

Characteristics and outcomes of community-onset septic arthritis in adults

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Background and purpose: Failure to recognize and to appropriately treat septic arthritis results in substantial morbidity rates. This study compared the demographic characteristics, risk factors, and outcomes of patients with community-onset septic arthritis due to Gram-positive and Gram-negative bacteria.

Methods: The medical charts of 51 adults with culture-proven community-onset septic arthritis treated at a tertiary medical center in northern Taiwan from January 1, 2004 through December 31, 2007 were retrospectively reviewed. The demographic data and clinical features were analyzed.

Results: There were 39 patients with septic arthritis caused by Gram-positive cocci (76.4%) and 12 with septic arthritis caused by Gram-negative bacteria (23.6%). The most common pathogen was *Staphylococcus aureus* (n = 30; 58.9%). The most frequently involved joint was the knee (n = 33; 63.5%). By multivariate logistic regression analysis, age (odds ratio [OR], 1.07; 95% confidence interval [CI], 1.01-1.13; $p = 0.024$) and range of motion limitation (OR, 8.23; 95% CI, 1.14-59.49; $p = 0.037$) were independent predictive factors for septic arthritis caused by Gram-positive cocci. Diabetes mellitus with end-organ damage (OR, 0.03; 95% CI, 0.00-0.39; $p = 0.007$) and malignancy (OR, 0.04; 95% CI, 0.00-0.66; $p = 0.025$) were negative predictive factors for septic arthritis caused by Gram-positive cocci. There were no significant differences in outcomes for patients with Gram-positive and Gram-negative septic arthritis.

Conclusions: In adult patients with community-onset septic arthritis, older age and limited range of motion predict for Gram-positive cocci as the causative pathogen, while underlying diabetes mellitus with end-organ damage and malignancy predict for Gram-negative bacteria as the causative pathogen.

Key words: Arthritis, infectious; Diabetes mellitus; Gram-negative bacteria; Gram-positive cocci; Neoplasms

Introduction

Septic arthritis is a rheumatologic emergency and can cause rapid joint destruction. In one study, approximately 27% of patients who presented to the emergency room with acute arthritis were found to have septic arthritis [1]. Children and elderly people are the most susceptible groups for septic arthritis [2,3]. The risk factors for septic arthritis include old age, immunocompromised status, and pre-existing joint disease [4]. Gram-positive bacteria, especially *Staphylococcus aureus*, are the leading causative pathogens, but Gram-negative bacteria, such as *Haemophilus influenzae*, *Escherichia coli*, *Neisseria*

meningitidis, and *Pseudomonas* spp. also cause septic arthritis [3]. Patients with a history of intravenous drug abuse, and those who are immunocompromised or elderly tend to have septic arthritis caused by Gram-negative pathogens [5]. The choice of antibiotic regimen is different for septic arthritis caused by Gram-positive or Gram-negative bacteria [6], and the outcomes are different for these 2 groups of patients [7]. In this study, the demographic characteristics, risk factors, and outcomes of patients with septic arthritis caused by Gram-positive cocci and Gram-negative bacteria are compared.

Methods

Patients

Patients with the International Classification of Diseases, Ninth Revision, diagnostic code for pyogenic

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arthritis (711.0) at discharge from the National Taiwan University Hospital, Taipei, Taiwan, from January 1, 2004 through December 31, 2007 were identified from the hospital database. All adult patients with culture-proven septic arthritis were enrolled. Culture-proven septic arthritis was defined as identification of a microbial pathogen in the synovial fluid or joint tissue, or typical features of septic arthritis with a pathogen isolated from the blood. Typical features of septic arthritis were defined as at least 1 of the compatible clinical symptoms and signs (redness, swelling, heat, pain, or limited range of motion [ROM]) and/or imaging documentation (computed tomography, magnetic resonance imaging, or bone scan). If a patient had multiple episodes of septic arthritis, only the first episode of infection was included.

Patients younger than 18 years were excluded. Those who had had a joint operation within 1 year, nosocomial infected septic arthritis, or incomplete medical records for evaluation of the initial presentation (transfer from another hospital) or outcome (non-critical discharge against medical advice) were excluded.

