Septic Arthritis Among Users of Injection Drugs: Clinical Course and Microbial Characteristics

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abstract

Injection drug use (IDU) is a risk factor for septic arthritis (SA) of native joints. Amid the opioid crisis, IDU rates have increased. This study assessed differences in preoperative characteristics, microbial characteristics, and postoperative outcomes of 177 cases of SA treated operatively from 2015 to 2019 at 3 US hospitals, by self-reported IDU status. Forty cases (23%) involved patients who reported IDU. Patient characteristics, comorbidities, microbial characteristics, duration of hospital stay, discharge destination, follow-up rates, and rates of persistent/secondary infection were compared by self-reported IDU status. Compared with non–IDU-associated SA (non–IDU-SA), IDU-associated SA (IDU-SA) was associated with female sex (P=.001), younger age (P<.001), lower body mass index (P<.001), tobacco use (P<.001), and psychiatric diagnosis (P=.04) and was more likely to involve methicillin-resistant *Staphylococcus aureus* (P<.001). The IDU-SA was associated with discharge to a skilled nursing facility or against medical advice (P<.001) and with loss to follow-up (P=.01). The 2 groups did not differ in terms of American Society of Anesthesiologists classification, joint involved, Gram stain positivity, presence of bacteremia, peripherally inserted central catheter placement, return to hospital within 3 months, or persistent/secondary positive results on culture within 3 months. Patients with IDU-SA were younger, were more likely to be female, had lower body mass index, and had fewer medical comorbidities but were more likely to use tobacco and to have a psychiatric diagnosis compared with patients with non–IDU-SA. Methicillin-resistant *S aureus* was more common in the IDU-SA group, as was discharge to a skilled nursing facility or against medical advice. Patients with IDU-SA were less likely to return for follow-up than patients with non–IDU-SA. [*Orthopedics*. 2021;44(6):e747-e752.]

Septic arthritis (SA) is among the few true orthopedic emergencies[1] and can lead to cartilage damage, permanent disability, and even death.[2] Patients with articular abnormalities, diabetes, low socioeconomic status, cutaneous ulcers or skin infections, or injection drug use (IDU) are at increased risk for SA.[1] Patients with IDU represent a unique population who may have characteristics and behaviors that predispose them to worse outcomes after SA. Injection drug use increases the risk of morbidity and death from drug overdose as well as the many acute and chronic diseases associated with recurrent hematogenous infections.[3]

Recent studies have linked the increasing rates of IDU in the United States to the opioid epidemic as more nonmedical users of prescription opioids have transitioned to injectable forms of narcotics.[4-6] Concurrent with the increase in IDU has been an increase in the incidence of SA among patients with IDU.[7] Nonsterile injection

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technique is a risk factor for SA because it can introduce skin flora into the bloodstream or tissue via primary inoculation.[8,9] Recent studies have noted a shift to more antibiotic-resistant or virulent pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), among patients with SA.[10-12] Septic arthritis caused by resistant organisms is associated with higher rates of complications, reoperation, and death, in addition to higher treatment costs.[7,13-15]

Studies have reported microbial trends in SA in the IDU population, but results have differed over time and by geographic location.[9,10,12,16-20] Rates of MRSA and methicillin-sensitive *S aureus* (MSSA) are reportedly higher in IDU-associated SA (IDU-SA) compared with non–IDU-associated SA (non–IDU-SA).[10,13,16] The differences in the clinical courses of these patients are poorly understood.

In this study, the authors analyzed the differences in preoperative characteristics, microbial characteristics, and postoperative outcomes between patients with IDU-SA and non–IDU-SA groups. They hypothesized that patients with IDU-SA would have higher rates of resistant pathogens, longer hospital stays, higher rates of discharge to a skilled nursing facility or against medical advice, lower rates of follow-up, and higher rates of persistent/secondary infections.

Materials and Methods

This study received institutional review board approval. The authors retrospectively reviewed the medical records of all 208 cases of operatively treated SA confirmed by positive culture between May 2015 and May 2019 at 2 academic urban hospitals and 1 community suburban hospital in 1 US health system. Cases were excluded if the patient was younger than 18 years (n=22) or if a prosthetic joint was involved (n=9). Overall, the authors included 177 cases of SA among 175 patients.

