Risk Factors for Failure of a Single Surgical Debridement in Adults with Acute Septic Arthritis

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Background: Acute septic arthritis in a native joint may require more than one surgical debridement to eradicate the infection. Our objectives were to determine the prevalence of failure of a single surgical debridement for acute septic arthritis, to identify risk factors for failure of a single debridement, and to develop a prognostic probability algorithm to predict failure of a single surgical debridement for acute septic arthritis in adults.

Methods: We collected initial laboratory and medical comorbidity data of 128 adults (132 native joints) with acute septic arthritis who underwent at least one surgical debridement at our institution between 2000 and 2011. Univariate and logistic regression analyses were used to identify potential risk factors for failure of a single surgical debridement. Stepwise variable selection was used to develop a prediction model and identify probabilities of failure of a single surgical debridement.

Results: Of the 128 patients (132 affected joints) who underwent surgical debridement for acute septic arthritis, forty-nine (38%) of the patients (fifty joints) experienced failure of a single debridement and required at least two debridements (range, two to four debridements). *Staphylococcus aureus* was the most common bacterial isolate (in sixty, or 45%, of the 132 joints). Logistic regression analysis identified five independent clinical predictors for failure of a single surgical debridement: a history of inflammatory arthropathy (odds ratio [OR], 7.3; 95% confidence interval [CI], 2.4 to 22.6; $p < 0.001$), the involvement of a large joint (knee, shoulder, or hip) (OR, 7.0; 95% CI, 1.2 to 37.5; $p = 0.02$), a synovial-fluid nucleated cell count of >85.0 x 10^9 cells/L (OR, 4.7; 95% CI, 1.8 to 17.7; $p = 0.002$), *S. aureus* as the bacterial isolate (OR, 4.6; 95% CI, 1.8 to 11.9; $p = 0.002$), and a history of diabetes (OR, 2.6; 95% CI, 1.1 to 6.2; $p = 0.04$).

Conclusions: Most (62%) of the septic joints were managed effectively with a single surgical debridement. Adults with a history of inflammatory arthropathy, involvement of a large joint, a synovial-fluid nucleated cell count of >85.0 x 10^9 cells/L, an infection with *S. aureus,* or a history of diabetes had a higher risk of failure of a single surgical debridement for acute septic arthritis and requiring additional surgical debridement(s).

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

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Septic arthritis is an orthopaedic emergency requiring prompt treatment. Treatment with a single surgical irrigation and debridement with antibiotics is usually effective, but more than one debridement may be necessary to eradicate the infection[1].

The bacterial inoculation of a joint can develop from hematogenous seeding, direct introduction, or extension from a contiguous focus of infection[2]. A joint infection may damage cartilage directly by bacterial enterotoxins and indirectly from the host immune response to bacteria[3]. Delayed treatment of septic arthritis can result in joint degeneration, osteonecrosis, or joint instability[4-6].

The clinical evaluation of a patient with suspected septic arthritis begins with a clinical examination and assessment of

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laboratory data[7]. The serologic testing consists of a white blood-cell (WBC) count, measurement of the C-reactive protein (CRP) level and of the erythrocyte sedimentation rate (ESR), and performance of aerobic and anaerobic blood cultures. Arthrocentesis is also performed to determine synovial-fluid nucleated cell count, to test for crystals, and for a Gram stain and cultures. The standard for the diagnosis of septic arthritis is a positive Gram stain or subsequent positive cultures from the arthrocentesis. A high nucleated cell count (that is, $>50 \times 10^9$ cells/L) is also strongly correlated with infection[2]. Treatment consists of emergency surgical irrigation and debridement, followed by a course of antibiotics based on culture results[8-12]. Successful treatment results in the resolution of symptoms (which include pain, fever, inability to bear weight, and limited motion in the affected joint). Some patients (23% to 48%) do not improve after a single debridement and require additional debridements to treat the infection[13-15].

Several studies have identified risk factors for the development of septic arthritis in adults, including diabetes mellitus[16], rheumatoid arthritis[17], intravenous drug use[16,18], poor socioeconomic status[12,19], concurrent infection, and immunosuppression[17]. We are aware of no published literature regarding risk factors associated with the failure of a single surgical debridement for the treatment of acute septic arthritis of a native joint. The goals of the present study were to determine the prevalence of failure of a single surgical debridement for acute septic arthritis, to identify risk factors for failure of a single surgical debridement, and to develop a prognostic probability algorithm for failure of a single surgical debridement.

