# The long-term time course of septic arthritis

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Cite this article: *Bone Jt Open* 2024;5(9): 785–792.

DOI: 10.1302/2633-1462.59.BJO-2024-0048.R1

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## Aims

The aims of this study were to: 1) report on a cohort of skeletally mature patients with native hip and knee septic arthritis over a 14-year period; 2) to determine the rate of joint failure in patients who had experienced an episode of hip or knee septic arthritis; and 3) to assess the outcome following septic arthritis relative to the infecting organism, whether those patients infected by *Staphylococcus aureus* would be more likely to have adverse outcomes than those infected by other organisms.

## Methods

All microbiological samples from joint aspirations between March 2000 and December 2014 at our institution were reviewed in order to identify cases of culture-proven septic arthritis. Cases in children (aged < 16 years) and prosthetic joints were excluded. Data were abstracted on age at diagnosis, sex, joint affected (hip or knee), type of organisms isolated, cause of septic arthritis, comorbidities within the Charlson Comorbidity Index (CCI), details of treatment, and outcome.

## Results

A total of 142 patients were confirmed to have had an episode of septic arthritis in a native hip (n = 17) or knee joint (n = 125). *S. aureus* accounted for 57.7% of all hip and knee joint infections. There were 13 inpatient deaths attributed to septic arthritis. The median age of the patients who died was 77.5 (46.9 to 92.2) and their median age-adjusted CCI was 8 (6 to 12). A failure of the joint occurred in 26 knees (21%) and nine hips (53%). Of the knee joints infected by *S. aureus* (n = 71), 23 knees (32%) went into failure of joint, whereas of those infected by other organisms (n = 54), only three knees (6%) failed.

## Conclusion

Based on our study findings, hip and knee septic arthritis long-term outcomes were substantially worse than their immediate outcome suggested. Failure of knee joint is 6.1 times more likely to occur in those infected with *S. aureus*.

## Take home message

- Septic arthritis outcomes were substantially worse than previously demonstrated in the literature postulated to be due to secondary damage to articular cartilage caused by the initial infection.
- *Staphylococcus aureus* was associated with a considerably higher level of joint damage compared to other organisms.
- Early and aggressive treatments of septic arthritis to protect the articular cartilage is inferred.

## Introduction

The advent of antibiotics has revolutionized the management and outcome of septic arthritis.[1,2] In the pre-antibiotic era, to control the infection and to reduce the mortality of septic arthritis, massive, debilitating, but potentially life-saving surgical treatments were employed.[3,4] Antibiotics have been instrumental in improving these initial outcomes so successfully that there has not been a perceived need for any further major advances in the treatment for septic arthritis since their introduction. The majority of cohort studies investigating septic arthritis consider a treatment success to be the resolution of infection, and in today's antibiotic era most patients appear to have a satisfactory outcome. There have, however, been few studies that have examined

**Table I.** Causative organisms in native knee or hip septic arthritis.

| Group | Organism isolated | Joint affected | | Total, n (%) |
|---|---|---|---|---|
| | | Hip, n | Knee, n | |
| | All organisms | 17 | 125 | 142 (100) |
| 1 | Methicillin-sensitive *S. aureus* | 9 | 67 | 76 (53.5) |
| | Methicillin-resistant *S. aureus* | 2 | 4 | 6 (4.2) |
| | **Total Group 1** | **11** | **71** | **82 (57.7)** |
| 2 | Other staphylococcal species | 1 | 10 | 11 (7.7) |
| | *βhaemolytic streptococci* | 0 | 12 | 12 (8.5) |
| | *Streptococcus pneumoniae* | 0 | 2 | 2 (1.4) |
| | Other streptococci | 1 | 2 | 3 (2.1) |
| | *Enterococci* | 0 | 6 | 6 (4.2) |
| | *Neisseria species* | 1 | 5 | 6 (4.2) |
| | Mixed growth | 2 | 5 | 7 (4.9) |
| | Other | 1 | 12 | 13 (9.2) |
| | **Total Group 2** | **6** | **54** | **60 (42.3)** |

*S. aureus*, *Staphylococcus aureus*.

