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Infections after spine instrumentation: effectiveness of short antibiotic treatment in a large multicentre cohort

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Background and objectives: Available information about infection after spine instrumentation (IASI) and its management are scarce. We aimed to analyse DAIR (debridement, antibiotics and implant retention) prognosis and evaluate effectiveness of short antibiotic courses on early forms.

Methods: Multicentre retrospective study of patients with IASI managed surgically (January 2010–December 2016). Risk factors for failure were analysed by multivariate Cox regression and differences between short and long antibiotic treatment were evaluated with a propensity score-matched analysis.

Results: Of the 411 IASI cases, 300 (73%) presented in the first month after surgery, 48 in the second month, 22 in the third and 41 thereafter. Infections within the first 2 months (early cases) occurred mainly to older patients, with local inflammatory signs and predominance of Enterobacteriaceae, unlike those in the later periods. When managed with DAIR, prognosis of early cases was better than later ones (failure rate 10.4% versus 26.1%, respectively; $P = 0.02$). Risk factors for DAIR failure in early cases were female sex, Charlson Score, large fusions (>6 levels) and polymicrobial infections (adjusted HRs of 2.4, 1.3, 2.6 and 2.26, respectively). Propensity score matching proved shorter courses of antibiotics (4–6 weeks) as effective as longer courses (failure rates 11.4% and 10.5%, respectively; $P = 0.870$).

Conclusions: IASIs within the first 2 months could be managed effectively with DAIR and shorter antibiotic courses. Clinicians should be cautious when faced with patients with comorbidities, large fusions and/or polymicrobial infections.

Introduction

The use of orthopaedic devices in the axial skeleton has been increasingly used for health problems, but infections after spine instrumentation (IASI) are one of the most concerning complications, due to the frequent need of prolonged antibiotic treatment and high morbidity.[1,2] IASIs are typically classified as early, occurring within the first month after surgery, or delayed-late, occurring from the third month. However, these cut-off points have been defined on the basis of expert opinion or short case series, and no global picture of different patterns of IASI has been described.

Regarding surgical management, probably based on analogy to the treatment of prosthetic joint infection, early IASI with stable implants and young biofilms are usually managed with debridement, antibiotics and implant retention (DAIR).[3,4] While the main goal of DAIR is to eradicate infection, various factors could necessitate that the precise timing for DAIR in IASI be reconsidered. For example, bone infection can be eradicated easier in the well-vascularized cancellous vertebrae. Additionally, ensuring vertebral fusion is crucial in IASI, and removing spine instrumentation in the early stages may not be possible due to the risk of complications, such as an unstable spine; however, partial removal may be possible in the early stages and, if needed, removal can be delayed until fusion is confirmed. By contrast, the orthopaedic goal in prosthetic joint infections managed with DAIR is to allow optimal joint functionality with a permanent implant.

Finally, the most suitable duration of antibiotic therapy for IASIs managed with DAIR has not been established. Although prolonged therapy (3–6 months) has traditionally been used, the potential efficacy of shorter antibiotic courses has been recently postulated.[5–8] In the current era of great antibiotic consumption and MDR bacteria, antimicrobial stewardship policies based on shortening antibiotic therapies seem desirable.

Over recent years, the Spanish Network for Research in Infectious Diseases (REIPI) and the Spanish Study Group of Osteoarticular Infections (GEIO) have been working on several orthopaedic device-related infections through multidisciplinary collaboration. In this study, we analysed a large cohort of patients with IASIs from this network to define the outcomes of different clinical forms according to the surgical approaches. Among early IASI cases treated with DAIR, we also analysed the most appropriate timing, duration of concomitant antibiotic therapy and risk factors for failure.

Patients and methods

Study design, settings and inclusion/exclusion criteria

This was a multicentre, retrospective, observational study performed in 14 Spanish hospitals enrolled in the REIPI and/or GEIO groups. The local Ethics Committee approved the study (PR298/18). We included patients older than 16 years who presented with IASI between January 2010 and December 2016, regardless of the time that had elapsed since instrumentation. We excluded postoperative IASIs that had not undergone a surgical approach as well as cases in which infection was the indication for initial instrumentation surgery (e.g. vertebral osteomyelitis or new infection/persistence/relapse of a previous IASI).

Definitions

IASI was diagnosed based on the presence of two mandatory criteria: (i) presence of symptoms or signs compatible with a surgical site infection, such as localized pain or tenderness, purulent drainage from the incision or localized inflammatory signs, e.g. swelling, erythema, or heat; and (ii) intraoperative findings compatible with infection and/or the presence of positive intraoperative cultures (one positive culture for pathogenic microorganisms and two or more for less virulent species, such as coagulase-negative staphylococci or *Cutibacterium acnes*). In addition, cases could present laboratory findings such as WBC count >10 000/mm^3, C-reactive protein >10 mg/L, or radiological findings (e.g. deep tissue collection or material loosening), supporting the diagnosis of infection. Microbiological diagnosis was allowed with positive intraoperative cultures and/or aspirates from punctures of deep collections guided by computed tomography, and/or blood cultures in cases of concomitant bacteraemia. The use of imaging tests for diagnosis was at the discretion of the treating team. Superficial and deep infections were defined in accordance with the criteria of the CDC[9] and cases with vertebral osteomyelitis met main diagnostic criteria according to literature.[10]

Data collection

Patients' medical histories were analysed, including any major risk factors for infection, with specific attention on the use of immunosuppressive, antiplatelet, or anticoagulant treatment. Comorbidities were reported using the Charlson Comorbidity Index.[11] Finally, we collected relevant data about the surgical procedure.

