

Diagnosis and Management of Osteomyelitis Associated With Stage 4 Pressure Ulcers: Report of a Query to the Emerging Infections Network of the Infectious Diseases Society of America

Anjum S. Kaka,^{1,2} Susan E. Beekmann,³ Amy Gravely,¹ Gregory A. Filice,^{1,2} Philip M. Polgreen,³ and James R. Johnson^{1,2}

¹Veterans Affairs Medical Center, Minneapolis, Minnesota, USA, ²University of Minnesota, Minneapolis, USA, and ³Carver College of Medicine, Iowa City, Iowa, USA

Background. Few studies exist to guide the management of patients with stage 4 pressure ulcers with possible underlying osteomyelitis. We hypothesized that infectious disease (ID) physicians would vary widely in their approach to such patients.

Methods. The Emerging Infections Network distributed a 10-question electronic survey in 2018 to 1332 adult ID physicians in different practice settings to determine their approach to such patients.

Results. Of the 558 respondents (response rate: 42%), 17% had managed no such patient in the past year. Of the remaining 464 respondents, 60% usually felt confident in diagnosing osteomyelitis; the strongest clinical indicator of osteomyelitis reported was palpable or visible bone at the ulcer base. Approaches to diagnosing osteomyelitis in patients with visible and palpable bone varied: 41% of respondents would assume osteomyelitis, 27% would attempt pressure off-loading first, and 22% would perform diagnostic testing immediately. Preferred tests for osteomyelitis were bone biopsy (for culture and histopathology) and magnetic resonance imaging. Respondents differed widely on favored route(s) (intravenous, oral, or both) and duration of antimicrobial therapy but would treat longer in the absence, vs presence, of full surgical debridement ($P < .001$). Overall, 62% of respondents opined that osteomyelitis under stage 4 pressure ulcers is usually or almost always treated excessively, and most (59%) suggested multiple topics for future research.

Conclusions. Regarding osteomyelitis underlying stage 4 pressure ulcers, ID physicians reported widely divergent diagnostic and treatment approaches. Most of the reported practice is not supported by the available evidence, which is quite limited and of low quality.

Keywords. decubitus; infection; osteomyelitis; pressure ulcer; spinal cord injury.

Persons with spinal cord injury (SCI) have an ~85% lifetime risk of developing a pressure ulcer [1–5]. Stage 4 pressure ulcers, the most severe, involve full-thickness tissue loss, with exposed bone, tendon, or muscle [6]. About one-third of all stage 4 pressure ulcers may progress to osteomyelitis, which increases the risk of complications and treatment costs [7]. Costs associated with treating stage 4 pressure ulcers and related complications are substantial, by some estimates exceeding \$124 000 for hospitalized patients [8].

Despite osteomyelitis associated with stage 4 pressure ulcers being highly prevalent, costly, and morbid, few studies are available to guide its diagnosis and management. The authors of a recent systematic review on sacral stage 4 pressure ulcers

found 20 relevant studies, mostly small case series, with no prospective randomized trials [9]. Based on the available evidence regarding management of stage 4 pressure ulcers, the authors concluded that (i) no clinical exam or diagnostic study other than bone biopsy can accurately predict the presence of underlying osteomyelitis, (ii) there is no role for antimicrobial therapy for >6 weeks, and (iii) addressing psychosocial factors that lead to the mechanical development of a stage 4 pressure ulcer may be most important. The authors urged the performance of randomized controlled trials addressing (i) the impact of bone biopsy on diagnosis and (ii) the spectrum and duration of antimicrobial therapy [9].

Accordingly, we surveyed members of the Emerging Infections Network (EIN) of the Infectious Diseases Society of America to determine, regarding osteomyelitis underlying stage 4 pressure ulcers, infectious disease (ID) specialists' (i) level of confidence, (ii) approach to diagnosis and treatment, (iii) concerns regarding antimicrobial use, and (iv) suggestions for future research. We hypothesized that ID physicians would vary widely in their approach to such patients.

Received 28 June 2019; editorial decision 6 September 2019; accepted 10 September 2019.