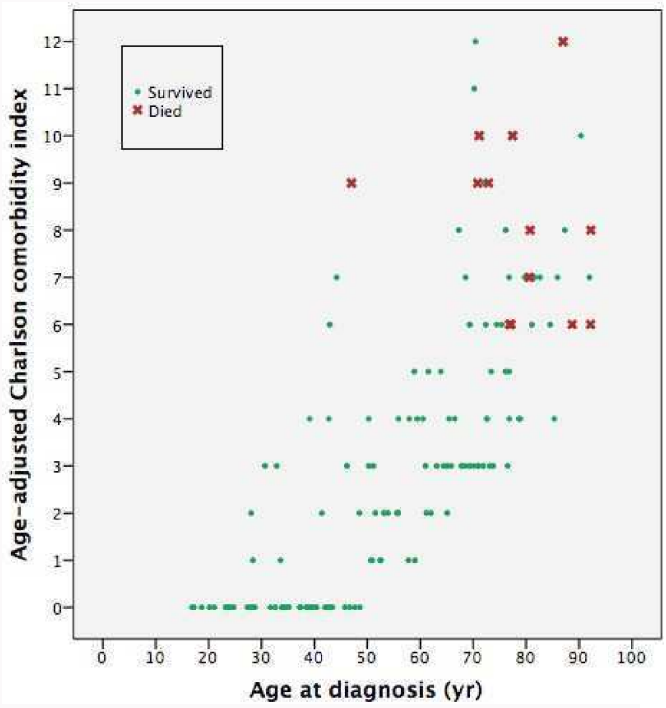


**Fig. 1**
Scatterplot of patients according to age at diagnosis and Charlson Comorbidity Index. There was generally higher morbidity and older age in those who died as a result of septic arthritis.

**Table II.** Causes of knee sepsis initiated through the direct route.

| Cause | Group 1 (*Staphylococcus aureus*), n | Group 2 (Other), n | Total, n |
|---|---|---|---|
| Fracture fixation | 7 | 1 | 8 |
| Arthroscopy | 16 | 9 | 25 |
| Penetrating trauma | 2 | 1 | 3 |
| Therapeutic injection | 5 | 2 | 7 |
| Direct spread from contiguous source | 4 | 0 | 4 |
| **Total** | **34** | **13** | **47** |

the functional loss of an infected joint over a long time period.[5-8] Of these, a smaller number of studies have suggested that there may be a high proportion of patients who go on to experience symptoms of osteoarthritis (including pain, stiffness, and/or limitation of function) in their infected joints. Limited conclusions can be drawn from these studies because of either short follow-up periods,[7,9,10] low patient numbers,[11] or suboptimal assessment methods.[5,11,12] Despite this, at least one animal study has indicated that significant damage occurs to the cartilage during septic arthritis, and it is possible that this would not be recognized at the time the infection had resolved.[13] If the damage subsequently led to secondary degeneration of the joint, then the outcomes in clinical studies could be far worse than reported if cohorts were followed up for longer. Moreover, *Staphylococcus aureus* has been shown to be a highly virulent organism that produces exotoxins which lead to cartilage destruction and possibly poorer outcomes.[14] A recent in vivo study has shown that haemolysin (Hla) toxin is a major cause of chondrocyte death in murine joints, which may lead to subsequent joint damage.[15]

## Methods

An ethical application for this study was submitted to the South East Scotland Research Ethics Service, who kindly advised that formal ethical approval was not required.

### Inclusion and exclusion criteria

Periprosthetic joints were excluded and only cases of septic arthritis in original/native joints were included. The effect of sepsis on the growing physis was not the focus of this study, and therefore only skeletally mature patients aged over 16 years (the age of legal consent in Scotland) were included.

### Identification of patients

Within NHS Lothian, all microbiological samples are coded and recorded in a universal database that was initiated in the year 2000. There were 107,601 specimen results identified between March 2000 and December 2014.

We retrieved all microbiology specimens in which any bacteria had been isolated from any culture, leaving 5,729 results. Removal of results that did not correspond to a potential joint aspirate (for example, specimens from the breast or neck) produced 2,805 results. After reviewing the patients' electronic records to remove periprosthetic joint infection and alternative pathology (infected bursitis or soft-tissue abscess), a total of 225 cases of native joint septic arthritis were identified. Based on these cases, we then isolated the knee and hip septic arthritis cases (n = 142).