Data collection

Demographic data, presenting symptoms and signs, duration of symptoms before admission, underlying disease, Charlson comorbidity score [8], health care exposure history, and prior surgery were collected from the medical records. The involved joint and microbiologic culture results for synovial fluid and blood were recorded. Initial blood examination included white blood cell count, hemoglobin, platelets, C-reactive protein, creatinine, and analysis of synovial fluid (synovial white blood cell count, differential count, and Gram stain). The outcomes were documented from the medical records, and included medical and surgical treatment, mortality, complications (shock, acute respiratory failure, acute renal failure, and intensive care unit admission), and duration of hospital stay.

Statistical analysis

Means \pm standard deviation (SD) were calculated for continuous variables, and percentages were used for categorical variables. Categorical variables were examined using chi-squared test or Fisher's exact test. The associations between the potential risk factors for Gram-positive cocci and Gram-negative bacteria for septic arthritis were investigated using univariate and multivariate logistical regression analyses. Risk factors

of $p < 0.2$ in the univariate analysis were included in the multivariate logistic analysis. A p value of < 0.05 was defined as statistically significant. Data were analyzed with the Statistical Package for the Social Sciences software, version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

249 patients with a definitive diagnosis of pyogenic arthritis were identified. 198 patients were excluded: for 46 patients, the admissions identified were not their first episodes; 117 patients did not have positive culture results; 3 patients had joint surgical intervention within the previous year, 16 patients had incomplete medical records for evaluation of initial presentation or outcome, 7 patients had nosocomial septic arthritis; 8 patients were children, and 1 had tuberculous septic arthritis (Fig. 1). Therefore, 51 patients were eligible for inclusion. There were 28 men (54.9%), the mean age was 59 years, and 27 patients (52.9%) were older than 60 years. Thirty two patients (62.7%) had not been admitted to hospital within the previous year. Thirteen patients (25.5%) had a previous history of joint operation, but none of them were within the year prior to the onset of the current episode. Eleven patients (21.6%) had a history of joint trauma within the previous 3 months. Most of the patients ($n = 50$; 98%) had involvement of a single joint, and only 1 patient (2%) had multiple joint involvement (Table 1). The most frequently involved joints were the knee ($n = 33$; 63.5%), shoulder ($n = 10$; 19.2%), hip ($n = 4$; 7.7%), and ankle ($n = 2$; 3.8%) [Table 2].

Twenty six patients (51%) had a positive blood culture, 40 (78.4%) had a positive synovial fluid culture, and 15 (29.4%) had both. Thirty nine patients (76.5%) had septic arthritis caused by Gram-positive cocci and 12 (23.5%) were caused by Gram-negative bacteria. *S. aureus* was the most common etiological agent, being isolated from 30 patients (58.9%); 24 were methicillin-susceptible *S. aureus* (MSSA) and 6 were methicillin-resistant *S. aureus* (MRSA). The second most common Gram-positive pathogen was *Streptococcus* spp. being isolated from 6 patients (11.8%); 2 were group B *Streptococcus*, 2 were group G *Streptococcus*, 1 was *Streptococcus pneumoniae*, and 1 was viridians streptococci. Twelve patients (23.5%) had Gram-negative bacteria. For these patients, the causative agents were more diverse. Two patients (3.9%) each had *Aeromonas* spp., *Escherichia* spp., *Pseudomonas* spp., and *Salmonella* spp., and 1

