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MAJOR ARTICLE

Microbes Causing Spinal Epidural Infection in Patients Who Use Drugs

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Background. The incidence of spine infections has increased due to the surge in injection drug use driven by the opioid epidemic. Few recent studies have evaluated the microbiology of spinal epidural infections among people who inject drugs compared to the microbiology of such infections among the general population.

Methods. We performed a retrospective chart review to identify patients with a spinal epidural abscess or phlegmon unrelated to recent spine surgery between 2015 and 2023.

Results. Of 346 initial records, 277 met inclusion criteria for demographic analyses. Of the 229 patients with microbiologic results, details regarding possible drug use were available in 227 patients. Patients with no documented history of drug use were categorized as non-PWUD, while patients who use drugs (PWUD) were separated based on whether drug use was active or not. Patients with prior histories of injection or noninjection drug use were categorized as nonactive PWUD, while those with injection or snorting drug use reported in the past 3 months were categorized as active PWUD. Thirty-nine percent of patients with spinal epidural infection had substance use disorder. Most patients with monomicrobial cultures were infected with gram-positive, aerobic bacteria (86%). Active PWUD were more likely to have methicillin-resistant *Staphylococcus aureus* compared to non-PWUD (36% vs 13%, respectively, $P = .002$). Nonactive PWUD were more likely to have non–*Escherichia coli* gram-negative bacterial infections than non-PWUD (18% and 4.4%, respectively, $P = .01$).

Conclusions. More than 1 in 3 patients with a spinal epidural infection unrelated to recent surgery had substance use disorder. These patients are more likely to have infections due to MRSA and gram-negative bacteria other than *E coli* such as *Serratia marcescens*.

Keywords. epidural abscess; epidural infection; injection drug use; spine infection; substance use disorder.

In parallel with the opioid epidemic of the past 2 decades, injection drug use and its infection-related sequelae have emerged as a pressing public health issue [1]. While illicit drug overdose remains the leading cause of drug-associated deaths, of particular concern is the precipitous increase in associated spine infections that has largely gone underreported [2]. These infections are associated with high rates of morbidity, mortality, and long-term disability [3]. However, some of these outcomes may be less prevalent among people who use drugs (PWUD), who are younger, and have fewer comorbidities [4]. Nevertheless, the financial burden on health systems is significant, as hospital charges may be as much as $31 000 higher for PWUD [5]. Treatment of spine infections among this highly stigmatized population is further complicated by the frequency of discharge against medical advice (AMA) [6], high rates of human immunodeficiency virus and hepatitis C virus infections [7], and clinician concern that PWUD may utilize intravascular catheters used for outpatient parenteral microbial therapy to inject drugs [8].

Staphylococcus aureus is the most common cause of epidural abscess among PWUD [9]. This reflects the fact that PWUD may have an increased likelihood of *S aureus* colonization, while skin and nasal epithelial damage associated with repeated injections and drug inhalation, respectively, allow entry into subcutaneous tissue and beyond [10]. Poor hygiene associated with housing instability may also be a contributing factor [11]. Additionally, there may be microbial contamination of syringes, drugs used as cutting or diluting agents, or contamination that occurs during storage or manufacturing [12–14]. PWUD

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may attempt to clean needles with tap, puddle, or toilet water contaminated with various gram-negative bacteria such as *Pseudomonas aeruginosa* and *Serratia marcescens* and they may do so in settings with heavy environmental contamination such as bathrooms [9, 15]. Oral flora such as *Eikenella corrodens*, *Haemophilus* spp, *Prevotella* spp, and viridans group streptococci may be introduced into the injection site from the skin or needle licking. Last, inexperienced PWUD may resort to "skin-popping," or subcutaneous injection if veins appear nonviable [15]. All of these behaviors can result in skin and soft tissue inoculation with risk of secondary bacteremia and hematogenous seeding of the spine [9]. Accordingly, injection drug use has been independently associated with hematogenous vertebral osteomyelitis [16].