Medical and surgical management

The surgical treatment strategy and antibiotic scheme were planned by the treating clinicians, according to previous evidence.[5–8] Cases were classified according to the duration of the antibiotic therapy, i.e. in short courses when received for 4–6 weeks and long courses if received for more than 6 weeks. Two surgical strategies were considered: (i) DAIR, comprising the debridement of all necrotic tissue and thorough irrigation of the surgical site with pulse saline serum (6–9 L), with or without antiseptic solution (povidone–iodine or chlorhexidine) in accordance with the reference centre protocol, and closed-suction drains were used and maintained until drainage was less than 30–50 cc per day without exceeding 4–5 days; and (ii) debridement with total removal of spine instrumentation, with or without new arthrodesis. Minor removals of some loosened screws were considered as the DAIR strategy.

Follow-up and outcome

Patients were followed-up for at least 12 months after the end of antibiotic treatment. Failure was defined as: (i) primary failure, need for a new surgical debridement beyond 30 days from the initial, but before the end of antibiotic treatment because of uncontrolled symptoms or signs of infection with intraoperative samples growing the same microorganism; (ii) relapse, when symptoms or signs of infection reappeared after the end of antibiotic treatment and the same microorganism was obtained in surgical or tissue samples; (iii) superinfection, as new infection by a different pathogen appeared after antibiotic treatment of the initial one; (iv) death related to infection or its treatment; and (v) suppressive treatment because of difficulty controlling the infection. The need for new surgery due to mechanical problems or plastic surgery for wound coverage was not considered a failure if there was no microbiological or clinical evidence of infection.

Statistical analysis

Data were analysed with Stata 14.2 (Stata Corporation, USA). Categorical variables are described by counts and percentages, while means and SDs or medians and IQRs are used to summarize continuous variables. Comparisons between groups were performed with either the χ^2 test or Fisher's exact test for categorical variables, or the *t*-test or Mann–Whitney *U*-test for continuous variables, Bonferroni correction was applied in order

to control the inflation of Type I error. Kaplan–Meier curves and the log-rank test were used to compare the cumulative likelihood of failure between groups. A P value ≤ 0.05 was considered statistically significant.

For the study of risk factors for failure in early infection managed by DAIR, multivariate Cox regression models were built to estimate the unadjusted and adjusted hazard ratios (HRs and aHRs, respectively) with their 95% CIs. Clinically relevant variables associated with the outcome in the univariate analysis were employed in the multivariate model. The likelihood ratio test was utilized to obtain P values. Failure rates according to antibiotic treatment duration (4–6 weeks versus >6 weeks) were also evaluated. To minimize imbalances between patients receiving short or long treatment courses ($\leq$6 weeks versus >6 weeks), a propensity score-matching analysis was performed. The propensity score matching included factors that could potentially affect the decision of extending the antibiotic treatment beyond 6 weeks. Clinically relevant variables were introduced in the propensity model, together with baseline characteristics found to have a univariate association with antibiotic duration ($P < 0.1$). We performed 1:1 nearest neighbour matching without replacement with a maximum caliper of 0.1. We identified the variables resulting in an imbalance between the groups after matching ($P < 0.2$) and included these in subsequent Cox proportional hazards model as covariates.

Results

Comparative analysis of the different forms of IASI

During the study, 14 255 spinal instrumentation surgeries were performed at the participating centres, and the average rate of infection was 3.4% (range 1.2%–6.4%). Overall, 485 cases of infection were included, among which 74 were excluded because they were managed with antibiotics only. Thus, 411 cases were finally included for our analysis, most occurring in the first month after surgery ($n = 300$, 73%; this interval included the time between instrumentation surgery and the first infection control surgery), and fewer occurring in the second month ($n = 48$; 11.7%), third month ($n = 22$; 5.4%) and beyond ($n = 41$; 10%).

Regarding the clinical presentation (Table 1), wound inflammatory signs, fever and bacteraemia were most common in the first and second months, whereas fistula, mechanical deformity, implant loosening, or secondary vertebral osteomyelitis were more predominant from the third month.