**Table III.** Univariate analysis of risk factors for inpatient death following septic arthritis.

| | | Inpatient death, n (%) | | | | | |
|---|---|---|---|---|---|---|---|
| **Risk of death** | | **No** | **Yes** | **Total %** | **Odds ratio** | **95% CI** | **p-value** |
| **Condition** | | | | | | | |
| *Staphylococcus aureus* as cause | No | 55 (91.7) | 5 (8.3) | 60 | 1.000 | | |
| | Yes | 74 (90.2) | 8 (9.8) | 82 | 1.189 | 0.369 to 3.834 | 0.772 |
| Cardiac failure | No | 111 (94.9) | 6 (5.1) | 117 | 1.000 | | |
| | Yes | 18 (72.0) | 7 28.0) | 25 | 7.194 | 2.170 to 23.857 | 0.001 |
| Vascular compromise | No | 114 (93.4) | 8 (6.6) | 122 | 1.000 | | |
| | Yes | 15 (75.0) | 5 (25.0) | 20 | 4.750 | 1.374 to 16.419 | 0.014 |
| Diabetes | No | 113 (91.9) | 10 (8.1) | 123 | 1.000 | | |
| | Yes | 16 (84.2) | 3 (15.8) | 19 | 2.119 | 0.526 to 8.527 | 0.291 |
| Immunocompromise | No | 122 (93.1) | 9 (6.9) | 131 | 1.000 | | |
| | Yes | 7 (63.6) | 4 (36.4) | 11 | 7.746 | 1.905 to 31.495 | 0.004 |
| Active cancer | No | 121 (92.4) | 10 (7.6) | 131 | 1.000 | | |
| | Yes | 8 (72.7) | 3 (27.3) | 11 | 4.537 | 1.038 to 19.840 | 0.045 |
| Dialysis | No | 126 (93.3) | 9 (6.7) | 135 | 1.000 | | |
| | Yes | 3 (42.9) | 4 (57.1) | 7 | 18.667 | 3.612 to 96.481 | < 0.001 |
| Charlson Comorbidity Index | Per unit increase | 369 (77.7) | 106 (22.3) | 475 | 1.880 | 1.407 to 2.510 | < 0.001 |
| Age at diagnosis, yrs | Per year | 6,993.9 (87.3) | 1,014.72 (12.7) | 8,008.6 | 1.103 | 1.043 to 1.166 | 0.001 |

### Data abstracted

The electronic medical records were examined in a structured fashion using a standard proforma and the following were abstracted: age at diagnosis, sex, organism isolated, cause of septic arthritis, route of infection, comorbidities within the Charlson Comorbidity Index (CCI),[16,17] details of treatment, and outcomes.

Medical notes were reviewed for comorbidities at the time of septic arthritis, which was then used to calculate the age-adjusted CCI. The CCI is a method of predicting mortality by classifying or weighting comorbid conditions for use in longitudinal studies.[18] The higher the sum of all of the scores, the more likely the predicted outcome will result in mortality.[17]

Treatments for septic arthritis were coded as serial joint aspirations, arthroscopic washout, or open washout. Septic arthritis was considered to have contributed to death where it was listed as one of the causes on the death certificate and occurred during the same hospital admission. Patients who had undergone an excision arthroplasty, total joint replacement (TJR), surgical arthrodesis, or natural ankylosis were recorded. Patients who had been recommended a TJR, and those with chronic infection such as a secondary osteomyelitis, were also considered to be a failure of the joint. Patients who had significant pain, stiffness, functional limitation, or recurrence of infection on follow-up were considered failure of the joint and offered surgical intervention. Patients who had attended for a medical review without recommendation for surgical intervention were not considered as a failure of the joint.

### Statistical analysis

For the data analysis, patients were allocated to Group 1 (caused by *S. aureus*) or Group 2 (caused by any other organism). Statistical analysis was performed using SPSS Statistics v. 21 for Mac (IBM, USA). Chi-squared tests were used for comparison of nominal data between the groups, and the independent-samples *t*-test or Mann-Whitney U tests were used for continuous variables. Univariate predictors of inpatient death and failure of the joint were analyzed using a binomial logistic regression model, and multivariate predictors were inputted into a forward stepwise regression model. For all tests the significance level was set at $p < 0.05$. Joint survival with 95% CIs was calculated according to the Kaplan-Meier survivorship analysis using Graphpad Prism v. 5.0 for Mac (GraphPad Software, USA).