Data were obtained from the authors' institutional electronic medical record system. They recorded preoperative characteristics, comorbidities, current tobacco use, American Society of Anesthesiologists classification, year of surgery, causative organism(s), joint involved, presence of instrumentation from previous procedures, patient-reported IDU, peripherally inserted central catheter placement, duration of hospital stay (from initial operation to discharge), discharge destination, follow-up within 3 months, return to hospital for SA-related treatment within 3 months, and persistent/secondary infection (defined as positive results on culture within 6 weeks after the first aspiration). Cases were assigned to 2 groups according to IDU status. The groups were analyzed for key differences in demographic, clinical, and microbial characteristics, which included Gram stain positivity, antibiotic resistance, and concomitant bacteremia (defined as a positive blood culture result within the same hospital stay). The ratios of MRSA to MSSA were calculated for each group.

Statistical Analysis

Categorical variables were analyzed with Pearson's chi-square and Fisher's exact tests, and continuous variables were analyzed with Student's *t* tests. Significance was set at $P<.05$. All analyses were conducted with JMP software, version 15.2.1 (SAS Institute Inc).

Results

Preoperative Characteristics

The IDU-SA cases (n=40) were not significantly different from the non–IDU-SA cases (n=137) in terms of American Society of Anesthesiologists classification ($P=.22$), but IDU-SA cases were more likely to involve patients who were female ($P=.001$), who were younger ($P<.001$), and who had lower body mass index ($P<.001$) (**Table 1**). Compared with non–IDU-SA, IDU-SA occurred among patients who were less likely to have medical comorbidities, including chronic kidney disease ($P=.01$) and diabetes ($P=.02$), and more likely to be current tobacco users ($P<.001$) and to have a psychiatric diagnosis ($P=.04$). Compared with non–IDU-SA, IDU-SA was less likely to involve joint instrumentation from a previous surgery ($P=.02$), but the authors found no difference in the type of joint involved ($P=.40$). They also found no change in the rates of SA during the study period among patients with self-reported IDU ($P=.05$).

Microbial Characteristics

The authors found no difference in Gram stain positivity ($P=.17$) or presence of bacteremia ($P=.58$) between the groups. For the IDU-SA cases, the cause was more likely to be MRSA ($P<.001$). Although the MRSA-to-MSSA ratio was higher for IDU-SA cases (1.3) than for non–IDU-SA cases (0.57), this difference was not significant ($P=.08$).

Postoperative Outcomes

The authors found no difference in duration of hospital stay ($P=.66$) or peripherally inserted central catheter placement ($P=.28$) between the 2 groups. Compared with patients with non–IDU-SA, those with IDU-SA were more likely to be discharged to a skilled nursing facility or to leave the hospital against medical advice, less likely to be discharged home, and more likely to be lost to follow-up (all $P=.01$; **Figure 1**). The authors found no differences between the groups for rate of return to the hospital for SA-related treatment within 3 months ($P=.20$) or rate of persistent/secondary infection ($P=.82$).

Discussion

Because of recent concern about increased rates of IDU stemming from the opioid epidemic, it is essential to understand the challenges of treating SA for patients who inject drugs. Patients with IDU-SA have reportedly higher rates of complications and death compared with non–IDU-SA groups.[7] Given the rising prevalence and unique challenges of treat-

Table 1

Characteristics of 177 Cases of Septic Arthritis From 2015 to 2019 by Patient-Reported Injection Drug Use Status

