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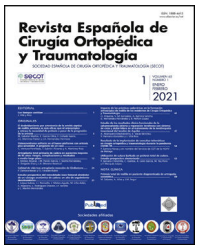

ORIGINAL PAPER

# [Translated article] Descriptive study of spinal instrumentation-related infections in a tertiary hospital

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**KEYWORDS**
Spinal instrumentation;
DAIR;
Infection;
Bone graft

**Abstract**
*Introduction:* Spinal instrumentation-related infections (SIRI) are one of the main causes of post-surgical complication and comorbidity. Our objective was to describe the clinical and microbiological characteristics, treatment and prognosis of these infections.
*Material and methods:* We conducted a retrospective study in our institution (2011–2018) including adult patients undergoing spinal instrumentation who met the diagnostic criteria for confirmed infection. Superficial surgical wound and deep intraoperative samples were processed for microbiological culture. The medical and orthopaedic team was always the same.
*Results:* Forty-one cases were diagnosed of which 39 patients (95.1%) presented early infection (<3 months after initial surgery) with symptoms in the first two weeks, mean CRP at diagnosis was 133 mg/dl and 23% associated bacteremia. The remaining two patients (4.8%) were chronic infections (symptoms >3 months after surgery). The treatment of choice in early infections was the Debridement, Antibiotics and Implant Retention (DAIR) strategy without removal of the bone graft, which successfully resolved 84.2% of the infections. The main aetiology was gram-positive (*Staphylococcus aureus*: 31.7%), followed by gram-negative and polymicrobial flora. Antibiotics were optimised according to cultures with a mean duration of 12 weeks.
*Conclusions:* In early infections, early diagnosis and DAIR strategy (with bone graft retention) demonstrated a healing rate higher than 80%.


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**PALABRAS CLAVE**
Instrumentación columna;
DAIR;
Infección;
Injerto óseo

**Estudio descriptivo de las infecciones asociadas con instrumentación de columna en un hospital terciario**

**Resumen** Introducción Las infecciones asociadas con instrumentación de columna (IAIC) son una de las principales causas de complicación posquirúrgica y comorbilidad. Nuestro objetivo fue describir las características clínicas, microbiológicas, tratamiento y pronóstico de estas infecciones.
*Material y métodos:* Realizamos un estudio retrospectivo en nuestro hospital (2011-2018) e incluímos a pacientes adultos con cirugía instrumentada de columna, que cumplieran los criterios diagnósticos de infección confirmada. Se procesaron muestras de herida quirúrgica superficial y muestras intraoperatorias profundas para cultivo microbiológico. El equipo médico y traumatológico fue siempre el mismo.
*Resultados:* Se diagnosticaron 41 casos, de los que 39 pacientes (95,1%) presentaron infección precoz (<3 meses tras cirugía inicial) con síntomas en las 2 primeras semanas, la media de PCR al diagnóstico fue de 133 mg/dl y un 23% asoció bacteriemia. Los 2 pacientes restantes (4,8%) fueron infecciones crónicas (síntomas >3 meses tras cirugía). El tratamiento de elección en las infecciones precoces fue la estrategia *Debridement, Antibiotics and Implant Retention* (DAIR) sin retirada del injerto óseo, que demostró la curación en el 84,2% de los pacientes. La principal etiología fueron los grampositivos (*S. aureus:* 31,7%), seguido por los gramnegativos y la flora polimicrobiana. Los antibióticos fueron optimizados según los cultivos con una duración media de 12 semanas.
*Conclusiones:* En las infecciones precoces, el diagnóstico precoz y la estrategia DAIR (con retención del injerto óseo) demostró una tasa de curación superior al 80%.


## Introduction

The percentage of spinal instrumentation surgery associated infection varies, depending on the studies and population reviewed, ranging between .5% and 15%.[1,2] Risk factors are associated with pre-surgical conditions of the patients (comorbidity, immunosuppression, age, malnutrition, etc.), as well as intraoperative factors (surgical time, bleeding, fusion levels, approach, surgical location, etc.) and postsurgical factors (incontinence), healing, etc.).[1] Patients who present infection associated with spinal instrumentation (IASI) can present with pain, instability, dysfunction, neurological deficit, fever, inflammatory signs, sepsis and this may even lead to death. In most centres, the Centres for Diseases Control and Prevention (CDC) diagnostic criteria for spinal infection are adhered to, modified according to Kowalski et al. and Dubée et al. These include a clinical (presence of fistula, exposure of intraoperative material or pus), microbiological (at least $\geq$2 positive cultures for the same microorganism or one if it is a primary pathogen, positive sonication with $\geq$50 CFU/ml), or histological criteria to confirm the infection.[3–5]