Materials and Methods

Patients

At our institution, the orthopaedic service treats all patients diagnosed with septic arthritis with surgical debridement. Therefore, we queried our billing database to identify all patients at least eighteen years of age who were treated for septic arthritis between 2000 and 2011. We included patients for whom orthopaedic consultation was obtained; we did not include those who may have been treated nonoperatively with serial aspirations by other services because of high surgical risk or because the patient declined to undergo surgery. Exclusion criteria included a history of septic arthritis (nine patients), osteomyelitis of a bone contiguous with the affected joint (five patients), a history of fracture surgery with an arthrotomy of the joint/joint capsule (twenty patients), previous arthroplasty (seventy-three patients), a joint with an implanted foreign body (such as suture material) from a previous procedure (six patients), or a treatment plan at the time of the initial debridement that included conducting a subsequent second debridement (nineteen patients). The records of the remaining 128 patients (132 joints) were reviewed to obtain the results of serologic and joint-fluid analyses. Institutional review board approval for this study was obtained.

The diagnosis of septic arthritis was made when the patient had a clinical presentation consistent with acute septic arthritis (acute onset of pain, the inability to bear weight or move the affected joint, fevers, and joint effusion) and when any of the following occurred: (1) a positive Gram stain (that is, for bacteria) from joint aspiration; (2) aerobic or anaerobic cultures that grew bacteria; (3) aspirated fluid with a nucleated cell count of $>50.0 \times 10^9$ cells/L. To minimize information bias, patients with an incomplete work-up and follow-up history were excluded.

Data obtained for all of the patients included age, sex, race, date of presentation, duration of prodromal symptoms, history of fever (a temperature of >38.5°C), which joint was affected, history of any surgical procedures involving the affected joint, presence of concurrent infection, method of surgical debridement, and history of the following comorbidities: cancer, diabetes, insulin use, immunosuppression, HIV (human immunodeficiency virus), inflammatory arthropathy (such as rheumatoid arthritis or spondyloarthropathy), sickle cell disease, coronary artery disease, tobacco use, or obesity (a body mass index [BMI] of >30 kg/m^2).

Hospital Course

Surgery

All patients had either an open or an arthroscopic irrigation and debridement of the affected joint for the index procedure, as determined by the attending surgeon. Open debridement was the preferred initial treatment (68% of the affected joints). In general, the affected joints were debrided and then irrigated with sterile saline solution. With the exception of a few patients, in whom antibiotics were initiated prior to orthopaedic consultation, broad-spectrum antibiotics were routinely withheld preoperatively until deep intraoperative specimens for culture were obtained. Cultures were monitored, and antibiotic selection was later adjusted as necessary based on these results.

Postoperative Period

Patients were monitored in the hospital for at least forty-eight hours postoperatively to assess the success of the initial surgical debridement. For all patients, an infectious disease consultant determined the appropriate antibiotic regimen.

During the postoperative period, any of the following signs or symptoms were considered a recurrence of infection and failure of a single surgical debridement: persistent purulent discharge from a drain or incisional site(s), increasing pain, decreasing range of motion, persistent fevers, or persistent elevation of serologic inflammatory markers. Patients showing steady clinical improvement after forty-eight hours were discharged from our institution with continued antibiotic therapy. Serologic markers (ESR, CRP, and CBC [complete blood count]) were routinely monitored during antibiotic therapy in an outpatient setting to assess the patient's response to the treatment.

Outpatient Follow-up

Outpatient infectious disease and orthopaedic follow-up continued for the length of the antibiotic therapy (three to twelve weeks of oral or intravenous therapy, determined by infectious disease consultants on the basis of clinical examination and return of serologic markers to near-baseline values). Any increase in inflammatory markers prompted clinical reevaluation. Any patient with worsening symptoms was evaluated in the clinic and/or our emergency room. Repeat aspiration and serologic studies were performed. Those having recurrence of the infection were readmitted to the hospital, and an additional debridement was performed.

Statistical Analysis

Univariate analysis, using a two-tailed Student t test for continuous variables and Fisher exact test for binary variables, was performed. Variables with a p value of <0.20 were included as initial candidates in the stepwise variable selection. For all continuous laboratory variables (WBC, ESR, CRP, and synovial-fluid nucleated cell count), thresholds were created and optimized to detect a difference, thus allowing for variable inclusion in our model and assisting with risk stratification. Stepwise variable selection using logistic regression was performed to identify a subset of significant independent clinical variables present in individuals with failure of a single surgery.