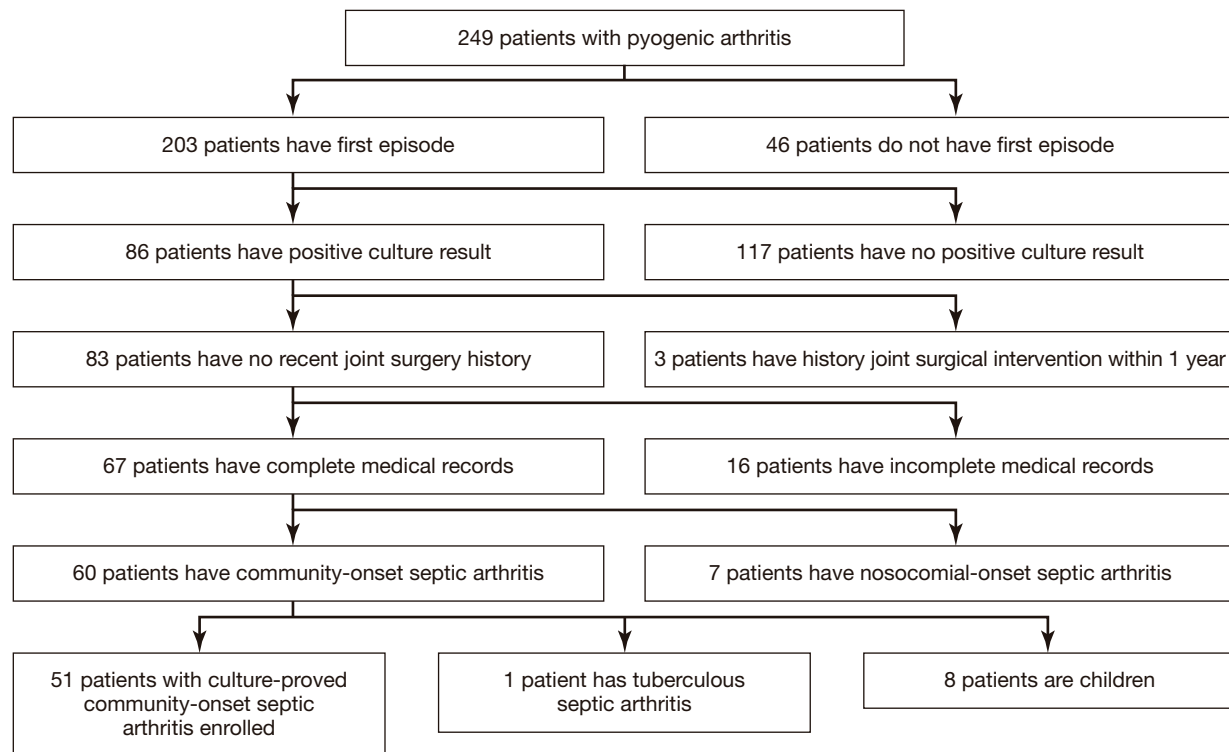


Fig. 1. Study enrollment.

had gonococcal septic arthritis identified; no *H. influenzae* was identified (Table 3).

The risk factors and outcomes for septic arthritis caused by Gram-positive and Gram-negative bacteria are shown in Table 4. Univariate analysis showed that old age was a predictive factor for septic arthritis

Table 1. Demographic data of patients with septic arthritis.

Variable	No. of patients (%)
Age (years)	
Mean \pm SD	59.0 \pm 20.1
>60	27 (52.9)
Male sex	28 (54.9)
Blood culture positive ^a	26 (65.0)
Synovial fluid culture positive ^a	40 (90.9)
Single joint involvement	50 (98.0)
Hospital admission history within 1 year	19 (37.3)
Nursing home resident	2 (3.9)
Hemodialysis	3 (5.9)
Health care associated risk factor ^b	21 (41.2)
Joint surgery history ^c	13 (25.5)
Trauma within 3 months	11 (21.6)

^aPositive rate for those who had a culture test.

^bHistory of hospital admission within 1 year, nursing home resident, or hemodialysis. Some patients had more than 1 risk factor.

^cJoint surgery history before 1 year.

Abbreviation: SD = standard deviation.

caused by Gram-positive cocci (odds ratio [OR], 4.8; 95% confidence interval [CI], 1.12-20.61; $p = 0.035$), while Charlson comorbidity score ≤ 4 (OR, 0.18; 95% CI, 0.04-0.76; $p = 0.019$), diabetes mellitus with end-organ damage (OR, 0.17; 95% CI, 0.03-0.90; $p = 0.037$), and underlying malignancies (OR, 0.08; 95% CI, 0.01-0.85; $p = 0.036$) had a negative prediction for septic arthritis caused by Gram-positive cocci (Table 4).

Univariate analysis found no statistically significant differences for sex, recent hospital admission history, health associated risk factors, joint operation history, recent trauma history, or other underlying diseases between patients infected with Gram-positive

Table 2. Distribution of involved joints of patients with septic arthritis.

Joint	No. of joints (%)
Knee	33 (63.5)
Shoulder ^a	10 (19.2)
Hip ^a	4 (7.7)
Ankle	2 (3.8)
Wrist	1 (1.9)
Sacroiliac	1 (1.9)
Distal interphalangeal	1 (1.9)

^aOne patient had 2 involved joints.

Table 3. Distribution of causative agents among patients with septic arthritis.