Variable	Cases involving injection drug use (n=40)	Cases not involving injection drug use (n=137)	*P*
Preoperative characteristics			
Age, mean±SD, y	39±11	50±18	<.001
Sex, No. (%)			.001
Male	17 (42.5)	96 (70)	
Female	23 (57.5)	41 (30)	
Body mass index, mean±SD, kg/m^2	24±4.7	28±7.5	<.001
ASA classification >2, No. (%)	30 (75)	82 (60)	.22
Chronic kidney disease, No. (%)	2 (5)	34 (25)	.01
Diabetes, No. (%)	4 (10)	39 (28)	.02
Current tobacco use, No. (%)	38 (95)	69 (50)	<.001
Psychiatric diagnosis, No. (%)	18 (45)	38 (28)	.04
Joint involved, No. (%)			.40
Ankle	5 (13)	14 (10)	
Knee	16 (40)	42 (31)	
Hip	4 (10)	23 (17)	
Shoulder	8 (20)	26 (19)	
Elbow	2 (5)	8 (6)	
Wrist	2 (5)	1 (1)	
Finger	2 (5)	12 (9)	
Other/polyarticular	1 (3)	11 (8)	
Periarticular instrumentation from previous surgery, No. (%)	1 (3)	23 (17)	.02
Microbial characteristics			
Gram stain			.17
Gram positive, No. (%)	32 (80)	88 (64)	
Gram negative, No. (%)	3 (8)	16 (12)	
Polymicrobial, No. (%)	5 (13)	33 (24)	
MRSA, No. (%)	18 (45)	17 (12)	<.001
MRSA:MSSA ratio	1.3	0.57	
Bacteremia present, No. (%)	11 (28)	44 (32)	.58
Postoperative characteristics			
PICC placement, No. (%)	24 (60)	68 (50)	.28
Duration of hospital stay, mean±SD, d	8.9±8.5	9.6±8.4	.66
Discharge destination, No. (%)[a]			<.001
Home	7 (18)	98 (73)	
Nursing facility/subacute rehabilitation	24 (60)	29 (22)	
Transferred	1 (3)	5 (4)	
Left against medical advice	8 (20)	2 (1)	
Follow-up within 3 mo, No. (%)	25 (63)	109 (79.5)	.01
Return to hospital within 3 mo, No. (%)	14 (35)	33 (24)	.20
Persistent/secondary positive culture at 3 mo, No. (%)	5 (13)	19 (14)	.82

Abbreviations: ASA, American Society of Anesthesiologists; MRSA, methicillin-resistant Staphylococcus aureus*; MSSA, methicillin-sensitive* S aureus*; PICC, peripherally inserted central catheter.*

[a]*This was unknown for 3 patients.*

ing this patient population, the authors explored their distinct characteristics in this study. They focused on differences that have treatment implications and that can influence clinical care.

Patients with non–IDU-SA had more medical comorbidities, with higher proportions of chronic kidney disease and diabetes than those with IDU-SA. This difference is likely attributable in part to the difference in mean age between the groups. Diabetes and chronic kidney disease have been recognized as independent predictors of death among patients with SA.[21] Compared with the non–IDU-SA

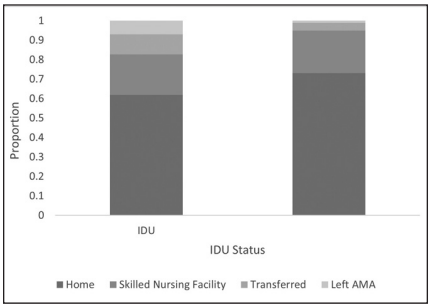

Figure 1: Discharge destination by self-reported injection drug use (IDU) status for 177 cases (175 patients) of operatively treated septic arthritis. Abbreviation: AMA, against medical advice.

group, those with IDU-SA had higher rates of psychiatric diagnoses and tobacco use, which is consistent with results of previous studies.[22,23] Mertz et al[24] showed that for patients with IDU who were being treated for infectious disease, the presence of psychiatric disorders was an independent predictor of reduced compliance with antibiotic treatment regimens. Additionally, in a study by Jennings et al,[25] smoking was an independent predictor of SA of the wrist. Tobacco use has numerous consequences for orthopedic patients, including higher rates of fracture nonunion, deep infection, and osteomyelitis.[26,27] For the current patient population, fracture healing was not a concern, but the higher rates of persistent infection seen in smokers are particularly concerning. Finally, tobacco use is independently associated with greater odds of poor wound healing, which can complicate recovery from surgery.[28]