A prognostic model for failure of a single surgery was created using the identified risk factors. The Hosmer-Lemeshow goodness-of-fit test was performed to detect any departure from a good model fit. A receiver operating characteristic (ROC) curve was constructed to determine the diagnostic performance for identifying patients who may experience failure of a single surgery. A two-sided p value of <0.05 was considered significant for all tests.

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TABLE I Univariate Analysis of Demographic Variables for Successful Versus Failed Single Surgical Debridement

Variable	Successful Single Surgical Debridement	Failed Single Surgical Debridement	P Value
Male*	47 (59.5%)	35 (71.4%)	0.28
Age* *(yr)*	53.8 ± 19.0	57.1 ± 18.6	0.12
Race*			
Caucasian	52 (65.8%)	36 (73.4%)	0.32
African-American	19 (24.1%)	12 (24.5%)	1.00
Hispanic	8 (10.1%)	1 (2.0%)	0.15
Duration of prodromal symptoms* *(d)*	6.2 ± 5.4	5.3 ± 4.5	0.14
Large joint involvement*	64 (81.0%)	46 (93.9%)	0.08
Recent arthroscopy*	15 (19.0%)	13 (26.5%)	0.46
Concurrent infection*	30 (38.0%)	24 (49.0%)	0.33
History of cancer*	17 (21.5%)	11 (22.5%)	1.00
History of diabetes*	36 (45.6%)	32 (65.3%)	0.05
Current insulin use*	10 (12.7%)	11 (22.5%)	0.24
History of immunosuppression*	18 (22.8%)	20 (40.8%)	0.054
HIV positive*	5 (6.3%)	2 (4.1%)	0.87
Inflammatory arthropathy*	13 (16.5%)	19 (38.8%)	0.01
Sickle cell disease*	2 (2.5%)	2 (4.1%)	1.00
Coronary artery disease*	12 (15.2%)	15 (30.6%)	0.07
Tobacco use*	15 (19.0%)	12 (24.5%)	0.63
BMI >30 kg/m^2*	21 (26.6%)	14 (28.6%)	1.00
Fever >38.5°C*	12 (15.2%)	9 (18.4%)	0.85
Cell count >85.0 × 10^9 cells/L*	11 (13.9%)	17 (34.7%)	0.011
CRP >180 mg/L*	52 (65.8%)	25 (51.0%)	0.14
WBC >11.5 × 10^9/L*	48 (60.8%)	17 (34.7%)	0.007
Positive blood culture*	7 (8.9%)	11 (22.5%)	0.06
Presence of crystals in synovial fluid†	10 (12.2%)	10 (20.0%)	0.47
Positive Gram stain†	31 (37.8%)	28 (56.0%)	0.05
S. aureus infection†	27 (32.9%)	33 (66.0%)	<0.001
Methicillin-resistant *S. aureus* infection†	16 (19.5%)	24 (48.0%)	<0.001

*Values are given as the mean number of patients and standard deviation for continuous variables and as the number and percentage of patients for categorical variables. N = 79 patients in the successful group, and N = 49 patients in the failed group. †Values are given as the number and percentage of affected joints. N = 82 joints in the successful group, and N = 50 joints in the failed group.

Results

Univariate Analysis

No difference in the effectiveness of a single surgical debridement was seen with regard to sex, race, or age ($p > 0.05$). We were unable to demonstrate any difference in the effectiveness of a single surgical debridement between open and arthroscopic debridement ($p > 0.05$). The forty-nine patients (fifty joints) with a failed single debridement differed from the seventy-nine patients (eighty-two joints) with a successful single debridement (using $p < 0.20$) by duration of prodromal symptoms (5.3 ± 4.5 compared with 6.2 ± 5.4 days, respectively), positive Gram stain from arthrocentesis (56% compared with 38%, respectively), history of diabetes (65% compared with 46%, respectively), history of immunosuppression (41% compared with 23%, respectively), history of inflammatory arthropathy (39% compared with 17%, respectively), coronary artery disease (31% compared with 15%, respectively), *Staphylococcus aureus* infection (66% compared with 33%, respectively), methicillin-resistant *S. aureus* (MRSA) infection (48% compared with 20%, respectively), positive blood culture (23% compared with 9%, respectively), large joint involvement (94% compared with 81%, respectively), an initial CRP level of >180 mg/L (51% compared with 66%, respectively), a WBC of >11.5 × 10^9/L (35% compared with 61%, respectively), and a synovial-fluid nucleated cell count