Causative agent	No. of pathogens (%)
Gram-positive bacteria	39 (76.5)
MSSA	24 (47.1)
MRSA	6 (11.8)
MRCNS	1 (2.0)
<i>Streptococcus</i> spp.	6 (11.8)
<i>Enterococcus</i> spp.	1 (2.0)
<i>Peptostreptococcus</i> spp.	1 (2.0)
Gram-negative bacteria	12 (23.5)
<i>Aeromonas sobria</i>	2 (3.9)
<i>Escherichia</i> spp.	2 (3.9)
<i>Pseudomonas</i> spp.	2 (3.9)
<i>Salmonella</i> spp.	2 (3.9)
<i>Proteus</i> spp.	1 (2.0)
<i>Klebsiella pneumoniae</i>	1 (2.0)
<i>Neisseria</i> spp. ^a	2 (3.9)

^aOne *Neisseria gonorrhoeae*, and 1 *Neisseria meningitidis*.

Abbreviations: MSSA = methicillin-susceptible *Staphylococcus aureus*; MRSA = methicillin-resistant *Staphylococcus aureus*; MRCNS = methicillin-resistant coagulase-negative staphylococci.

and Gram-negative organisms. There was a trend for more patients with prosthesis infection to have Gram-positive pathogens than Gram-negative pathogens, but this did not reach statistical significance ($p = 0.094$).

For the initial presenting symptoms and signs, there was no differentiation between Gram-positive and Gram-negative pathogens, except for limitation in ROM [Table 4]. Patients presenting with limited ROM tended to have Gram-positive pathogens (OR, 4.06; 95% CI, 1.05-15.73; $p = 0.043$). The initial laboratory data also showed no significant differences between the groups (Table 4).

The factors for which univariate analysis showed $p < 0.2$ were included in the multivariate analysis. Age (OR, 1.07; 95% CI, 1.01-1.13; $p = 0.024$) and ROM limitation (OR, 8.23; 95% CI, 1.14-59.49; $p = 0.037$) were independent predictive factors for septic arthritis caused by Gram-positive cocci. Diabetes mellitus with end-organ damage (OR, 0.03; 95% CI, 0.00-0.39; $p = 0.007$) and malignancy (OR, 0.04; 95% CI, 0.00-0.66; $p = 0.025$) were independent negative predictive factors for Gram-positive septic arthritis.

There were no significant differences in clinical outcomes, including days to defervescence, duration of hospital stay, surgical interventions, complications, intensive care unit admission, and in-hospital mortality between patients with Gram-positive and Gram-negative septic arthritis (Table 5).

Discussion

In this study of adult patients with culture-proven community-onset septic arthritis in Taiwan, the most common pathogen was *S. aureus* (58.9%) followed by streptococci (11.8%), and Gram-negative bacteria caused 23.5% of all culture-proven septic arthritis. The distribution of causative pathogens was similar to many other studies, in which *S. aureus* was the predominant cause of septic arthritis, accounting for 37% to 56% [3,9,10], followed by *Streptococcus* spp. Gram-negative bacilli caused fewer cases of septic arthritis than Gram-positive cocci, accounting for 10% to 20% of patients [9-11].

In this study, age was an independent factor predicting for Gram-positive cocci septic arthritis. Regarding the age predisposition of Gram-positive or Gram-negative septic arthritis, previous studies demonstrated conflicting results [3,7,11]. Goldenberg et al described 13 patients with septic arthritis due to Gram-negative bacilli with a mean age of 56 years, and only 1 pediatric patient, aged 10 years [7]. However, in another study, Gram-negative bacteria predominated in patients younger than 5 years (60/114; 50%), and staphylococci and streptococci accounted for only 43% (49/114). In patients older than 60 years, staphylococci and streptococci predominated [3]. Deesomchok and Tumrasvin demonstrated that younger patients with septic arthritis were more frequently affected by Gram-negative bacilli [11].

In this study, patients with diabetes mellitus with end-organ damage and malignancy tended to have septic arthritis caused by Gram-negative bacteria. This finding is compatible with other studies [7,12,13]. In those studies, underlying immunocompromised status was associated with septic arthritis caused by Gram-negative bacilli in 66% of patients with septic arthritis, of whom 22% had malignancy, 16% had diabetes mellitus, and 28% had other chronic disorders, such as connective tissue disease, heroin abuse, or sickle cell anemia [7]. As nearly all cases of Gram-negative bacillary septic arthritis are a consequence of hematogenous spread, factors that predict for Gram-negative bacteremia also predict for Gram-negative bacillary septic arthritis [7]. Some studies have shown that a history of intravenous drug abuse is associated with a higher percent of Gram-negative bacillary septic arthritis, especially *Pseudomonas aeruginosa* [14]. As there was only 1 intravenous drug abuser in this series, it was not possible to demonstrate a

Table 4. Characteristics of patients with septic arthritis caused by Gram-positive and Gram-negative bacteria.