Regarding the microbiology [Table 2 and Table S1 (Table S1 is available as Supplementary data at *JAC* Online)], Gram-negative bacilli due mainly to the Enterobacteriaceae group were most common overall ($n = 321$; 53.2%). However, this predominance was greatest in the first and second months (58.2% and 52.3%, respectively), with Gram-positive cocci presenting more frequently in the third month and beyond (79.2% and 77.8%, respectively). Among the cocci, *Staphylococcus aureus* ($n = 124$) accounted for 19%–20% in first and second months and 29%–33% in third month and beyond; additionally, there was an elevated percentage of coagulase-negative staphylococci and *C. acnes* in the latter group. Finally, the proportion of polymicrobial infections was higher in early IASI. Among the whole cohort there were only 11 cases (2.7%) without a microbiological diagnosis.

Besides the relationship between time from surgery to IASI and the microbiology, we also observed a potential relationship of both with the initial indication for surgery and the surgical site (Table 1). IASIs occurring in the first and second months were mainly related to degenerative problems on the lumbar spine in older patients, whereas those occurring in the third month and especially thereafter were mainly among younger patients submitted to surgery because of trauma or deformities, who require larger instrumentations and greater dorsal spine involvement.

Outcome of IASIs with a focus on cases managed with DAIR

The median follow-up of the whole cohort was 860 days (IQR 429–1369). Global failure for IASI, independent of the surgical strategy, occurred in 11.5% ($n = 47$) of cases and without differences among the diverse clinical forms (Table 1). Excluding those cases with failure because of death ($n = 5$) or suppressive treatment ($n = 2$), failures once antibiotic treatment was concluded occurred 67.5% ($n = 27$) during the first year, increasing to 87.5% ($n = 35$) in the second year of follow-up. The DAIR strategy was used most often in the first, second and third months after surgery, whereas implant removal was the main surgical strategy thereafter. Of note, the failure rate of DAIR ($n = 39$) did not differ between the first (10%) and second (13.5%) months (Figure 1), but cases had worse outcomes by the third month (23.1%) and beyond (30%) that clearly differed compared with cases in the first 2 months (Figure 1). In addition, among cases managed with DAIR, most of the failures were diagnosed after 2 years of follow-up (87.5%; $n = 28$).

Further analyses were performed with IASIs occurring in the first 2 months after surgery and managed with DAIR. Of 317 cases, there were 33 failures (10.4%): 16 relapses, 8 superinfections, 4 primary failures, 4 related deaths, and 1 with suppressive therapy (see Table S2). In the univariate analysis (Table 3), factors associated with failure were female sex, the presence of comorbidities measured by Charlson Score Index, immunosuppressive treatment, large instrumentation (>6 intervertebral levels), bacteraemia and polymicrobial infection. In particular, mixed polymicrobial infections with Gram-positive cocci (especially *S. aureus*) and Gram-negative bacilli had the highest failure rates among the polymicrobial infections. Of note, the use of irrigation with serum saline and antiseptic solution (73.7% of cases) was not associated with a different outcome. Female sex, Charlson Score, large instrumentations and polymicrobial infections retained their associations with higher failure rates (aHR, 2.35, 95% CI 1.02–5.37; aHR, 1.27, 95% CI 1.03–1.56; aHR, 2.63, 95% CI 1.15–5.97; aHR, 2.26, 95% CI 1.09–4.65, respectively) after adjusting for age, immunosuppressive treatment, the presence of bacteraemia and antibiotic treatment duration. Risk factors for failure with DAIR were also evaluated in those cases with deep infection with similar findings (Table S3).

There were 303 cases of IASI in which the duration of antibiotic treatment was evaluable. Most were treated with long antibiotic courses that lasted more than 6 weeks (74.9%, $n = 227$) rather than shorter courses of 4–6 weeks (25.1%, $n = 76$). Figure S1 shows median duration treatment and IQR for the whole cohort and both groups mentioned. Among cases receiving long-term antibiotics courses, more than half ($n = 151$; 66.5%) were treated for more than 8 weeks. The most widely used families of antibiotics were the β-lactams (88%), quinolones (73%) and lipo-glycopeptides (44.2%). Median duration of parenteral antibiotic therapy was 17 days (IQR 9–30), which differed between cases receiving shorter courses of antibiotics (12.5 days, IQR 7–20) and those with longer treatments (19 days, IQR 11–37; $P < 0.001$).

Table 1. Comparison of baseline characteristics, instrumentation, clinical features and surgical management by time of presentation