## Results

### Culture-positive hip or knee septic arthritis

A total of 142 patients had an episode of septic arthritis in a native hip (n = 17) or knee (n = 125) joints. The infecting organisms were divided into two study groups (*S. aureus* vs others, Table I) given that *S. aureus* is the most common pathogen in adult acute septic arthritis and also the predominant producer of α haemolysin.[19]

There were 82 patients (59 males, 72%) infected by *S. aureus* (Group 1) and 60 patients (40 males) infected by other organisms (Group 2). The median age at diagnosis for Group 1 (*S. aureus*) was 53.1 (17.1 to 92.2) and for Group 2 (other organisms) was 61.8 (16.9 to 92.2) with no significant difference between the groups ($p = 0.307$).

**Table IV.** Multivariate logistic regression for risk of inpatient death following septic arthritis.

| | Estimate | Standard error | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| Age at diagnosis per year | 0.101 | 0.032 | 0.002 | 1.106 | 1.039 to 1.177 |
| Dialysis impairment | 2.754 | 0.992 | 0.006 | 15.713 | 2.247 to 109.858 |
| Constant | -9.571 | 2.472 | 0.000 | 0.000 | |

For each year increase in age, the likelihood of death secondary to septic arthritis increased by 1.1%. The risk of death was 15 times higher in the presence of dialysis.

**Table V.** Outcomes following septic arthritis categorized into those that were deemed to constitute a failure of the joint and those that were not.

| Outcome | | Group 1 (*Staphylococcus aureus*), n (%) | | Group 2 (Other organisms), n (%) | |
|---|---|---|---|---|---|
| | | **Knee** | **Hip** | **Knee** | **Hip** |
| | Arthroplasty (TJR) | 8 (35) | 2 (29) | 1 (33) | 0 |
| | Excision arthroplasty | 0 | 5 (71) | 0 | 1 (50) |
| | Arthrodesis/ankylosis | 3 (13) | 0 | 0 | 0 |
| | Waiting list for TJR | 4 (17) | 0 | 1 (33) | 0 |
| | Not well enough for TJR | 3 (13) | 0 | 0 | 0 |
| | "Too young" for TJR | 3 (13) | 0 | 0 | 1 (50) |
| | Recurrence of infection/osteomyelitis | 2 (8) | 0 | 1 (33) | 0 |
| Failure of the joint | **Total (n = 35)** | **23 (100)** | **7 (100)** | **3 (100)** | **2 (100)** |
| | Inpatient death | 7 (14) | 1 (25) | 5 (10) | 0 |
| | Outpatient death with no reported joint problems | 9 (19) | 1 (25) | 6 (12) | 1 (25) |
| | Had formal follow-up and no problems recorded | 3 (6) | 0 | 0 | 0 |
| | Mobility limited secondary to other health concern | 4 (8) | 0 | 0 | 0 |
| | Reported reduction in activities or increase in pain | 13 (27) | 1 (25) | 8 (16) | 0 |
| | No subsequent contact after initial post-sepsis review | 12 | 1 (25) | 32 (63) | 3 (75) |
| Not a failure of the joint | **Total (n = 107)** | **48 (100)** | **4 (100)** | **51 (100)** | **4 (100)** |

The outcome for patients from Group 1 (*Staphylococcus aureus* infection) was much worse than those from Group 2 (other organisms) for both knee and hip joint septic arthritis.
TJR, total joint replacement.

### Comorbidities

The mean age-adjusted CCI for Group 1 was 3.33 (SD 3.07; 0 to 12) and for Group 2 was 3.37 (SD 3.14; 0 to 12). There was no statistical difference between groups (p = 0.941) for the overall CCI. The only statistically significant difference between the groups in relation to individual comorbidities was an increased number of patients from Group 1 who were immune-compromised (p = 0.020).

### Route of infection

All cases of hip septic arthritis were due to haematogenous spread, with four of these cases secondary to intravenous drug use. There were 78 cases of knee septic arthritis caused by haematogenous spread and 47 by direct spread. The various causes of direct spread in knee septic arthritis are presented in Table II. The percentage of cases caused by direct spread was statistically higher in Group 1 than Group 2 (p = 0.002, chi-squared test).