Characteristic	Gram-positive (n = 39) No. (%)	Gram-negative (n = 12) No. (%)	Univariate odds ratio (95% CI)	<i>p</i>	Multivariate ^a odds ratio (95% CI)	<i>p</i>
Demographics						
Age (years) [mean ± SD]	61.5 ± 19.7	51.1 ± 20.1	1.03 (0.99-1.06)	0.122	1.07 (1.01-1.13)	0.024
Age >60 years	24 (61.5)	3 (25.0)	4.80 (1.12-20.61)	0.035		
Male sex	21 (53.8)	7 (58.3)	0.83 (0.23-3.09)	0.785		
Prosthesis infection	9 (23.1)	0 (0)		0.094		
Past history and underlying disease						
Hospital admission within 1 year	13 (33.3)	6 (50.0)	0.50 (0.13-1.86)	0.301		
Health care associated risk ^b	15 (38.5)	6 (50.0)	0.63 (0.17-2.30)	0.479		
Joint surgery history	12 (30.8)	1 (8.3)	2.21 (0.75-6.50)	0.149		
Trauma history within 3 months	8 (20.5)	3 (25.0)	0.77 (0.17-3.54)	0.741		
Charlson comorbidity score >4	6 (15.4)	6 (50.0)	0.18 (0.04-0.76)	0.019		
Diabetes mellitus	11 (28.2)	4 (33.3)	0.79 (0.20-3.15)	0.733		
Diabetes mellitus with end-organ damage	3 (7.7)	4 (33.3)	0.17 (0.03-0.90)	0.037	0.03 (0.00-0.39)	0.007
Liver cirrhosis	4 (10.3)	2 (16.7)	0.57 (0.09-3.59)	0.550		
Hypertension	21 (53.8)	4 (33.3)	2.33 (0.60-9.05)	0.220		
Coronary artery disease	3 (7.7)	1 (8.3)	0.92 (0.09-9.73)	0.942		
Chronic renal insufficiency	12 (30.8)	3 (25.0)	1.33 (0.31-5.81)	0.702		
Autoimmune disease	2 (5.1)	1 (8.3)	0.59 (0.05-7.19)	0.683		
Immunosuppressant	2 (5.1)	2 (16.7)	0.27 (0.03-2.16)	0.218		
Malignancy	1 (2.6)	3 (25.0)	0.08 (0.01-0.85)	0.036	0.04 (0.00-0.66)	0.025
Initial symptoms, signs, and laboratory data						
Pain	38 (97.4)	10 (83.3)	7.60 (0.62-92.54)	0.112		
Fever	22 (56.4)	10 (83.3)	0.26 (0.05-1.34)	0.107		
Swelling	34 (87.2)	9 (75.0)	2.27 (0.45-11.33)	0.319		
Heat	25 (64.1)	7 (58.3)	1.28 (0.34-4.78)	0.718		
Redness	21 (53.8)	6 (50.0)	1.17 (0.32-4.26)	0.816		
Limited range of movement	29 (74.4)	5 (41.7)	4.06 (1.05-15.73)	0.043	8.23 (1.14-59.49)	0.037
C-reactive protein (mg/dL) [mean ± SD]	14.2 ± 8.9	15.7 ± 10.2	0.98 (0.91-1.07)	0.665		
Blood culture positive	18 (60.0)	8 (80.0)	0.38 (0.07-2.08)	0.262		
Synovial fluid culture positive	31 (91.2)	9 (90.0)	1.14 (0.11-12.42)	0.909		
Anemia ^c	20 (51.3)	7 (58.3)	0.75 (0.20-2.78)	0.669		
Leukocytosis (>10,000 cells/μL)	30 (76.9)	6 (50.0)	3.33 (0.86-12.91)	0.082		
Thrombocytopenia (<130,000 cells/μL)	31 (79.5)	8 (66.7)	1.94 (0.46-8.10)	0.365		
Synovial fluid white blood cell count (>100,000 cells/μL)	9 (45.0)	2 (25.0)	2.45 (0.40-15.25)	0.335		

^aFactors that univariate logistic analysis showed *p* < 0.2 were included in the multivariate logistic regression.

^bHistory of admission within 1 year, nursing home resident, and hemodialysis.

^cWorld Health Organization criteria.