The authors found that cases of IDU-SA were more likely to be caused by antibiotic-resistant organisms compared with non–IDU-SA. Among the IDU-SA group, 78% of cases involved *S aureus* compared with 33% of the non–IDU-SA group. Forty-five percent of IDU-SA cases involved MRSA, with a MRSA-to-MSSA ratio of 1.3 compared with 12% and a MRSA-to-MSSA ratio of 0.57 for the non–IDU-SA group. Available evidence is inconsistent in terms of microbial trends in SA. Geographic location and the local microbiome may affect microbial patterns because studies conducted in different geographic regions have reported different findings. In a 5-year study of 58 cases of hematogenous SA at a hospital in the United Kingdom, Al-Nammari et al[16] reported higher rates of MSSA (49%) compared with MRSA (7%) among patients reporting IDU. Peterson et al[9] reviewed 96 patients with IDU who were undergoing treatment for SA at a US hospital at two different times (during the 1980s and 2000s) and found that MRSA was the most common causative pathogen. They also reported a 5% increase in the prevalence of MRSA among patients with IDU-SA from the 1980s to the 2000s, suggesting a temporal trend because injectable substances and antibiotic regimens have changed over time.[9] The greater prevalence of *S aureus* in the IDU-SA group may be explained by the introduction of skin flora into the bloodstream via needle punctures. The continued increase in the prevalence of resistant bacteria, such as MRSA, is concerning because patients infected with resistant organisms have worse clinical outcomes and higher mortality rates and are more costly to treat compared with patients without these infections.[14] Infections with resistant pathogens are often first treated empirically with ineffective antibiotics.[16] Because SA can cause rapid destruction of articular cartilage, the initial use of ineffective antibiotics can be devastating.[2] The use of ineffective antibiotics also leads to further resistance, particularly when the treatment course is not completed.[10]

For postoperative outcomes, the authors found no differences in peripherally inserted central catheter placement rates or duration of hospital stay between the 2 groups. Peripherally inserted central catheter placement for patients with a history of IDU is sometimes avoided because of concern about relapse and infection.[29,30] The authors' health system's policy mandates against discharge to home for patients with IDU and indwelling catheters, and this policy likely contributed to differences in discharge destination. The authors found no difference in duration of hospital stay, which may be attributable in part to the discharge patterns seen for this population. The IDU-SA group had higher rates of discharge against medical advice and discharge to a skilled nursing facility, which may have shortened hospital stay. Additionally, the IDU-SA group had lower rates of follow-up compared with the non–IDU-SA group. These findings are consistent with previous research on SA among patients with IDU. Although their study was limited to SA of the knee, Oh et al[7] also reported higher rates of discharge to postacute care facilities for patients with IDU. Injection drug use has been associated with lower follow-up rates in the settings of HIV care and orthopedic trauma.[31,32] When patients leave the hospital against medical advice, there is concern about the development of resistant organisms because of the greater likelihood that antimicrobial therapy will not be completed as prescribed.[24,33] Lack of follow-up can lead to suboptimal care and potentially avoidable complications[31] and may be particularly detrimental for patients with IDU, for whom continued IDU may increase the risk of morbidity. Injection drug use can also lead to more advanced presentation, which can be challenging and costly to treat. These factors suggest that patients with IDU may warrant more aggressive treatment. The authors recommend the empirical use of vancomycin for IDU-SA, followed by an antibiotic chosen according to culture results. Finally, contrary to what they expected, the authors found no difference in persistent/secondary infections between the 2 groups. However, their ability to draw conclusions about persistent/secondary infection rates was limited because nearly 40% of patients with IDU did not return for follow-up.

This study had several limitations. The authors analyzed operatively treated and culture-positive SA to facilitate identification of cases of SA at their institution.

They may have missed culture-negative cases of SA that resulted from antibiotic exposure before operative intervention, and this possibility may limit the generalizability of these results. Additionally, the retrospective design of the study limited the data to information previously collected in medical records. Finally, IDU was self-reported, which can lead to reporting bias. Despite these limitations, this study allowed the authors to analyze several factors that are not routinely reported in large data sets, such as IDU status, peripherally inserted central catheter placement, and follow-up rates. In the context of the opioid epidemic, it is important to compare IDU-SA and non–IDU-SA groups to help clinicians to recognize the differences between their clinical courses and provide more effective treatment.

Conclusion

Patients with IDU-SA had fewer underlying medical comorbidities but higher rates of tobacco use and psychiatric diagnoses compared with the non–IDU-SA group. Patients with IDU-SA had higher rates of MRSA, were more likely to leave the hospital against medical advice or to be discharged to a skilled nursing facility, and were less likely to return for follow-up. If untreated, SA can cause severe morbidity and death. To promote appropriate antimicrobial stewardship and provide more effective patient care, special attention must be given to patients with IDU who present with SA.

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