The purpose of this study was to evaluate the microbiology of spinal epidural infections (ie, epidural abscess or phlegmon) in PWUD compared to the general population. We hypothesized that methicillin-susceptible *S aureus* (MSSA) and methicillin-resistant *S aureus* (MRSA) will predominate among gram-positive bacteria across both groups. We anticipated that infections with *Escherichia coli* will be more common in non-PWUD as a result of hematogenous spread from the gastrointestinal or genitourinary tracts [17], while other gram-negative bacteria such as *S marcescens* would predominate among PWUD and nonactive PWUD. A secondary aim of this project was to evaluate differences in AMA discharge and demographic data between the 2 study populations.

METHODS

We searched admission diagnoses and problem lists in the electronic medical records of patients admitted to Rhode Island Hospital between 2015 and 2023 for the presence of epidural abscess (Figure 1, Table 1). All previous surgeries in the 90 days prior to hospital admission at any of the 3 acute care hospitals in our healthcare system (Lifespan Healthcare) were assessed to ensure that the diagnosis was not related to a recent surgical procedure. Similarly, for patients transferred from another hospital, the available medical records were reviewed to assess for spine surgery over the prior 90 days. Patients were excluded if they had a cranial epidural abscess or phlegmon, or if they had a surgical site infection related to spine surgery in our hospital system or another facility over the prior 90 days. Some patients were originally admitted with what appeared to be an epidural abscess, but ultimately determined to have a noninfectious etiology (eg, metastatic cancer; Figure 1). After determining that a patient met study criteria, further medical record review ensued including assessing infectious diseases consult notes, as well as neurosurgery, psychiatry, addiction medicine consult notes, and discharge summaries. Patients were categorized by no history of injection or snorting drug use (non-PWUD), history of injection or noninjection drug use (nonactive PWUD), and patients with active snorting or injection drug use within the past 3 months (active PWUD). Information was gathered from these sources on infection type(s) and microorganism(s), age, race/ethnicity, sex, smoking status, anatomic level of spine infection, AMA discharge, and comorbidities. Patients with spinal epidural infections were defined by (1) presence of microbial growth in epidural or paravertebral culture, culture of vertebral bone, and/or blood cultures), and/or (2) magnetic resonance imaging findings, and/or (3) infectious diseases consultation. Substance use data were primarily collected from addiction medicine or psychiatry consult notes. If neither was present, data were obtained from the infectious diseases consultation note, and to a lesser extent, the primary care team admission and discharge notes. Source of infection data were collected predominantly from infectious diseases consultation notes. If this was not present, information was obtained from the discharge summary, history and physical note, internal medicine progress notes, and psychiatry consultation notes.

Wilcoxon rank-sum tests were used for statistical tests for continuous variables, while Fisher exact tests were used for categorical variables given the small sample size. For comparisons of categorical variables involving >2 groups, log-binomial regression models were used instead of Fisher exact tests.

Ethical Considerations

The study was approved by the Lifespan Rhode Island Hospital Institutional Review Board as a minimal risk project. As a retrospective chart review, patient consent was not required for this project.

RESULTS

Demographics and Patient Characteristics

For demographic information, 277 patients were evaluated, including 169 non-PWUD and 108 PWUD (Figure 1). The majority of spinal epidural infections among PWUD occurred in people aged 50 years or younger (mean age, 48 years). Conversely, non-PWUD with spinal epidural infections were on average 64 years old (Table 2). PWUD were far more likely than non-PWUD to have prior histories of AMA discharge (34% and 4.7%, $P < .001$) or current discharge AMA (12% and 1.2%, $P < .001$). A total of 52 patients were designated as having active injection drug use. Of these patients with active injection drug use, 45 also had culture results, representing 87% of the active-PWUD category.

PWUD were more likely to have lumbosacral epidural infections (27% vs 15%, $P = .02$). Sixty percent of PWUD had toxicology screening compared to 8.9% of non-PWUD (Table 2, $P < .001$). Among PWUD with a toxicology screening, 48%, 7.7%, and 3.1% tested positive for cocaine, amphetamines, and barbiturates, respectively, compared to 0% for non-PWUD. PWUD were more likely than non-PWUD to test positive for fentanyl (49% vs 20%, respectively, $P = .047$).