### Treatments

A total of 94 patients were treated with arthroscopic washout with standard normal saline, 16 had open washout, and the remaining 32 underwent serial aspiration. The time to washout (data available for 60 patients) from the presentation was 2.1 days (SD 1.7; 0 to 8). The mean number of washouts (data for 72 patients) was 1.9 (SD 1.3; 1 to 6). There was no statistical difference (p = 0.325) between the treatments of patients from Group 1 compared to those from Group 2.

### Inpatient deaths

There were 13 inpatient deaths (9.1%) in nine males and four females attributed to septic arthritis (eight were from Group 1 (*S. aureus*) and five from Group 2 (other organisms)). These occurred in 12 patients with knee septic arthritis and one with hip septic arthritis. The median age of the patients who died was 77.5 years (46.9 to 92.2) and their median age-adjusted CCI was 8 (6 to 12). The relationship of age and comorbidity to mortality in septic arthritis is illustrated in Figure 1.

The median time from presentation to death was 20.5 days (0 to 159). All cases of septic arthritis in those who died were acquired via the haematogenous route. Six patients had arthroscopic washouts, and seven were treated with serial aspiration.

Univariate analysis of factors affecting risk of death is presented in Table III.

Based on the results of univariate analysis, a forward stepwise multivariate logistic regression was performed to ascertain the effects of age at diagnosis, dialysis, cardiac failure, vascular compromise, immunosuppression, and active cancer on the likelihood that patients would die from septic arthritis. The logistic regression model was statistically significant (p < 0.005). Of the five predictor variables, only two were statistically significant and included in the model, which were age at diagnosis and dialysis (Table IV).

### Failure of the joint

A failure of the joint occurred in 26 knees and nine hips, as detailed in Table V. A further 22 patients reported either decreased function or increased pain in the affected joint during a subsequent clinical visit.

The outcome of septic arthritis in native hip joints did particularly badly, with 9/17 patients going on to a failure of the joint (an example is shown in Figure 2). Resection arthroplasty was required in six of these cases due to

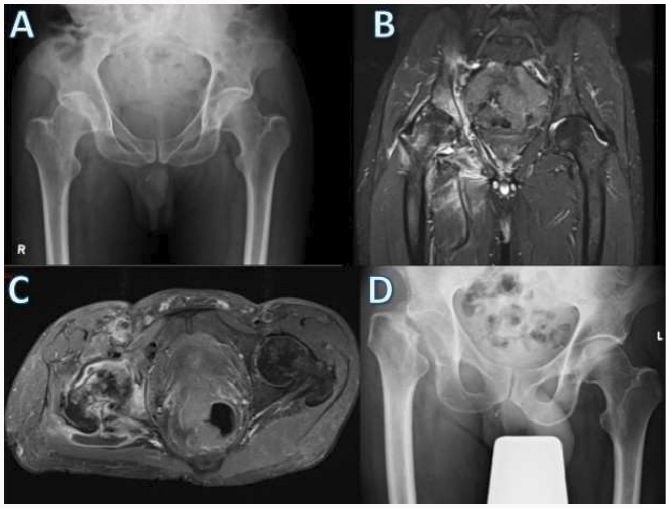


**Fig. 2**
Sequalae of hip sepsis example. a) Initial (total anteroposterior (AP)) pelvis radiograph of 49-year old female at presentation. b) Coronal slice and axial slice. c) Taken from an MRI performed at the same time, demonstrating signal change in the right femoral head indicating bone involvement. d) Postoperative AP radiograph following an excision arthroplasty performed to control the infection.