N = 411	First month, *N* = 300 (73%)	Second month, *N* = 48 (11.7%)	Third month, *N* = 22 (5.4%)	Beyond third month, *N* = 41 (10%)	*P* value[a]
Age (years), median (IQR)[d,e]	61.3 (49–71.5)	58.2 (47.6–70.9)	67.5 (37.4–73.2)	40.5 (18.4–65.7)	0.001
Women	163 (54.3)	22 (45.8)	13 (59.1)	24 (58.5)	NS
Obesity[e]	108 (46)	14 (30.4)	4 (25)	5 (16.1)	0.003
Diabetes mellitus	61 (20.3)	12 (25)	7 (31.8)	7 (17.1)	NS
Spine instrumentation surgery					
degenerative problems[e]	176 (58.7)	31 (64.6)	13 (59.1)	14 (34.2)	<0.001
trauma	45 (15)	3 (6.3)	6 (27.3)	6 (14.3)	
malignancies	22 (7.3)	4 (8.3)	0	2 (4.9)	
deformity problems	34 (11)	7 (14.6)	3 (13.6)	17 (41.5)	
other surgery indication[f]	24 (8)	3 (6.25)	0	2 (4.9)	
location on lumbar spine[e]	183 (61)	31 (64.6)	12 (54.6)	15 (36.6)	0.021
large fusions (>6 levels)[d,e]	48 (16.6)	8 (17)	2 (10)	16 (40)	0.003
revision surgery	68 (22.7)	16 (33.3)	4 (18.2)	8 (19.5)	NS
Diagnostic and clinical presentation					
inflammatory signs[c–e]	281 (93.7)	42 (87.5)	15 (68.2)	13 (31.7)	<0.001
surgical wound dehiscence[e,h]	151 (50.7)	24 (50)	9 (40.9)	7 (17.1)	0.001
purulent drainage[d,e]	249 (83.6)	37 (80.4)	14 (63.6)	6 (14.6)	<0.001
fistula[c,e,i]	4 (1.3)	3 (6.4)	3 (13.6)	17 (41.5)	<0.001
mechanical deformity[c,e]	5 (1.7)	1 (2.1)	4 (18.2)	11 (26.8)	<0.001
fever	140 (46.8)	22 (45.8)	6 (28.6)	10 (26.3)	0.048
bacteraemia	61 (20.3)	8 (16.7)	2 (9.1)	4 (9.8)	NS
vertebral osteomyelitis[b,c,e]	3 (1)	5 (10.4)	5 (22.7)	7 (17.1)	<0.001
implant loosening[e]	6 (2)	1 (2.1)	2 (9.1)	6 (14.6)	<0.001
Surgical treatment					
DAIR[b–e]	280 (93.3)	37 (77.1)	13 (59.1)	10 (24.4)	<0.001
material withdrawal[g]	20 (6.6)	11 (22.9)	9 (40.9)	31 (75.6)	
failure (all causes)	31 (10.4)	8 (16.7)	4 (18.2)	4 (9.8)	NS
failure with DAIR	28 (10)	5 (13.5)	3 (23.1)	3 (30)	NS

Data are presented as *n* (%) unless otherwise noted. NS, non-significant for *P* values >0.05.
[a]*P* value of the comparison between four groups.
[b]Significant differences between cases from the first and second months after applying the Bonferroni correction ($P \leq 0.05$).
[c]Significant differences between early cases (first and second months) and those from the third month after applying the Bonferroni correction ($P \leq 0.05$).
[d]Significant differences between cases from the third month and those from beyond the third month after applying the Bonferroni correction ($P \leq 0.05$).
[e]Significant differences between early cases and those from beyond the third month after applying the Bonferroni correction ($P \leq 0.05$).
[f]Pseudoarthrosis, osteoporotic fractures.
[g]With or without new arthrodesis.
[h]Surgical wound dehiscence was defined as the rupture or splitting open of a previously closed surgical incision site.[9]
[i]Fistula or sinus tract was defined as an abnormal channel of communication between the skin and the deeper implants of the spine once the surgical wound has completely healed.[30]

The use of long or shorter antibiotic therapies differed by participant centre and for particular difficult-to-treat situations (Table 4). Of note, failure rates among IASI cases due to *S. aureus* and treated with short antibiotic schemes were significantly higher (28.6% versus 10.3% in longer schemes, $P = 0.038$). There were no significant differences in failure rates between cases treated with short or long antibiotic courses (9.7% versus 7.9%, respectively; $P = 0.872$; Figure 1). In the propensity score-matched cohort (matching by age, Charlson Score, centre, immunosuppressive treatment, larger fusions, wound dehiscence, deep infections, bacteraemia, polymicrobial infection and *S. aureus* infection), we found no association between short treatment courses and failure (aHR 1.51; 95% CI, 0.45–5.04; $P = 0.503$; Tables 4 and 5).

Discussion

In the present work including what we believe is the largest series of IASI cases to date, we provided data to support the optimal timing of DAIR and the effectiveness of short antibiotic courses.

After surgery, 75% of IASIs presented in the first month, and the majority (90%) had presented by the end of the first 3 months. These findings are difficult to compare with previous studies, which