Abbreviation: CI = confidence interval; SD = standard deviation.

significant association of intravenous drug abuse with any specific pathogen.

According to previous reports, any joint can be affected by septic arthritis, with 80% to 90% being monoarticular [10,15-17]. The most frequently involved joint was the knee, which accounted for approximately 50% of the affected joints [2]. Hips, especially in children [5,9,18], and ankles [11] are also

frequently involved. In this study, only 1 patient had more than 1 involved joint, and the most frequently involved joint was the knee (63.5%), followed by the shoulder (19.2%), hip (7.7%), and ankle (3.8%). Part of the reason why the shoulder was more frequently involved in this series than in other studies might be because pediatric patients and those who had recently had joint operations were excluded.

Table 5. Comparison of outcomes for patients with septic arthritis caused by Gram-positive and Gram-negative bacteria.

Outcomes	Gram-positive (n = 39) No. (%)	Gram-negative (n = 12) No. (%)	Univariate odds ratio (95% CI)	<i>p</i>
Duration of fever (days) [mean ± SD]	4.5 ± 3.6	5.0 ± 4.7		0.744
Duration of hospital stay (days) [mean ± SD]	36.7 ± 22.6	27.6 ± 12.0	1.03 (0.99-1.07)	0.194
Duration of hospital stay >30 days	18 (48.6)	4 (33.3)	1.89 (0.49-7.40)	0.358
Surgical intervention	13 (33.3)	2 (16.7)	2.50 (0.48-13.12)	0.279
Complications ^a	8 (20.5)	4 (33.3)	0.52 (0.12-2.16)	0.365
Intensive care unit admission	6 (15.4)	2 (16.7)	0.91 (0.16-5.23)	0.915
In-hospital mortality	2 (5.1)	0 (0)		1.000
14-day mortality	1 (2.6)	0 (0)		1.000
30-day mortality	2 (5.1)	0 (0)		1.000

^aComplications: septic shock, acute respiratory failure, acute renal failure, and mortality.

Abbreviation: CI = confidence interval; SD = standard deviation.

Typical symptoms and signs of septic arthritis include joint pain, heat, redness, swelling, decreased ROM, and fever [6,19,20]. Joint pain is the most sensitive symptom for diagnosing septic arthritis, with an 85% sensitivity rate (95% CI, 78-90) reported by Margaretten et al [21]. In this study, 94% of patients had joint pain, 84% had joint swelling, 67% had limited ROM, 63% experienced warmth, and 53% had joint erythema. This result was compatible with those of previous studies that showed that a significant number of patients do not have heat and redness around the affected joint [5,22]. Limited ROM was an independent risk factor for septic arthritis caused by Gram-positive cocci (OR, 8.23; 95% CI, 1.14-59.49; *p* = 0.037). This was probably because there were more patients with prosthetic infection in the Gram-positive group, and Gram-positive cocci cause more severe inflammation. The number of synovial white blood cells was greater in the Gram-positive group, although this did not reach statistical significance (*p* = 0.255).

There are several limitations to this study. First, because this was a retrospective study, the record keeping for clinical symptoms and signs might vary between different doctors. Second, a small number of patients were enrolled, only 51, and only 12 patients had septic arthritis caused by Gram-negative bacteria. This may have affected the statistical power. In addition, there was 1 patient with gonococcal septic arthritis in this study, which might have affected the characteristics of the Gram-negative group. However, even when this patient was excluded, age older than 60 years was still an independent risk factor for septic arthritis caused by Gram-positive cocci (OR, 26.89; 95% CI, 1.46-500.50; *p* = 0.027). Diabetes mellitus with end-organ damage

(OR, 0.01; 95% CI, 0.00-0.70; *p* = 0.011) and malignancy (OR, 0.01; 95% CI, 0.00-0.25; *p* = 0.006) were still independent negative predictive factors for septic arthritis caused by Gram-positive cocci. The third limitation of this study is that the treatment of these patients was not analysed. Due to the limited number of patients for each individual pathogen, it was difficult to compare the effect of different treatment regimens.

In conclusion, when patients have community-onset septic arthritis, those older than 60 years tend to have septic arthritis caused by Gram-positive cocci. Patients with diabetes mellitus with end-organ damage and malignancy tend to have septic arthritis caused by Gram-negative bacteria. The treatment should be different for these 2 groups. Although this study did not show outcome differences between the 2 groups, further study to analyse the relationship between treatment and outcome within these groups is needed.

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