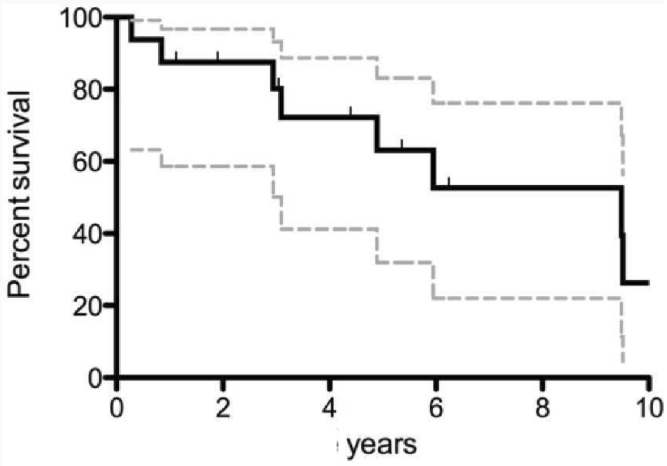


**Fig. 4**
Kaplan-Meier joint survival analysis following septic arthritis of the hip. At one year, the mean survival of hip joints was 87.5% (95% CI 58.6 to 96.7) based on 15 subjects at risk, and by five years was 63.1% (95% CI 31.944 to 83.115) based on eight subjects at risk.

the development of osteomyelitis and failure to control the infection.

### Kaplan-Meier survival curves

Knee joint survival following septic arthritis was calculated using Kaplan-Meier survival analysis. The 13 patients who died as a direct result of septic arthritis were excluded from the analysis, leaving 113 with knee septic arthritis (Figure 3) and 16 with hip septic arthritis (Figure 4). Patients were censored following their most recent follow-up, whether death had occurred or not. Failure of the joint for any of the reasons outlined in the Methods was considered as an event. The time at which the event occurred was calculated in years.

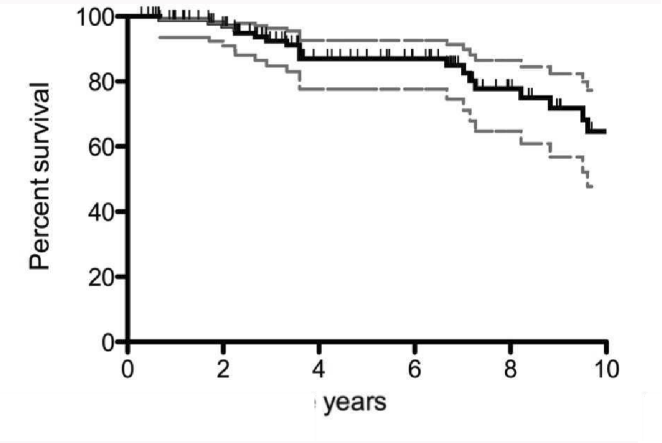


**Fig. 3**
Kaplan-Meier joint survival analysis following septic arthritis of the knee. Mean survival of the knee joint at five years was 88.3% (95% CI 79.2 to 93.6) with 53 subjects at risk at this time, and at ten years was 65.5% (95% CI 48.4 to 78.2) with 18 subjects at risk at this time.

### Risk factors for failure of the joint

Univariate risk factors for failure of the joint are presented in Table VI.

A forward stepwise multivariate logistic regression was performed to ascertain the effects of a pre-existing arthritic condition, *S. aureus* as causative organism and hip versus knee infection on the likelihood of developing a failure of the joint. The logistic regression model was statistically significant ($p < 0.001$). All the predictor variables were statistically significant and included in the model (as shown in Table VII).

Failure was 3.2 times higher in patients with pre-existing osteoarthritis, 6.1 times higher if the infecting organism was *S. aureus,* and 7.2 times higher if it involved the hip rather than the knee.

## Discussion

Our results show that mortality rate is high following septic arthritis with an initial death rate of 9.1% in this large cohort study. Furthermore, mortality following septic arthritis was more commonly seen in elderly patients with a high number of comorbidities. All the patients who died had an age-adjusted CCI score of 6 or higher, indicating that they all had severe comorbidities.

For every unit increase in CCI score, odds of inpatient death was 1.88 times more likely. These results correlate with those of Weston et al,[7] who found that age greater than 65 years was associated with increased mortality. Weston et al[7] did not, however, investigate dialysis as a predictor of inpatient death, which was found to be significant (odds ratio of 15.7) in our study. This concurs with the findings of Gupta et al,[20] who found impaired renal function in 7/8 patients who died of septic arthritis, compared to only 14/67 who survived, indicating that renal dysfunction is a poor prognostic sign in septic arthritis.[20] These studies indicate that particular attention should be paid to patients on haemodialysis as they have a high risk of inpatient mortality. Interestingly, in a small series of 15 patients who developed septic arthritis while being treated with haemodialysis for renal failure, Al-Nammari et al[21] only reported one death as a result of the infection,