Table 2. Microbiological findings by time of presentation

	All isolates[a]	First month	Second month	Third month	Beyond third month	*P* value[b]
Gram-positives[c,d]	277 (45.9)	192 (40.9)	31 (47.7)	19 (79.2)	35 (77.8)	<0.001
Staphylococcus spp.[c,d]	191 (31.7)	130 (27.7)	22 (33.9)	14 (58.3)	25 (55.6)	<0.001
S. aureus	124 (20.6)	89 (19)	13 (20)	7 (29.2)	15 (33.3)	NS
coagulase-negative staphylococci[c,d,e]	67 (11.1)	41 (8.7)	9 (13.9)	7 (29.2)	10 (22.2)	0.001
Cutibacterium spp.[d,f]	27 (4.5)	15 (3.2)	3 (4.6)	2 (8.3)	7 (15.6)	<0.001
Gram-negatives[c,d]	321 (53.2)	273 (58.2)	34 (52.3)	4 (16.7)	10 (22.2)	<0.001
Enterobacteriaceae[c,d]	243 (40.3)	214 (45.6)	21 (32.3)	2 (8.3)	6 (13.3)	<0.001
P. aeruginosa	62 (10.3)	45 (9.6)	11 (16.9)	2 (8.3)	4 (8.9)	NS
Polymicrobial infections	135 (32.9)	114 (38)	12 (25)	2 (9.1)	7 (17.1)	0.002

Data are presented as number of isolates and percentage. NS, non-significant for *P* values >0.05.
[a]There was a total of 604 isolates in the IASI cases ($n = 411$); there were 11 cases without microbiological diagnosis.
[b]*P* value of the comparison between four groups. No differences were found in the remaining comparisons among groups after applying the Bonferroni correction unless indicated.
[c]Significant differences between early cases (first and second months) and those from the third month ($P \leq 0.05$).
[d]Significant differences between early cases and those from beyond the third month ($P \leq 0.05$).
[e]*Staphylococcus epidermidis*, $n = 63$; *Staphylococcus lugdunensis*, $n = 3$; *Staphylococcus capitis*, $n = 1$.
[f]*Cutibacterium acnes*, $n = 25$; *Cutibacterium granulosum*, $n = 1$; *Cutibacterium avidum*, $n = 1$.

mostly comprise small case series that focus on particular types of IASI. In our cohort, we noted that cases were very similar in the first 2 months with regards to age (older adults), site (lumbar spine) and the presence of inflammatory signs. By contrast, the remaining late IASIs, and especially those after the third month, more frequently involved younger patients requiring surgery for deformity or trauma, and in these, fistula, osteomyelitis and implant loosening were more common, which is consistent with earlier research.[12–14]

Our microbiological findings also support the differences between forms of IASI, showing that the earlier the infection, the more common are Enterobacteriaceae and polymicrobial infections. This pattern has been highlighted in other recent works.[6,8] In fact, an increased frequency of Gram-negative infection has been noticed[15] and associated with the lumbar location and colonization from the perineal area.[16,17] As is widely reported, *S. aureus* was the more frequent isolate in early infections,[18–20] but it was causing more late IASI cases where less virulent microorganisms, such as *C. acnes* or coagulase-negative staphylococci, were otherwise more relevant.[5,14] These findings reflect that, depending on the IASI, clinicians may be more used to dealing with a particular epidemiological setting.

Surgical management of early device-related infections can be performed successfully with DAIR.[5–7,18,19,21] In particular, DAIR for IASIs should aim to achieve vertebral fusion, and the removal of any spinal instrumentation can be delayed to avoid mechanical complications.[22] At this point, in addition to orthopaedic criteria, providing an accurate definition of early IASI may be essential for clinicians given that it can influence the decision about DAIR and affect the prognosis. However, the precise cut-off is still unclear, and the need to limit early infections within the first 30 days after surgery or to extend it to 90 days has been discussed widely.[3] Of interest, we did not observe significant differences in the outcome of IASI cases managed by DAIR in the first 2 months, which contrasted with the higher failure rates in late cases, although lower when comparing with other osteoarticular infections. Thus, we conclude that these results provide robust data for an accurate cut-off, allowing DAIR to be offered with a reasonable expectation of success within the first 2 months.

We identified risk factors for failure of the DAIR strategy that depended on host (female sex, Charlson Score), surgical (large instrumentation) and virulence (polymicrobial infections) factors, which were also valid for the subgroup of patients with deep infections. To our knowledge, limited data exist about the risk factors for failure with DAIR, but this seems to be in line with our results. Polymicrobial infection and long instrumentations were previously identified as risk factors in a study of early and late infections.[23] Other research has also shown polymicrobial infection to be associated with worse outcomes, together with a previous history of smoking, extended vertebral arthrodesis and certain etiologies (Enterobacteriaceae and Enterococci).[7,24] Lastly, most of the failures once antibiotic treatment was concluded occurred in the first 2 years (86%, $n = 24$), so it seems appropriate to recommend a minimum 2-year follow-up for these patients.