IASIs can be early, and are those that occur before 3 months, usually in the first 6 weeks after surgery, and usually present with acute symptoms, as well as an increase in acute phase reactants (CRP, ESR) in analysis. Up to 25% may be bacteraemia-associated. The main aetiology is *Staphylococcus aureus*,[6] followed by gram-negative bacilli and polymicrobial flora.[2] In these patients, Debridement, Antibiotics and Implant Retention (DAIR) and antibiotics with the capacity to diffuse into the bacterial biofilm ensure cure in more than 80% of patients.[7] From a surgical point of view, aggressive debridement must be performed with retention of the implant, cleaning of purulent material and resection of necrotic tissue. The surgical wound must be thoroughly explored, both superficially and deep to the muscle fascia. The need to remove bone grafts is debated.[8] Some series document the need to remove the bone graft for healing, as well as prolonged antibiotic treatment for at least 12 weeks.[8]

Chronic infections would therefore be those that present more than 3 months after surgery with more latent and insidious symptoms over time and less systemic and analytical repercussions. The aetiological agents are usually less virulent gram-positive agents such as *Cutibacterium acnes* or negative *Staphylococcus coagulasa*. In most cases, it is necessary to remove the implant if the spine is already fused or to replace the implant in one or two stages if there is instability or pseudoarthrosis, all of which implies greater morbidity, mortality and orthopaedic sequelae.[9]

Our purpose was to review the IASIs that occurred in our centre, to describe the clinical, microbiological, surgical and prognostic characteristics, as well as to investigate the success rate of our therapeutic protocol.

## Material and methods

A retrospective descriptive study of IASIs diagnosed in a tertiary hospital was carried out over 8 years, from 2011 to 2018. The medical records of those adult patients (>18 years) with a confirmed diagnosis were reviewed following the international IASI consensus: that they met a

clinical (presence of peri-implant fistula or pus), histological (presence of inflammation in peri-implant tissues) or microbiological criteria (at least ≥2 positive intraoperative cultures with the same species and sensitivity or one positive culture if primary pathogen, sonication fluid positive for >50 CFU/ml).

Demographic criteria, information on the primary surgery (reason for the intervention, fused levels, surgical prophylaxis) were recorded, as well as several major risk factors such as: diabetes mellitus, neoplasia or immunosuppression (treatment with chemotherapy, biological agent or corticosteroid at high doses). Microbiological aspects and antibiotic treatments received by patients were also reviewed.

All patients were diagnosed and treated by the same medical (infectious unit) and surgical (trauma spine unit) team following the protocols established for osteoarticular infections and endorsed by the hospital's Infections Commission. The patients had a 5-year follow-up by traumatology with an initial joint follow-up with the infectious unit for one year until resolution of the infection.

Surgical treatment of the infection consisted of lavage, extensive debridement, and excision of necrotic tissues. The bone grafts were removed and washed with saline solution, then immersed for 20 min in antibiotic solution with 240 mg gentamicin and after rinsing with saline solution, they were reintroduced to the surgical bed. A minimum of 3−5 intraoperative samples were always taken for microbiological culture. After surgery all patients remained with an external lavage system through the surgical wound, which consisted of a cranial inlet drain connected to a continuous infusion of physiological saline at 21 ml/h for 3 days and an aspirating caudal outlet drain. On the fourth day, both drains became aspiration and, depending on the drainage volume, they were removed on progressive days (when the aspirated volume was less than 100 ml/day).

Samples for culture were taken from the superficial surgical wound at the onset of symptoms, using a syringe with aspiration, under aseptic conditions. In the revision surgery, deep wound samples were taken during exposure and prior to any lavage.

Blood cultures were also obtained in febrile patients or with clinical signs of sepsis. No patient was administered antibiotics until the samples were taken.