**Table VI.** Univariate analysis for risk factors predictive of failure of the joint.

| Risk of poor outcome | | Poor local outcome, % | | Odds ratio | 95% CI | p-value |
|---|---|---|---|---|---|---|
| **Condition** | | **No** | **Yes** | | | |
| Pre-existing arthritic condition | No | 75 | 17 | 1.000 | | |
| | Yes | 32 | 18 | 2.582 | 1.136 to 5.421 | 0.023 |
| *Staphylococcus aureus* as causative organism | No | 55 | 5 | 1.000 | | |
| | Yes | 52 | 30 | 6.346 | 2.289 to 17.596 | < 0.001 |
| Hip joint affected | No | 99 | 26 | 1.000 | | |
| | Yes | 8 | 9 | 4.284 | 1.505 to 12.189 | 0.006 |
| Surgical cause of infection | No | 82 | 27 | 1.000 | | |
| | Yes | 25 | 8 | 0.972 | 0.392 to 2.408 | 0.951 |
| Time from onset, days | Per day | | | 1.070 | 1.010 to 1.134 | 0.023 |
| Age at diagnosis, yrs | Per year | | | 1.000 | 0.982 to 1.020 | 0.970 |

**Table VII.** Multivariate regression model for risk of joint failure.

| Condition | Estimate | Standard error | p-value | Odds ratio | 95% CI |
|---|---|---|---|---|---|
| Pre-existing arthritic condition (impairment) | 1.161 | 0.465 | 0.012 | 3.193 | 1.284 to 7.938 |
| *Staphylococcus aureus* as cause | 1.811 | 0.550 | 0.001 | 6.119 | 2.082 to 17.984 |
| Hip vs knee | 1.974 | 0.625 | 0.002 | 7.197 | 2.116 to 24.484 |
| Constant | -5.143 | 1.007 | 0.000 | 0.006 | |

which they attributed to close vigilance and early aggressive treatment.

The second aim was to determine the rate of joint failure (as indicated by a salvage procedure being carried out on that joint) in patients who had experienced an episode of septic arthritis. The survival of joint arthroplasties after a previous episode of septic arthritis has been reported,[22] but the survival of the native joint has not been detailed. There was a high number of patients who went on to develop catastrophic failure of the joint following septic arthritis, and the perceived good results experienced initially were misleading.[23] In a cohort study of the subset of native knee septic arthritis treated by arthroscopic washout with follow-up of over one year,[24] Abram et al[24] found that 8% of patients required subsequent arthroplasty within 15 years. This is comparable to our arthroplasty rate of 7.7% at long-term follow-up. However, our study has demonstrated that survival of native knee joints decreased to 65.5% at ten years (Figure 4), which suggests a process of secondary degenerative process after the initial episode of septic arthritis.

Poor outcomes were seen in all age groups but occurred more frequently in those with pre-existing joint disease, which was predictive of joint failure (Table VI). A possible explanation for this was that the effects of septic arthritis on arthritic cartilage were more severe than on healthy cartilage, therefore leading to accelerated decline.

Infected hip joints tended to do very badly, with 9/17 cases progressing on to a failure of the joint in this small series. This added to the findings of Matthews et al,[25] who reported excision arthroplasty in 25% of patients with hip septic arthritis, and suggested that the increased difficulty in making the diagnosis of hip (compared to knee) infection led to delays in treatment and accounted for the poorer outcomes. An alternative theory might be that there were intrinsic differences in the susceptibility of the hip joint to infection when compared to the knee.

The third aim was to assess the outcome following septic arthritis relative to the infecting organism. In particular, we wanted to test whether those patients infected by *S. aureus* would be more likely to have adverse outcomes than those infected by other organisms. To the author's knowledge, this is the first study to link the infecting organism to poor outcomes following septic arthritis in skeletally mature patients. *S. aureus* took a more destructive course, with 37% of patients developing joint failure compared to only 8% of patients whose infections were caused by other organisms (Table V). This is due to α Hla production by *S. aureus* which has been shown to have a catastrophic influence on chondrocyte viability.[19,26] Utilizing a selection of isogenic mutants originating from *S. aureus* 8,325-4, Smith et al[19] isolated Hla as the toxin primarily responsible, and showed that there was minimal chondrocyte death resulting from exposure to the other haemolysins (β and γ). In a review article by Gredlein et al,[27] it was shown that two out of 37 clostridial septic arthritis had joint destruction, although direct causal relationship to Clostridium's α haemolysin production could not be established from the series of case reports. Whereas in septic arthritis caused by *Pseudomonas aeruginosa*, the

other α haemolysin-producing organism, they tend to occur in institutionalized elderly patients or the immunocompromised, in whom poorer outcomes are expected.[28,29]

