitis. Multidrug-resistant infection, polymicrobial growth, segmental bone loss and recurrence of osteomyelitis were independently associated with an increased risk of deformity. Patients receiving combined systemic and local antibiotic therapy had a substantially lower deformity rate than those treated with systemic antibiotics alone. These findings support the use of multiple deep cultures, culture-directed antimicrobial therapy, thorough surgical debridement, effective dead-space management and early reconstruction of bone and soft-tissue defects. A multidisciplinary approach incorporating combined antibiotic delivery and appropriate skeletal stabilization may improve infection control and reduce malalignment, shortening, malunion and non-union after chronic osteomyelitis surgery.

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