All samples were processed according to the usual procedures of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), with Gram staining and cultures in solid (aerobic and anaerobic) and liquid (enrichment broth) media. The identification of the microorganisms grown in culture was carried out by mass spectrometry (MALDI-TOF) and the antibiotic sensitivity of the isolates was carried out using broth microdilution systems (MicroScan® WalkAway® and Wider®).[10,11]

Antimicrobial treatment consisted of the use of an empirical lipopeptide/glycopeptide (vancomycin or daptomycin) and antipseudomonal beta-lactam (cefepime/piperacillin−tazobactam/meropenem) with subsequent optimisation according to cultures. Antibiotherapy was administered intravenously with oral sequencing of antibiotics with good bioavailability and biofilm diffusion, giving preference to rifampicin in gram-positive infections and quinolones in those caused by gram-negative infections[12] when the patient presented a good evolution of the surgical wound and a decrease in inflammatory markers.

Treatment success in IAICs was defined as:

- Cure: absence of local and/or systemic clinical signs, as well as a decrease or normalisation of inflammatory parameters maintained over time for at least 6 months after the completion of antibiotic treatment.
- Failure: reappearance of clinical signs and/or increase in analytical parameters during treatment or after its completion. Causes:
- Persistence of infection: infection not cured by the same initial microorganism.
- Superinfection: infection by new microorganisms different from the initial ones.

### Statistical analysis

A descriptive-univariate analysis of all the clinical variables studied was performed. These are presented in absolute and relative frequencies in the case of qualitative variables and the main measures of centralisation and dispersion (mean, standard deviation) in the case of quantitative variables.

### Ethical aspects

The study was approved by the Ethics Committee of our hospital and was developed in accordance with the protocol and ethical considerations applicable in the Declaration of Helsinki and the ethical guidelines of the International Council of Medical Associations (CIOMS).

## Results

In the study presented we reviewed all instrumented spine surgeries performed from 2011 to 2018 (8 years). Forty-one cases of IASI were diagnosed out of 1680 total interventions, obtaining an average annual incidence of 2.43%. The cases of infection and incidence are detailed in Fig. 1.

The average age was 59 years, with the prevalence being slightly higher in women at 53.7%. Of the 41 infected patients, the most affected segment was the lumbar spine with 34 patients (82.9%), then the thoracic spine with 12 patients (29.2%), the cervical spine with 5 patients (12.1%). %) and localisation in more than one segment in 8 patients (19.5%).

Among the risk factors analysed, it was found that 24.4% had diabetes mellitus, 24.4% were receiving immunosuppressive treatment and 22% had some type of active neoplasia or were undergoing treatment.

Regarding surgical prophylaxis, during the first part of the study (2011−2014), cefazolin 2 g was administered according to international recommendations, with 22 infections being diagnosed (incidence 2.61%). At the end of that year, the surgical prophylaxis protocols were reviewed by the Infection Commission of our hospital and the prophylaxis regimen was modified to cefazolin 2 g + gentamicin 240 mg (single intravenous doses during anaesthesia induction). In the second period of the study (2015−2018) we diagnosed 19 cases of infections, observing an incidence of 2.25%

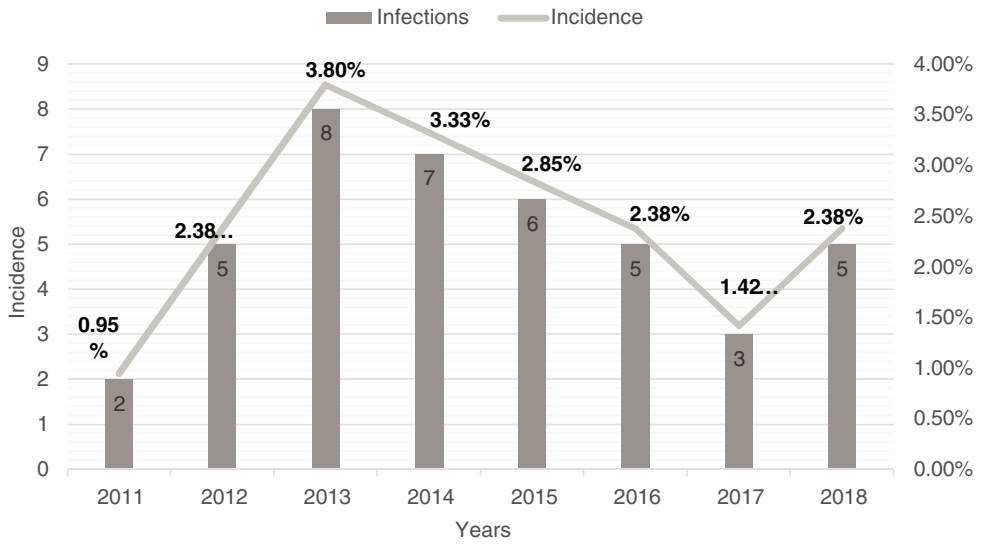


**Figure 1** Rate of IASI between 2011 and 2018 in our hospital.

**Table 1** Clinical presentation of the IASI.

| *N* = 41 | Early infections *N* = 39 (95.1%) | Late infections *N* = 2 (4.9%) |
|---|---|---|
| Start of symptoms (days) | 14.5 | 455 |
| CRP (mg/dl) | 133 | 12 |
| Bacteraemia (%) | 23 | 0 |