TABLE II Univariate Analysis of Serologic and Arthrocentesis Variables for Successful Versus Failed Single Surgical Debridement

Variable	Successful, N = 79*	Failed, N = 49*	P Value
WBC *(× 10^9/L)*	12.3 ± 5.1	14.0 ± 4.7	0.004
Platelets *(× 10^9/L)*	284.2 ± 142.5	275.9 ± 157.7	0.62
ESR *(mm/hr)*	75.0 ± 36.7	77.0 ± 34.0	0.66
CRP *(mg/L)*	171.2 ± 113.9	195.9 ± 104.9	0.07
Cell count *(× 10^9 cells/L)*	70.6 ± 58.3	89.4 ± 68.8	0.02

*Values are given as the mean and standard deviation for continuous variables.

of >85.0 × 10^9 cells/L (35% compared with 14%, respectively) (Table I).

When expressed as continuous variables, the mean nucleated cell count (70.6 ± 58.3 compared with 89.4 ± 68.8 × 10^9 cells/L; p = 0.02) and WBC (12.3 ± 5.1 compared with 14.0 ± 4.7 × 10^9/L; p = 0.004) differed significantly between the groups, with both markers trending higher in patients who failed a single debridement. The CRP level tended to be higher in the patients who failed a single surgical debridement, but this difference between the groups did not reach significance (171.2 ± 113.9 compared with 195.9 ± 104.9 mg/L; p = 0.07) (Table II).

Arthrocentesis was performed on all 128 patients (132 affected joints). For forty-seven joint aspirations (36%), bacteria did not grow on aerobic/anaerobic culture. A sterile or negative culture was more common in patients successfully treated with a single debridement (thirty-seven of seventy-nine [47%] compared with nine of forty-nine [18%]; p = 0.001).

S. aureus was the most common isolate, found in sixty (45%) of the 132 joints and fifty-eight (68%) of the eighty-five joints with a positive culture from aspiration. *S. aureus* was identified in twenty-seven (33%) of the eighty-two joints treated successfully with a single debridement compared with thirty-three (66%) of the fifty joints failing initial debridement (p < 0.001). Among the sixty joints for which *S. aureus* grew on culture, forty (67%) were identified as having MRSA. MRSA was also identified significantly more often in the joints experiencing a failed single surgical debridement (48% compared with 20%; p <0.001). No other significant differences were observed between the two groups on analysis of culture data (p > 0.05). Culture results are summarized in Figure 1.

The most commonly affected joint was the knee (ninety-four, or 71%, of the 132 joints). Other affected joints were the shoulder (seventeen, or 13%), the ankle (eight, or 6%), the elbow (eight, or 6%), the hip (three, or 2%), and the wrist (two, or 2%). Larger joints (knee, shoulder, and hip)