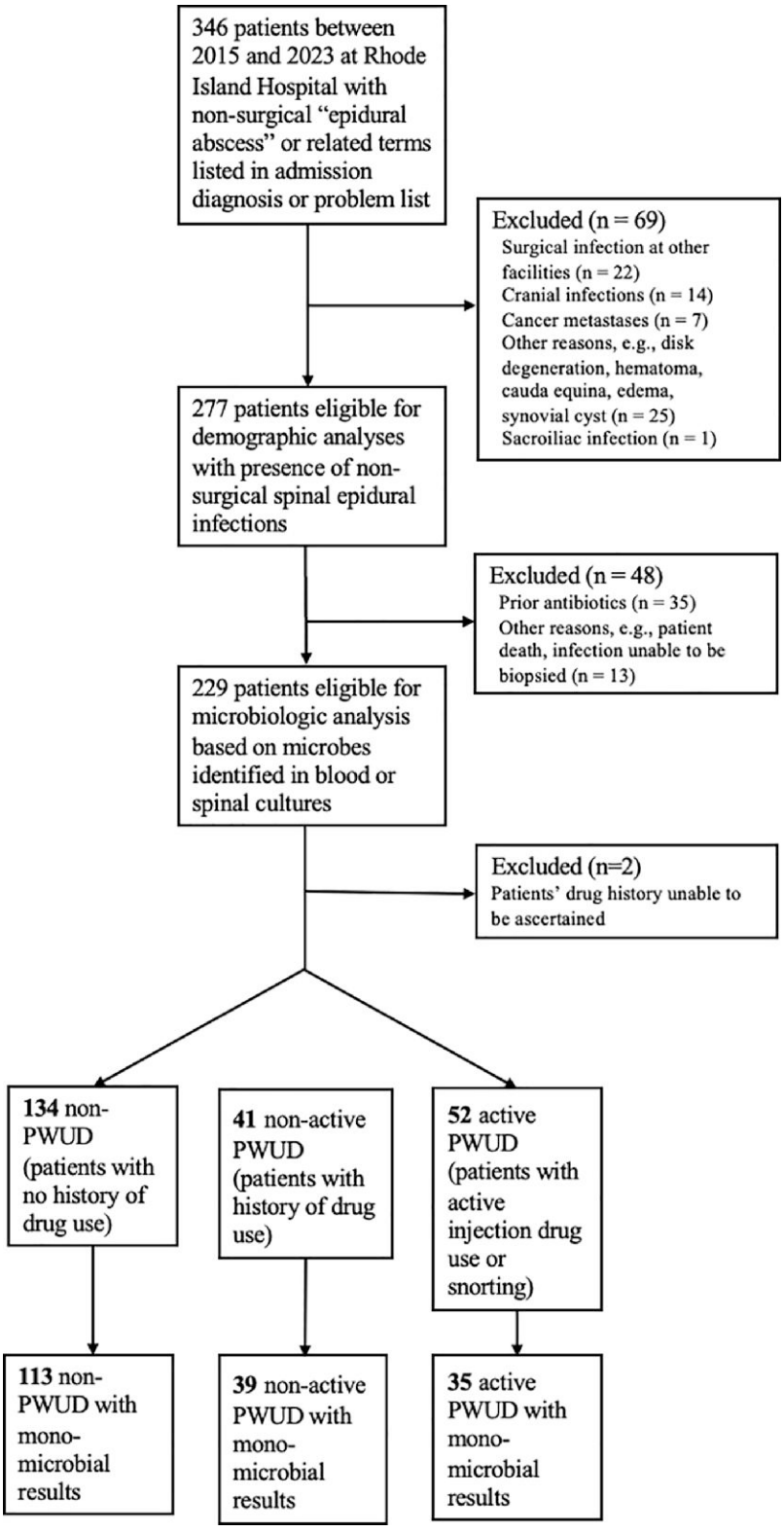

Figure 1. Flowchart of exclusion criteria. Abbreviation: PWUD, people who use drugs.