CRP: C reactive protein; IASI: infections associated with spinal instrumentation.

Of the 41 infections diagnosed, 39 were early presentation. Of them, one was a superficial infection and 38 were early and deep infections with involvement of the fascia and implants (92.7%). In these early infections, the days until the onset of symptoms was 14.51 days, the mean CRP value was 133 mg/dl, and up to 23% of patients associated secondary bacteraemia. There were 2 late-onset infections that had a mean symptom onset of 455 days and a mean CRP value of 12 mg/dl (Table 1).

On average 6 samples were sent for culture for microbiological diagnosis, and the diagnostic profitability was 86%, profitability being understood as the number of positive cultures with respect to the total samples sent from a patient. We did not have any patients without a microbiological diagnosis. There was microbiological discordance in 10 patients (24.9%) where the results of the cultures obtained from the superficial wound were not concordant with the intraoperative samples. Regarding the microbial aetiology, of the 41 infected patients, 32 cases (78%) were monomicrobial infections: *S. aureus*,[13] negative *S. coagulasa*,[5] *Streptococcus oralis*,[1] *Escherichia coli*,[2] *Proteus mirabilis*,[2] *Hafnia alvei*,[1] *Klebsiella pneumoniae*,[1] *Pseudomonas aeruginosa*,[4] *C. acnes*[2] and *Mycobacterium fortuitum*[1]; whilst 9 cases (22%) were polymicrobial infections where *S. aureus*,[2] negative *S. coagulasa*,[2] *Enterococcus faecium*,[1] *P. aeruginosa*,[3] *Proteus mirabilis*,[4] *E. coli*,[3] *K. pneumoniae*,[3] *Morganella morganii*[1] and *Corynebacterium striatum*[1] were isolated.

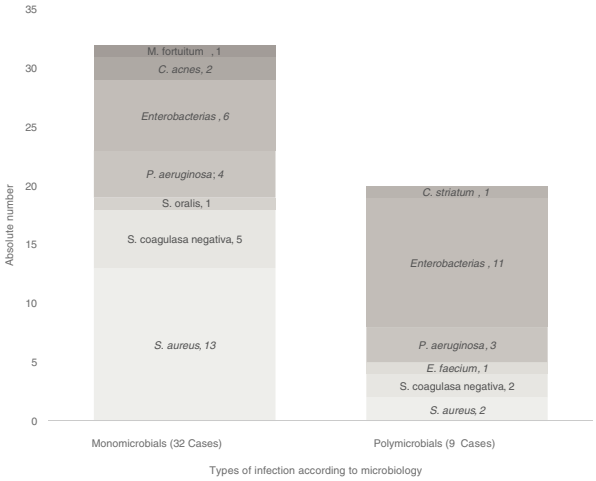


**Figure 2** Microbial aetiology of the IASI.

Globally, the most isolated microorganisms were staphylococci,[14] mainly *S. aureus*, followed by enterobacteria,[15] in our case the most frequent being *P. mirabilis*. The microbiological findings are detailed in Fig. 2.

We had a prevalence of methicillin-resistant *S. aureus* (MRSA) of 17.6%, enterobacteria with resistance to cephalosporins of 16% and resistance to quinolones between 20% and 30% depending on the microorganism. Of the 41 patients with IASI, 34 of them (82.9%) received empirical treatment after taking intraoperative cultures, with the majority, 32 (94.1%), having adequate empirical antibiotic coverage for the microorganism responsible for the infection.