There are no clear recommendations about the length of antibiotic therapy for IASI, and in particular, those managed by DAIR.[25] Classically, prolonged therapy from 3 to 6 months was advocated,[6,19,24,26,27] but recent studies have reported the efficacy of shorter regimens lasting 6–8 weeks when infections occur in the first month after surgery.[7,8] Shorter durations of antibiotic therapy have shown good outcomes in several scenarios, including bone and joint infections, with regards antibiotic consumption, adverse effects and ecological pressures on multidrug resistance.[28,29]

Supporting these recent works,[7,8] we found similar outcomes for early IASIs managed by DAIR with short (4–6 weeks) or long (>6 weeks) courses (success rates of 92.1% and 90.3%, respectively). Moreover our results show similar success rates to those reported in the literature, with also short course of 6 weeks of antibiotic therapy,[7] and when longer antibiotic treatments were evaluated.[5,6,19]

We noted that the prescription of longer rather than shorter courses differed by centre, instrumentation extent, wound

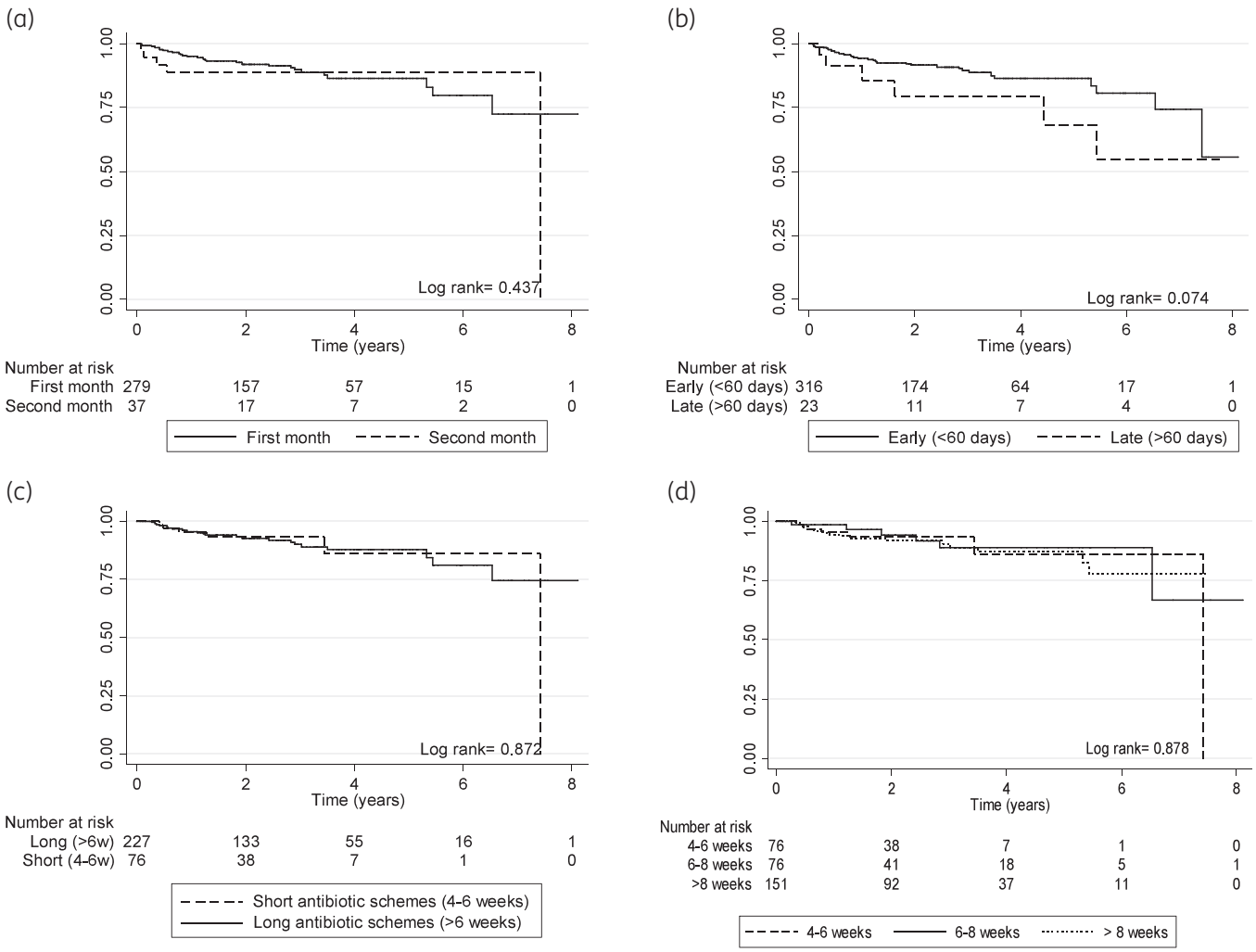

Figure 1. Kaplan–Meier survival estimates of surgical management by DAIR for different time of presentation and antibiotic schemes in IASI. (a) Prognosis of DAIR in Months 1 and 2 (early group). (b) Prognosis of DAIR in Early versus Delayed and Late infections. (c) Short versus Long antibiotics schemes. (d) Comparison between three antibiotic schemes: 4–6 weeks, 6–8 weeks, and >8 weeks. DAIR, debridement, antibiotics and implant retention; IASI, infection after spine instrumentation.