Table 1. Findings Using Epidural Abscess as a Search Term

	Diagnosis
1	Epidural abscess
2	Epidural abscess of spine due to infective embolism
3	Epidural abscess, L2–L5
4	Bacterial spinal epidural abscess
5	Cranial epidural abscess
6	Epidural intracranial abscess
7	Epidural intraspinal abscess
8	Mycobacterial spinal epidural abscess
9	Spinal epidural abscess
10	Intracranial epidural abscess due to infective embolism
11	Supratentorial epidural abscess due to pyogenic organism
12	Abscess in epidural space of cervical spine
13	Abscess in epidural space of L2–L5 lumbar spine
14	Abscess in epidural space of lumbar spine
15	Abscess in epidural space of spine
16	Abscess in epidural space of thoracic spine
17	Abscess of epidural space of spine due to bacteria
18	Abscess of epidural space of spine due to fungus
19	Abscess of epidural space of spine due to mycobacteria
20	Tuberculous abscess of epidural space

PWUD were less likely than non-PWUD to have previous skin or soft tissue infections acknowledged as a source (7% and 18%, $P = .02$) and less likely to have "no direct cause" of infection (27% and 44%, $P = .003$) (Table 2).

Microbiology

Of the 229 patients with microbiologic culture results, 1 patient had a positive culture result from another hospital, but the source was not specified. Of the remaining 228 patients, 25 patients had growth only in blood cultures, 106 patients had growth only in cultures other than blood, and 60 patients had growth both in blood cultures and cultures other than blood. An additional 4 patients did not have blood cultures but had growth in a culture other than blood. Last, 33 patients had blood cultures but did not have other cultures obtained. All cultures from sites other than blood involved the spine (eg, epidural fluid, bone) with only 3 exceptions: urine in a patient with a urinary tract infection associated with an epidural infection; a knee culture in a patient with a septic knee in addition to their epidural infection; and another patient with recent intravenous drug use, epidural infection, and a culture of the infected forearm injection site.

Of these 229 patients, details regarding possible drug use were available in 227 patients. Regarding these latter patients, 197 had monomicrobial culture results and 30 had polymicrobial culture results. Among all 3 cohorts, aerobic gram-positive bacteria predominated, comprising 86% of all monomicrobial cultures (Table 3). Active PWUD and nonactive PWUD were more likely to have *S marcescens* infections (11% and 10%, respectively) compared to non-PWUD (0.88%). However, only nonactive

Table 2. Demographics and Patient Characteristics

Characteristic	Total Cohort (n = 277)	Non-PWUD (n = 169)	PWUD (n = 108)	*P* Value
Age, y				
Mean (SD)	58 (15)	64 (14)	48 (12)	<.001[a]
Median (Q1–Q3)	59 (48–70)	65 (56–72)	50 (36–58)	
Range (Min–Max)	(20–95)	(21–95)	(20–74)	
Sex				
Male	188 (68)	110 (65)	78 (72)	.24[b]
Race				
Non-Hispanic White	221 (80)	136 (80)	85 (79)	.73
Black	23 (8.3)	12 (7.1)	11 (10)	
Other/Unknown	14 (5.1)	8 (4.7)	6 (5.6)	
Hispanic	19 (6.9)	13 (7.7)	6 (5.7)	
History of discharges AMA	45 (16)	8 (4.7)	37 (34)	<.001
Smoking status				
Current smoker	108 (39)	34 (20)	74 (69)	<.001
Former smoker	74 (27)	59 (35)	15 (14)	
Never smoker	91 (33)	75 (44)	16 (15)	
Unknown	4 (1.4)	1 (0.59)	3 (2.8)	
Spinal location[c]				
Cervical	88 (32)	54 (32)	34 (31)	1.00
Thoracic	126 (45)	80 (47)	46 (43)	.46
Lumbar	154 (56)	94 (56)	94 (56)	1.00
Sacrum	55 (20)	26 (15)	29 (27)	.02
Multiple spine location involvement	119 (43)	69 (41)	50 (46)	.39
Patients with toxicology screening,[d]	80 (29)	15 (8.9)	65 (60)	<.001
Positive toxicology results				
Amphetamine	5 (6.3)	0 (…)	5 (7.7)	
Barbiturate	2 (2.5)	0 (…)	2 (3.1)	
Benzodiazepine	28 (35)	4 (27)	24 (37)	.56
Cocaine	31 (39)	0 (…)	31 (48)	
Opiate	44 (55)	6 (40)	38 (59)	.25
Cannabinoids	26 (33)	4 (27)	22 (34)	.76
Fentanyl	35 (44)	3 (20)	32 (49)	.047
Methadone	12 (15)	0 (…)	12 (19)	
Oxycodone	12 (15)	2 (13)	10 (15)	1.00
Suboxone	2 (2.5)	0 (…)	2 (3.1)	
Buprenorphine	1 (1.3)	0 (…)	1 (1.5)	
Current discharge AMA	15 (5.4)	2 (1.2)	13 (12)	<.001
Most likely source of infection[e]				
Poor dentition	28 (10)	14 (8.3)	14 (13)	.23
Drug use	59 (21)	0 (…)	59 (55)	
Skin and soft tissue infection	38 (14)	30 (18)	8 (7.4)	.02
Gastrointestinal source	5 (1.8)	4 (2.4)	1 (0.93)	.65
Genitourinary source	19 (6.9)	19 (11)	0 (…)	
Steroid injections	8 (2.9)	6 (3.6)	2 (1.9)	.49
Physical trauma	28 (10)	21 (12)	7 (6.5)	.15
No direct cause	104 (38)	75 (44)	29 (27)	.003
Other	9 (3.3)	8 (4.7)	1 (0.93)	.09