Regarding the treatment strategy and prognosis, of the total of 41 patients:

- Thirty-nine (95.12%) patients presented early infections, of which one (2.63%) was a superficial infection receiving only antibiotics with cure and 38 (92.6%) were managed with DAIR, cure being obtained in 32 patients (84.2%). Dur-

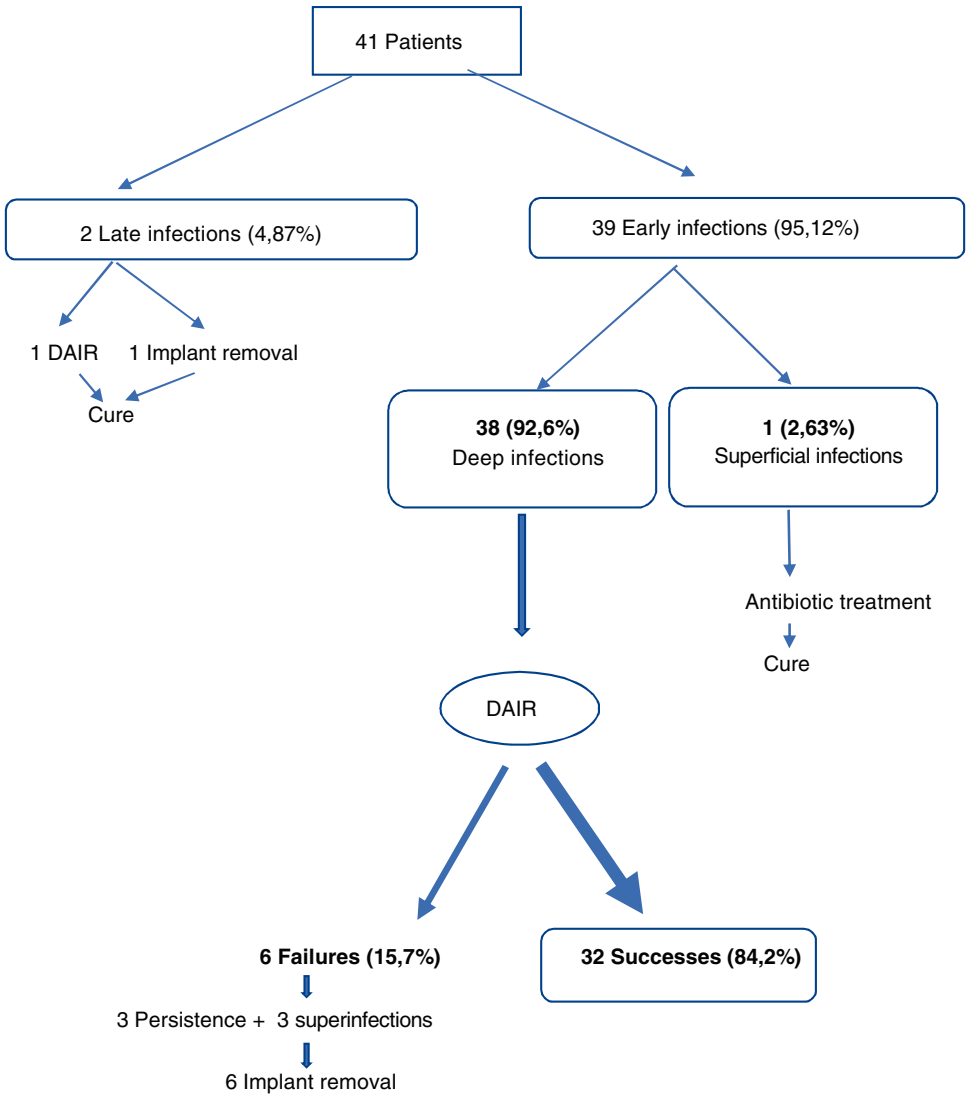


**Figure 3** Algorithm of surgical medical management of patients with spinal infection.

**Table 2** Patients with failed DAIR.

| | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Age | 64 a | 72 a | 29 a | 76 a | 80 a | 82 a |
| Initial surgery | LD | LD | LD | Metastasis | LD | LD |
| Risk factor | Neoplasm | NK | NK | Neoplasm | DM | DM, ID |
| Microbiology | *S. aureus* | Polymicrobial | *S. aureus* (+bacteraemia) | *P. aeruginosa* | *P. mirabilis* (+bacteraemia) | Polymicrobial |
| Persistence | *S. aureus* | Polymicrobial | *S. aureus* | No | No | No |
| Superinfection | No | No | No | *E. faecium* | *P. aeruginosa* | Polymicrobial |

DAIR: Debridement, Antibiotics and Implant Retention; DM: diabetes mellitus; ID: immunosuppression; LD: lumbar degenerative NK: not known.

ing surgery, no bone grafts had to be removed; they were all washed, disinfected, and reintroduced to the surgical bed.