dehiscence and infection depth. After propensity score matching, failure rates were no higher when cases were managed with short courses of antibiotics. It was notable that vertebral osteomyelitis secondary to IASI occurred anecdotally in the first 2 months, and this fact may also help clinicians to feel more comfortable with the use of short treatments. Indeed, our data should be interpreted with caution in difficult scenarios, such as when risk factors for failure are present or when the infection is caused by *S. aureus*. Further studies must better establish if specific populations with IASI benefit from prolonging the antibiotic schedules beyond 4–6 weeks, and indeed, if the cut-off of 6–8 weeks is preferable in those difficult scenarios. This is relevant because the latest evidence and our own results agree that longer treatments offer no benefits[7,8] and because prolonged antibiotic therapy could increase other adverse effects.[28,29]

The main limitations of this study result from its retrospective design. In addition, a comparatively small number of cases was available for some of the clinical forms defined as those from the third month onwards, which means that our conclusions are speculative. A detailed analysis of the prognosis or etiology based management was beyond the scope of the present work. Despite these limitations, the strengths of our study are that it includes the largest known cohort of IASIs and that all cases were followed by multidisciplinary teams with broad experience in managing these infections.

In conclusion, a global perspective of IASI indicates that a cut-off between early and late cases appears to be 2 months after surgery. Early IASI cases can be successfully managed by DAIR with shorter antibiotic courses than classically recommended. However, clinicians should take care in cases with higher comorbidities, large vertebral instrumentations, bacteraemia, polymicrobial infection and *S. aureus* infection, which were associated with treatment failure. We believe that the information provided in this research can be useful for

Table 3. Risk factors for failure in early infections managed by DAIR ($n = 317$)

	Success, $N = 284$ (89.6%)	Failure, $N = 33$ (10.4%)	Univariate analysis		Multivariate analysis	
			HR (95% CI)	*P*	adjusted HR (95% CI)	*P*
Age (years), median (IQR)	61.1 (47.3–70.7)	63.4 (52.6–71.6)	1.01 (0.99–1.04)	NS	1.01 (0.99–1.04)	NS
Sex (women)	150 (53)	24 (72.7)	2.24 (1.04–4.82)	0.030	2.35 (1.02–5.37)	0.035
Charlson Score, median (IQR)	0.5 (0–2)	1 (0–2)	1.20 (1.01–1.41)	0.052	1.27 (1.03–1.56)	0.033
Obesity	98 (43.8)	11 (37.9)	0.87 (0.41–1.87)	NS		
Diabetes	62 (21.9)	6 (18.2)	0.87 (0.36–2.13)	NS		
Cardiopathy	30 (10.6)	3 (9.1)	1.07 (0.32–3.53)	NS		
COPD	33 (11.7)	4 (12.1)	1.21 (0.42–3.48)	NS		
Immunosuppressive treatment	23 (8.1)	7 (21.2)	3.66 (1.56–8.58)	0.009	2.06 (0.80–5.32)	NS
Surgical indication						
degenerative	168 (59.4)	16 (48.5)	1	NS		
trauma	41 (14.5)	5 (15.2)	1.38 (0.51–3.78)			
malignancies	22 (7.8)	4 (12.1)	1.92 (0.64–5.82)			
deformity problems	30 (10.6)	5 (15.2)	1.52 (0.55–4.16)			
others	22 (7.7)	3 (9.1)	1.43 (0.41–4.90)			
revision surgery	68 (24)	10 (30.3)	1.17 (0.55–2.47)	NS		
large fusions of >6 levels	39 (14.4)	11 (33.3)	2.36 (1.13–4.91)	0.031	2.63 (1.15–5.97)	0.027
Diagnosis and clinical manifestation						
surgical wound dehiscence	144 (51.3)	22 (66.7)	1.69 (0.82–3.52)	NS		
deep infection	229 (80.9)	27 (81.8)	0.98 (0.41–2.39)	NS		
bacteraemia	50 (17.7)	12 (36.4)	2.18 (1.07–4.45)	0.041	2.23 (0.98–5.09)	0.064
Microbiology						
S. aureus	76 (26.9)	13 (39.4)	1.48 (0.74–2.99)	NS		
monomicrobial by *S. aureus*	61 (80.3)	5 (38.5)	1	0.016		
polymicrobial involving *S. aureus*	15 (19.7)	8 (61.5)	3.9 (1.27–12.01)			
Enterobacteriaceae	154 (54.4)	22 (66.7)	1.81 (0.87–3.75)	NS		
P. aeruginosa	46 (16.3)	6 (18.2)	1.02 (0.42–2.49)	NS		
polymicrobial infections	99 (35)	19 (57.6)	2.46 (1.21–4.99)	0.011	2.26 (1.09–4.65)	0.026
Antimicrobial treatment						
use of antiseptic solution in debridement surgery	193 (73.7)	23 (69.7)	0.95 (0.45–1.99)	NS		
long antibiotic courses (>6 weeks)	204 (74.5)	24 (72.7)	1			
short antibiotic courses (4–6 weeks)	70 (25.6)	9 (27.3)	1.43 (0.66–3.11)	NS	1.86 (0.82–4.22)	NS

Data are presented as *n* (%) unless otherwise noted. DAIR, debridement, antibiotics and implant retention; NS, non-significant for *P* values >0.1, for the multivariate analysis clinically relevant variables and those with *P* value <0.1 were taken into account.

the management of IASIs, but that further studies will be needed to define the impact of specific antibiotic treatments, and cases that may benefit from prolonging their antibiotic therapy.