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: AMA, against medical advice; Non-PWUD, person who does not use drugs; PWUD, person who uses drugs, including active and nonactive drug use; Q1, first quartile; Q3, third quartile; SD, standard deviation.

[a]Wilcoxon rank-sum test used for age comparisons of non-PWUD and PWUD.

[b]Fisher exact test used for all other comparisons of non-PWUD and PWUD.

[c]Patients may have >1 area of the spine involved such as lumbosacral epidural abscess.

[d]Patients may have had positive testing for >1 drug.

[e]Patients may have >1 possible source of infection.

Table 3. Monomicrobial Culture Results

Culture	Non-PWUD (n = 113)	Nonactive PWUD (n = 39)	*P* Value	Active PWUD (n = 45)	*P* Value
MRSA	15 (13)	6 (15)	.74[a]	16 (36)	.002[b]
MSSA	48 (42)	17 (44)	.90	19 (42)	.98
Serratia	1 (0.88)	4 (10)	.03	5 (11)	.02
Gram-positive aerobic bacteria including MRSA and MSSA	99 (88)	31 (79)	.27	39 (87)	.87
Gram-negative aerobic bacteria including *Serratia*	11 (9.7)	8 (21)	.08	6 (13)	.51
Anaerobic bacteria	3 (2.7)	0 (…)		0 (…)	
Gram-negative aerobic bacteria including *Serratia*, excluding *Escherichia coli*	5 (4.4)	7 (18)	.01	6 (13)	.058

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; Nonactive PWUD, person with a history of drug use who does not actively use drugs; Non-PWUD, person who does not use drugs; PWUD, person who uses drugs.

[a]Non-PWUD compared to nonactive PWUD assessed in a log-binomial regression model.

[b]Non-PWUD compared to active PWUD assessed in a log-binomial regression model.

Table 4. Polymicrobial Culture Results

Culture	Non-PWUD (n = 134)	Nonactive PWUD (n = 41)	*P* Value	Active PWUD (n = 52)	*P* Value
Polymicrobial, No. (%)	21 (16)	2 (4.9)	.11	7 (13)[a]	.71[b]

Abbreviations: Nonactive PWUD, person with a history of drug use who does not actively use drugs; Non-PWUD, person who does not use drugs; PWUD, person who uses drugs.

[a]Non-PWUD compared to nonactive PWUD assessed in a log-binomial regression model.

[b]Non-PWUD compared to active PWUD assessed in a log-binomial regression model.

PWUD were more likely to have non–*E coli* gram-negative infections relative to non-PWUD (18% vs 4.4%, $P = .01$). Active PWUD were more likely to have MRSA infections than non-PWUD (36% and 13%, respectively, $P = .002$). No significant differences were found in the incidence of polymicrobial, MSSA, or anaerobic bacterial infections (Table 3, Table 4).