- Two (4.87%) patients had chronic infections (one was treated with implant removal plus antibiotic therapy and the other with DAIR) with cure of the infection in both.

DAIR failure occurred in 6 patients (15.7%) due to persistence of the same initial microorganism or superinfection by different microorganisms. In these patients, the implants had to be removed to cure the infection (Fig. 3). During the follow-up period, no case of non-union or complication derived from the infection was observed.

The 6 patients with DAIR strategy failure are described below, with the most relevant aspects contained in Table 2. All started in the first 6 months after DAIR, and all ended up requiring removal of the material despite antimicrobial optimisation.

The empiric antibiotics used were mostly glucopeptic/lipopeptide (vancomycin or daptomycin) plus antipseudomonal beta-lactam (cefepime, piperacillin-tazobactam, meropenem) according to our osteoarticular infection protocol, for an average of 7 days until culture results and optimisation of targeted antibiotic therapy. The mean duration of IV antibiotic treatment was 21 days. The most prescribed oral antibiotics were quinolones, rifampicin and cotrimoxazole. The total duration (intravenous phase and oral sequencing) of early IASI treatment lasted for a mean of 86.4 days (12.3 weeks). No patient required suppressive treatment.

## Discussion

Within the retrospective nature of our study, we can conclude that being rigorous with the clinical/surgical and microbiological protocols ensures a high diagnostic yield and good clinical prognosis for patients suffering from IASI with a cure greater than 80%. Our main aetiological agent was *S. aureus* (more than 30%) followed by gram-negative bacilli and polymicrobial flora. Microbiological aspects are highly valuable to propose empirical treatments and local prophylaxis guidelines according to local epidemiology.

In IASI almost all the information regarding diagnosis, treatment and management has been extrapolated from national and international guidelines and consensus on prosthetic joint infection. There are no prospective studies or randomised clinical trials published for spine surgery, but most of our knowledge comes from retrospective and heterogeneous studies, which is why it is interesting and necessary to provide data on this condition.

The prevalence of IASI is variable, depending on factors intrinsic to the patient, as well as the complexity of the surgery, and can range between .5% and 15%.[2] In our review we obtained an annual incidence of 2.43%, which is in line with what has been published. With the change in presurgical prophylaxis carried out since 2014, when cefazolin + gentamicin began to be used, we had a slight decrease in infected patients (22 vs. 19 cases), but a similar incidence was maintained in both periods (2.61% vs. 2.25%). This could demonstrate that in lumbar spine surgeries, coverage against gram-negative bacteria should be expanded, the main aetiological culprits being in the form of monomicrobial or polymicrobial infection. Although consensus and international guidelines do not establish the addition of aminoglycoside, there are increasingly more manuscripts and expert opinions that recommend targeted prophylaxis based on the local epidemiology and clinical and surgical circumstances of the patient.[13,16,17] However, larger, controlled studies would be necessary to answer this question. The decrease we experienced may have been influenced by an unmeasured indirect effect such as reinforcement of other hygienic measures, pre-surgical preparation, early mobilisation of patients, removal of diapers, and the stability of health personnel.

Regarding microbiological diagnosis, between 3 and 5 intraoperative samples are always recommended (criteria of Atkins et al.), together with their processing in aerobic, anaerobic media and in blood culture bottles, since this appears to increase diagnostic sensitivity, maintaining incubation for up to 2 weeks. In some series, negative cultures can be up to 20% due to the use of previous antibiotics, lack of standardisation in sample taking or interference with the bacterial biofilm, having to resort to molecular CRP and sonication techniques to improve sensitivity,[9,10] if we have the implant.[18] The absence of or an incorrect microbiological diagnosis often leads to underdiagnosis of these infections, converting early infections into chronic ones with a poorer prognosis, and forcing the removal of the material in most cases. In our study, all patients had an aetiological diagnosis, so we consider that the sensitivity of our diagnostic and microbiological procedures was high.[17] It is important that work protocols and clinical pathways are established in the centres, as well as multidisciplinary teams for the early approach to these infections.[19–21]

If we compare the aetiology of our IASIs with that published in the literature, it is quite similar with a predominance of gram-positive cocci, with *S. aureus* as the main pathogen, being responsible for 31.7% of total infections. In our series we had a significant percentage of polymicrobial infections that would also be in accordance with the anatomical area most frequently operated on, that of the lumbar area.[15] Our microbial resistances were in accordance with our local epidemiology with a prevalence of 17.6% MRSA, 5% ESBL-producing enterobacteriaceae and a not insignificant 19.2% of gram-negative bacilli resistant to quinolones.