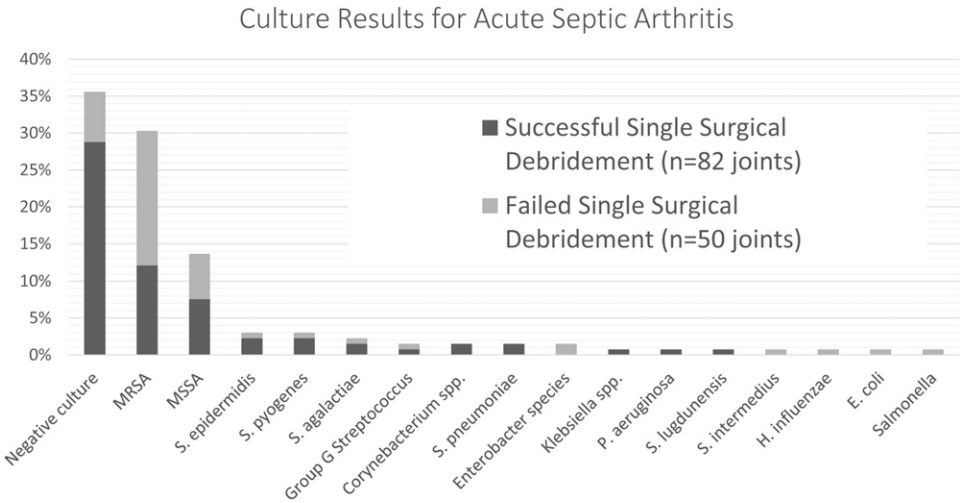

Fig. 1

The final culture results for adults with acute septic arthritis. Negative or sterile culture results were the most common. *Staphylococcus aureus* was the most common bacterial isolate identified (45%) and more common in joints that failed a single surgical debridement (66% compared with 33%; p < 0.001). No other significant differences were observed between the two groups on analysis of culture data (p > 0.05). MRSA = methicillin-resistant *S. aureus*, MSSA = methicillin-sensitive *S. aureus*, *S. epidermidis* = *Staphylococcus epidermidis*, *S. pyogenes* = *Streptococcus pyogenes*, *S. agalactiae* = *Streptococcus agalactiae*, *S. pneumoniae* = *Streptococcus pneumoniae*, *P. aeruginosa* = *Pseudomonas aeruginosa*, *S. lugdunensis* = *Staphylococcus lugdunensis*, *S. intermedius* = *Streptococcus intermedius*, *H. influenzae* = *Haemophilus influenzae*, and *E. coli* = *Escherichia coli*.

TABLE III Multivariate Logistic Regression of Identified Independent Risk Factors for Failure of a Single Surgery in Adults with Acute Septic Arthritis

Variable	Adjusted Odds Ratio	95% Confidence Interval	P Value
Inflammatory arthropathy	7.3	2.4-22.6	<0.001
Large joint involvement	7.0	1.2-37.5	0.02
Synovial-fluid nucleated cell count >85.0 × 10^9 cells/L	4.7	1.8-17.7	0.002
S. aureus	4.6	1.8-11.9	0.002
Diabetes	2.6	1.1-6.2	0.04

were more likely to fail a single surgical debridement compared with smaller joints (elbow, ankle, and wrist) (p = 0.02). Open surgical debridement was performed as the initial surgery for fifty-four (68%) of the seventy-nine patients in the successful single surgical debridement group and thirty-six (73%) of the forty-nine in the failed initial debridement group (p = 0.56).

Forty-nine (38%) of the patients (fifty joints) had a failed single surgical debridement. Thirty-three (67%) of these patients required two procedures, nine (18%) required three procedures, and seven (14%) had four procedures. Twenty-seven (55%) of the forty-nine patients had been discharged and required a hospital readmission for unplanned debridement. The second debridement occurred at a mean of 25.5 days after the initial debridement (range, two to 204 days). Five patients had a recurrence of septic arthritis more than 100 days after the initial debridement. All five recurrences occurred in the same joint and grew the same strain of bacteria identified at the initial debridement and, therefore, are considered a failure of a single debridement. There were four cases of polyarticular septic arthritis; one of these patients failed the initial debridement and three were successfully treated with a single surgery. All four cases involved one knee and one shoulder. The mean duration of follow-up was nine months (range, 1.5 to 69.5 months) for the successful single-surgery group and 4.9 months (range, 1.5 to fourteen months) for the failed single-surgery group.

Multivariate Analysis

We identified five independent predictors that were associated with failure of a single debridement: a history of inflammatory arthropathy (odds ratio [OR], 7.3; 95% confidence interval [CI], 2.4 to 22.6; p < 0.001), the involvement of a large joint (knee, shoulder, or hip) (OR, 7.0; 95% CI, 1.2 to 37.5; p = 0.02), a synovial-fluid nucleated cell count of >85.0 × 10^9 cells/L (OR, 4.7; 95% CI, 1.8 to 17.7; p = 0.002), *S. aureus* as the bacterial isolate (OR, 4.6; 95% CI, 1.8 to 11.9; p = 0.002), and a history of diabetes (OR, 2.6; 95% CI, 1.1 to 6.2; p = 0.04) (Table III).

Prognostic Model

We constructed a prognostic model with a scale of six points (range, zero to five points); one point was assigned for each risk factor noted. The predictive probabilities of failure of a single surgery based on this model and the analysis related to our study population are presented in the tables in the Appendix. The area under the ROC curve was calculated to be 0.79 for this model, demonstrating good-to-excellent prognostic capabilities (see Appendix). The Hosmer-Lemeshow goodness-of-fit test did not indicate any departure from a good model fit (p = 0.90).