DISCUSSION

We found a large number of patients with substance use disorder and spinal epidural infections (39% of the total cohort), highlighting that drug use is a major risk factor for the development of these infections [9]. We observed high rates of *S aureus* infections among all patient groups with a disproportionate number of MRSA infections in PWUD, consistent with recent literature [18]. However, we also found skin and soft tissue infections to be a less common infection source in PWUD compared to non-PWUD, possibly related to self-treatment [19]. We also observed a higher likelihood of infections due to gram-negative bacteria other than *E coli* among PWUD, including *S marcescens*, *Pantoea* spp, and other gram-negative bacteria found in the environment. This likely reflects *E coli* hematogenous seeding of the spine from genitourinary infections among older non-PWUD and exposure to these gram-negative pathogens in the surrounding environment in PWUD [9, 12–17]. This finding may inform clinicians initiating empiric antimicrobial therapy after appropriate cultures are obtained with coverage for MRSA and gram-negative bacteria, including *S marcescens*, in PWUD. Such cultures should include blood cultures and cultures of aspirated fluid or biopsied tissue from the affected site prior to initiation of antibiotics if at all possible. Cultures from remote sources of epidural infection such as an infected illicit drug injection site should also be obtained. Pathologic examination of tissue should be done, including special stains. Saving additional fluid or tissue is important if further studies are needed [20]. Last, nares screening for MRSA and MSSA may be helpful, along with decolonization if results are positive [10].

Our study has limitations. As this was a retrospective study, there was inconsistency in documentation regarding past medical and social histories. Although we found a higher likelihood of spinal epidural infections due to gram-negative bacteria other than *E coli* among PWUD, this difference did not reach significance likely due to our study being underpowered for this outcome measure. Additionally, while we observed a significantly higher rate of lumbosacral involvement among PWUD, we are unsure why this is the case. Data from future studies are needed to confirm this observation.

Data regarding drug history was inconsistent and not assessed in some cases, even among patients with presumed drug use. Only 60% of PWUD had toxicology screening. When toxicology panels were positive, it was not always evident if this reflected proper use of an agent that can be abused (eg, fentanyl) or if it reflected illicit drug use. For demographic and patient characteristics, we assumed that all PWUD, both active and nonactive, likely share similar characteristics and they were pooled together for those analyses; however, we realize that this may not be the case. Although our cutoff for active PWUD was at least within the prior 3 months, for 2 patients active use could only be confirmed within the prior 4 months.

Last, the general toxicology screening at our hospital does not detect heroin derivatives. However, Rhode Island Hospital has protocols for illicit drug testing in the emergency department to minimize errors of positive screening tests associated with opioid analgesics.

CONCLUSIONS

This study highlights the importance of individualized assessments of drug use habits and histories when patients present with back pain and fever. Patients with substance use disorder have a greater likelihood of MRSA and non–*E coli* gram-negative

bacterial infections, which in turn reflects psychosocial differences that require greater attention. We found a significant correlation between active drug use and MRSA; however, this was not found with MSSA. The reason for this difference is not well understood. Although some studies cite exposure to healthcare settings as a risk for MRSA infections, the risk is not too dissimilar from MSSA infections as noted in the Centers for Disease Control and Prevention Emerging Infections Program Network, which found that 62% of invasive MRSA infections were healthcare-associated, community-onset infections compared to 57% of invasive MSSA infections [21].

Uncovering substance use disorder in a patient should prompt timely addiction medicine consultation to assist in management to reduce the recurrence of spine infections or other infectious sequelae. Physicians should also inquire about drug use patterns such as needle sharing or licking, skin popping, and poor sterilization techniques and suggest safer ways to inject. The significance of nonsterile environments in driving infections underscores the need for a diverse set of interventions informed by a harm-reduction framework. Given the prevalence of needle reuse and sharing, syringe exchange programs and physician outreach on safer injection habits are effective harm-reduction techniques that may reduce risk for such infections and allow PWUD to identify early signs of infection.

Notes

Author contributions. A. P. and L. A. M. conceptualized the study. A. P. and D. A. performed data collection. A. P. and P. H. performed statistical analyses. A. P. and L. A. M. drafted the manuscript. All authors reviewed and edited the manuscript.

Potential conflicts of interest. L. A. M. is on the scientific advisory board of Citius Pharma and Destiny Pharma and serves as a consultant for CorMedix and Lightline Medical. All other authors report no potential conflicts.

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