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Table 4. Differences by length of antibiotic treatment in early cases managed with DAIR ($n = 303$)

	Overall cohort			Propensity score-matched cohort		
	long antibiotic schemes, >6 weeks, $N = 227$ (74.9%)	short antibiotic schemes, 4–6 weeks, $N = 76$ (25.1%)	P value[a]	long antibiotic schemes, >6 weeks, $N = 67$ (50.4%)	short antibiotic schemes, 4–6 weeks, $N = 66$ (49.6%)	P value[b]
Baseline characteristics and comorbidity						
age (years), median (IQR)	61.2 (49.4–70.8)	59.7 (43.4–70.3)	NS	57 (40–64.5)	62.6 (49.3–70.7)	NS
sex (women)	126 (55.5)	43 (56.6%)	NS	33 (49.3%)	36 (54.6)	NS
Charlson Score, median (IQR)	0 (0–2)	1 (0–1)	NS	0 (0–1)	1 (0–1)	NS
obesity	78 (43.3)	26 (41.9)	NS	20 (39.2)	23 (41.1)	NS
diabetes	46 (20.3)	17 (22.4)	NS	12 (17.9)	16 (24.2)	NS
cardiopathy	23 (10.1)	9 (11.8)	NS	7 (10.5)	9 (13.6)	NS
COPD	26 (11.5)	11 (14.5)	NS	5 (7.5)	10 (15.2)	NS
immunosuppressive treatment	21 (9.3)	7 (9.2)	NS	6 (9)	6 (9.1)	NS
Surgical indication						
degenerative	128 (56.4)	50 (65.8)	NS	37 (55.2)	44 (66.7)	NS
trauma	36 (15.9)	8 (10.5)		9 (13.4)	6 (9.1)	
malignancies	18 (7.9)	5 (6.6)		3 (4.5)	5 (7.6)	
deformity problems	26 (11.5)	7 (9.2)		11 (16.4)	5 (7.6)	
others	19 (8.4)	6 (7.9)		7 (10.5)	6 (9.1)	
revision surgery	54 (23.8)	23 (30.3)	NS	14 (20.9)	18 (27.3)	NS
large fusions of >6 levels	40 (18.3)	6 (8.3)	0.045	16 (23.9)	5 (7.6)	0.010
Diagnosis and clinical manifestation						
dehiscence of the surgical wound	127 (56.4)	30 (39.5)	0.010	31 (46.3)	27 (40.9)	NS
deep infection	200 (88.1)	49 (64.5)	<0.001	54 (80.6)	47 (71.2)	NS
bacteraemia	49 (21.6)	10 (13.2)	NS	12 (17.9)	10 (15.2)	NS
Microbiology						
S. aureus	69 (30.4)	19 (25)	NS	23 (34.3)	18 (27.3)	NS
Enterobacteriaceae	126 (55.5)	42 (55.3)	NS	38 (56.7)	35 (53)	NS
P. aeruginosa	39 (17.2)	13 (17.1)	NS	12 (17.9)	11 (16.7)	NS
Polymicrobial infections	86 (37.9)	27 (35.5)	NS	24 (35.8)	23 (34.9)	NS
Failure	22 (9.7)	6 (7.9)	NS	5 (7.5)	6 (9.1)	NS
primary failure or due to relapse	14 (63.6)	6 (100)	NS	4 (80)	6 (100)	NS
failure due to superinfection	8 (36.4)	0 (0)		1 (20)	0	

Data are presented as *n* (%) unless otherwise noted. DAIR, debridement, antibiotics and implant retention; NS, non-significant for *P* values >0.05.
[a]Difference when comparing cases treated with long schemes of antibiotic versus short schemes according to the different risk factors for failure with DAIR management in the whole cohort.
[b]Comparison of long schemes of antibiotic versus short schemes in the matched cohort after propensity score matching.

Table 5. HR for DAIR failure associated with the use of short courses of antibiotic therapy (4–6 weeks) as estimated using different analyses

Model	HR	95% CI	P
Overall cohort ($N = 317$)			
unadjusted	1.43	0.66–3.11	NS
Cox regression	1.86	0.82–4.22	NS
adjusted by PS	1.58	0.57–4.42	NS
Propensity matched cohort ($n = 133$)			
unadjusted	1.53	0.46–5.07	NS
Cox regression[a]	1.51	0.45–5.04	NS

NS, non-significant for *P* value >0.05; PS, propensity score.
[a]Adjusted by imbalanced variables in the propensity score-matched cohort ($P < 0.2$); age, COPD and number of levels fused.

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Transparency declarations

None to declare.

Supplementary data

Tables S1 to S3 and Figure S1 are available as Supplementary data at *JAC* Online.

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