Discussion

Septic arthritis often can be treated by a single surgical debridement with appropriate antibiotic therapy. Sometimes, however, a patient's clinical picture worsens and a second debridement becomes necessary. To our knowledge, risk factors for failure of a single surgical debridement have not previously been identified. The purpose of this study was to determine the prevalence of failure of a single surgical debridement, to identify risk factors associated with a failed single surgical debridement for the treatment of acute septic arthritis of a native joint, and to develop a prognostic probability algorithm.

In this study, 62% (eighty-two of 132) of the joint infections were successfully managed with a single debridement. Open debridement was the preferred initial treatment in 68% of affected joints, although we were unable to demonstrate any clinical differences between open and arthroscopic debridement (p > 0.05). This is in agreement with other studies that have demonstrated equal treatment efficacy between open and arthroscopic surgical debridement of the wrist, knee, shoulder, and hip[11,15,20-23].

In this study, 36% of joint aspirations did not yield a positive culture result despite a clinical scenario suggestive of septic arthritis. This is comparable with what has been published in other studies, in which the prevalence of no growth on culture has ranged from 0% to 40%[8,18]. The most common bacterial isolate was *S. aureus,* accounting for 45% (sixty of 132) of all samples. This is similar to reports from other countries (37% to 56%)[12,24,25]. When patients with no growth on culture (that is, sterile or negative culture) were excluded from analysis, *S. aureus* accounted for 68% (fifty-eight of eighty-five) of all positive cultures and was identified as a risk factor for failure in our study. MRSA represented 30% of all cultures, 47% of all positive cultures, and 67% of all *S. aureus* cultures, but was not an independent risk factor for failure of a single surgery by multivariate analysis. This prevalence of MRSA is substantially higher than previously reported in other studies[18,26] and raises concern that the prevalence of MRSA as a cause of septic arthritis continues to rise.

A synovial-fluid nucleated cell count of $>50 \times 10^9$ cells/L from aspiration is commonly cited as a threshold for diagnosing acute septic arthritis, even in the presence of a sterile Gram stain result[15,27]. Rashkoff et al. reported a variability from 20 to 150×10^9 cells/L in confirmed cases of septic arthritis[28]. Our study had a range of 2.0 to 294×10^9 cells/L for patients treated for septic arthritis. A threshold of 50×10^9 may not be as reliable as previously believed.

Our study had several limitations. It was retrospective in design and may have inherent bias from incomplete documentation in the medical record. The surgical procedures were performed by different surgeons, and some variability in patients' hospital course and treatment may have occurred during the perioperative period. Also, because a portion of the patients had negative cultures, it is possible that some of those treated surgically actually had an inflammatory arthropathy rather than septic arthritis. However, the generally accepted criteria for diagnosis of septic arthritis were used in this study. Although all patients were treated initially with broad-spectrum antibiotics, individual patient medication allergies and operative culture sensitivities meant that the selected antibiotic regimen could not be standardized, and it is beyond the scope of this project to be able to comment on the effectiveness of different antibiotic regimens. It is also possible that patients having one surgical debridement at our institution may have undergone an additional procedure elsewhere; however, this was never documented in their follow-up record.

Our small sample size limits our ability to perform internal validation and may have resulted in an over-fitted algorithm. Furthermore, although our data provide prognostic information on the risk that a patient will fail a single surgery, we do not have any data to support the concept that a planned second surgery, based on risk factors alone, will result in an improved clinical course or lead to a quicker resolution of the infection. Additional prospective studies should be performed to confirm our identified risk factors and prognostic algorithm for the risk of failure of a single surgical debridement in treating acute septic arthritis.

In summary, we found open and arthroscopic debridements similarly effective for the initial treatment of septic arthritis. *S. aureus* was the most common bacterial isolate (in 45%), and there was a high prevalence of MRSA (30% of all cultures). Adults with a history of inflammatory arthropathy, involvement of a larger joint, a synovial-fluid nucleated cell count of $>85.0 \times 10^9$ cells/L, infection with *S. aureus,* or a history of diabetes had a higher risk of failure of a single surgical debridement for acute septic arthritis in a native joint. We believe that the model we developed has prognostic value and may be useful to physicians in counseling their adult patients with acute septic arthritis, especially in the early treatment course.

Appendix

eA The ROC curve of our prognostic model and tables showing the predicted probabilities of failure of a single surgical debridement and the analysis related to our study population are available with the online version of this article as a data supplement at jbjs.org. ■

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