The most frequent clinical presentation was early, which began between 2 and 3 weeks after surgery and according to consensus is accepted within the first 3 months. The treatment of choice was a debridement, antibiotics and implant retention (DAIR) strategy, which ensured more than 80% cure. Our review supports these results, with an early diagnosis in 92.6% of patients, being treated with DAIR and reintroduction of the graft after washing with gentamicin, and managing to cure the infection in 84.2%, maintained over a period of 5-year clinical follow-up.

The need for bone graft removal is under debate. Spanish groups such as the Regional Hospital of Malaga advocate for their withdrawal in their own review published in this same journal (Gómez Caceres A. et al.).[14] In contrast, the International Consensus on Musculoskeletal Infections (Philadelphia 2018) proposes that bone graft does not need to be routinely removed after cleaning and debridement surgery, especially if it has been partially incorporated. However, loose or purulent graft must be removed. In our case, the bone grafts were not removed, maintaining the healing rate of the patients. We had a low DAIR failure rate (15.7%), with only 6 patients having to have their implant removed to cure the infection. The majority presented some risk factor such as immunosuppression or bacteraemia secondary to the infection as a factor of severity and possible poor outcome. In our series, the patients did not present major complications derived from the infection, but similar articles on deep infection in spinal surgery in Spain point out the not uncommon and serious complications associated with failure to treat the infection. These are especially deformity,[22,23] and mainly pseudoarthrosis, that requires subsequent corrective

surgeries and prolonged use of antibiotics, which increases the morbidity and mortality of these patients, as well as healthcare costs. Possibly having a coordinated and trained multidisciplinary team will allow us to optimise the diagnosis and treatment of these infections to improve our results.

Another important aspect is the total duration of antibiotic treatment, as well as the administration route, i.e. if oral sequencing is possible in these infections and at what time. In prosthetic joint infection we have at least one Spanish clinical trial that validates shorter treatments of 8 weeks after surgery.[24] We also have the English OVIVA clinical trial which demonstrates non-inferiority in oral treatment during the first 6 weeks in complex osteoarticular infections.[25] However, in spinal infection there is little evidence, although we are increasingly approaching the management we do in other osteoarticular infections. Recommendations in IASI range between 8 and 12 weeks of treatment, but increasingly more publications present good results with shorter periods.[16,17,26] Some Spanish publications from the last 2 years, such as those by Bosch-Nicolau P. and Benavent E.[27,28] show that 6–8 weeks would be sufficient in selected patients. Billières J. et al. already demonstrated in their study that some factors such as the duration of antibiotic treatment (2 weeks of intravenous treatment and 8 weeks of total treatment) were not related to recurrence, suggesting that individual risk factors could be more important than the duration of antibiotic administration.[29] In other publications, such as the clinical trial by Benkabouche M. et al., it is shown that even 4–6 weeks after implant removal are sufficient.[30] In our study, we remember that in patients with early infection who underwent DAIR, the average duration of treatment was 86.4 days (mean 12 weeks), very much in line with what international recommendations were until 2 years ago.

A weakness of the study is that we present a limited number of patients that makes statistical inference difficult, but not without important data that can support conclusions provided in previous studies. However, a strength is that all patients were always managed by the same medical team from the infectious unit and the spinal trauma team following the protocols established in our hospital for the management of this condition, which provides homogeneity in the management and clinical outcomes of these patients.

## Conclusions

Rigorous monitoring of diagnostic procedures and microbiological techniques guarantees high diagnostic sensitivity in IASIs, which added to a DAIR strategy (with graft retention) and optimisation of antimicrobials leads to therapeutic success above 80% in early infections after instrumented spine surgery.

It is necessary to review the duration of antibiotic therapy in the light of related studies published in the last 2 years, as well as to probe into the possible usefulness of antibiotic prophylaxis more optimised to the characteristics of surgery and local epidemiology to improve the course of these infections.

It is important to form multidisciplinary teams with the different specialists involved in the management of osteoarticular infection to improve the diagnosis, treatment and prognosis of these infections.

## Level of evidence

Level of evidence II.

## Conflict of interests

The authors have no conflict of interests to declare.

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