One of the advantages of only including microbiologically-confirmed cases of septic arthritis prevented the inclusion of clinically diagnosed septic arthritis, but were subsequently diagnosed with a rheumatological condition. This was estimated to occur in up to 14% of patients with negative microbiological specimens, and potentially acts as a confounder in other series.[30] The second advantage was that outcomes following infection with *S. aureus* could be compared to those following infection with other organisms. It was possible that 'cases', where there was contamination of the specimen, were erroneously included; however, this is likely very rare. Atkins et al[31] investigated the predictive value of microbiological specimens taken from 297 patients at the time of revision arthroplasty where multiple samples are taken. They considered that if growth occurred in a single microbiological specimen, it was likely to be a contaminant, and this occurred in 47 samples out of 1,206, giving a contamination rate of 3.9%.

The authors recognized that there are limitations of a retrospective study, such as incomplete data and difficulty with sub-group analysis. The authors also recognized that a prospective study would reduce some of the biases of a retrospective study; however, that in itself will likely require a multicentre study with prospective data collection which will only yield significant data in considerable number of years, making it less feasible for rare conditions. Our study has reported one of the largest case series of native joint septic arthritis, and we believe it is one of only a handful of studies to report on long-term outcomes following the resolution of initial infective symptoms. It is unique in providing the time course to failure in patients with different infecting organisms. In addition, the authors feel that the poor outcomes associated with septic arthritis are likely under-reported given the lack of complete follow-up, making it worth highlighting the likely worse outcomes than those reported in the current literature.

The microbiological data for this study were collected prospectively, but the clinical information was collected retrospectively and there was a possibility of comorbid conditions being missed; thus, the CCI scores might have been higher in some patients.

The question needs to be asked as to why these poor outcomes have occurred if the majority of patients were doing well at the time the infection had resolved. The answer may lie in the unique structure of articular cartilage. Chondrocytes are the only living component, and are responsible for the maintenance of the articular cartilage.[32,33] It is possible that during the acute phase of septic arthritis there is significant damage to chondrocytes leading to chondrocyte death. Evidence is accumulating that for *S. aureus,* at least, in an animal cartilage model, the potent toxin Hla causes rapid chondrocyte death.[19,26] If this occurs then there will be cumulative damage to the matrix caused by alterations to normal matrix metabolism, leading to mechanically weakened cartilage and ultimately the development of secondary degenerative change or even failure.[34] Further elucidation of the mechanism of cartilage damage during *S. aureus* infection would be of great benefit, so that chondroprotective treatment strategies can be developed to prevent the catastrophic joint failure that can cripple patients of all ages.

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## Funding statement

The authors disclose receipt of the following financial or material support for the research, authorship, and/or publication of this article: R. G. E. Clement discloses a Royal College of Surgeons of Edinburgh/Cutner Fellowship grant, a Tenovus small grant fund, and a Royal College of Edinburgh small grant fund related to this work.

## ICMJE COI statement

R. G. E. Clement discloses a Royal College of Surgeons of Edinburgh/Cutner Fellowship grant, a Tenovus small grant fund, and a Royal College of Edinburgh small grant fund related to this work. A. H. R. W. Simpson declares grants from RCUK, charities, and Stryker, unrelated to this paper.

## Data sharing

All data generated or analyzed during this study are included in the published article and/or in the supplementary material.

## Acknowledgements

The authors would like to thanks the NHS Lothian microbiology department for the access to the microbiological database from which we are able to derive our study sample.

## Ethical review statement

An ethical application for this study was submitted to the South East Scotland Research Ethics Service, who kindly advised that formal ethical approval was not required.

## Open access funding

For the open access funding for this manuscript, R. G. E. Clement discloses a Royal College of Surgeons of Edinburgh/Cutner Fellowship grant, a Tenovus small grant fund, and a Royal College of Edinburgh small grant.