Correspondence: A. S. Kaka, 1 Veteran's Drive, 111F, Minneapolis, MN 55417 (anjum.kaka@va.gov)

Open Forum Infectious Diseases®

Published by Oxford University Press on behalf of Infectious Diseases Society of America 2019. This work is written by (a) US Government employee(s) and is in the public domain in the US. DOI: 10.1093/ofid/ofz406

METHODS

The EIN

The EIN was established by the Centers for Disease Control and Prevention in 1995 to create a sentinel network of ID physicians in North America [10]. The EIN member database includes professional characteristics such as type of practice (adult ID vs pediatric ID), years in ID practice (<5 years, 5–14 years, 15–24 years, and ≥25 years), geographic location, hospital type, and size.

Survey

The survey was a 10-question, multiple-choice/open-comment survey (Supplementary Data). It was designed initially by 3 of the authors (A.S.K., J.R.J., and S.E.B.) and was subsequently revised based on input from 3 colleagues who piloted it and provided suggestions (which addressed mainly word choice for improved clarity).

Survey topics included how frequently respondents encountered patients with a stage 4 pressure ulcer and, regarding underlying osteomyelitis, respondents' opinions about making the diagnosis (level of confidence, physical findings, diagnostic tests), treatment (route and duration of antimicrobial therapy in relation to pathogen and extent of debridement, criteria for stopping antimicrobials), and how often such osteomyelitis is overtreated. Likert-type scale responses were used for questions with graded responses (eg, rarely/sometimes/usually/almost always and minimally/moderately/strongly). An open-text field allowed respondents to suggest questions for future research.

On July 10, 2018, we sent the confidential survey by e-mail link or by facsimile to EIN members with adult ID practices who had previously responded to 1 or more EIN surveys. The recipients represented nearly 20% of ID providers currently active in clinical practice in North America. No incentive for participation was provided. Nonresponders received 2 follow-up electronic reminders at 2-week intervals. The survey closed on August 7, 2018.

Statistical Analysis

Responses were compiled, and summary statistics were calculated for response rates (both overall and stratified by member characteristics) and survey content results. Categorical variables were compared using χ^2 tests, and differences were considered significant at $P < .05$. Statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA). Suggestions regarding future research were grouped according to common themes, which were sorted into broad categories, each with subcategories.

RESULTS

Survey Respondents

The survey was sent electronically to 1332 EIN physicians with adult ID practices, of whom 558 (42%) responded. We compared respondents and nonrespondents for years in ID practice, geographic region, and employment characteristics to assess for response bias (Table 1). Response rates were significantly higher for members with ≥25 years of ID experience (54%) compared

Table 1. Characteristics of Respondents and Nonrespondents Among 1332 Survey Recipients

Respondent Characteristics		No. With Characteristic (Row %)			P Value ^a
Category	Specific Characteristic	Total (n = 1332)	Responder (n = 558)	Nonresponder (n = 774)	
Experience	<5 y	261 (19.6)	112 (42.9)	149 (57.1)	<.001
	5–14 y	494 (37.1)	182 (36.8)	312 (63.2)	
	15–24 y	239 (18.0)	83 (34.7)	156 (65.3)	
	≥25 y	337 (25.3)	181 (53.7)	156 (46.3)	
Type of hospital	City/county	68 (5.1)	25 (36.8)	43 (63.2)	.008
	Community	390 (29.3)	143 (36.7)	247 (63.3)	
	Teaching, nonuniversity	327 (24.6)	158 (48.3)	169 (51.7)	
	University	464 (34.9)	190 (41.0)	274 (59.1)	
Hospital size	VA or DoD	82 (6.2)	42 (51.2)	40 (48.8)	.40
	<200	142 (12.9)	62 (43.7)	80 (56.3)	
	200–350	312 (28.4)	123 (39.4)	189 (60.6)	
	451–600	256 (23.3)	113 (44.1)	143 (55.9)	
Region ^b	>600	389 (35.4)	178 (45.8)	211 (54.2)	.32
	Midwest	311 (23.4)	144 (46.3)	167 (53.7)	
	Northeast	291 (21.9)	121 (41.6)	170 (58.4)	
	Puerto Rico	14 (1.1)	6 (42.9)	8 (57.1)	
	South	400 (30.1)	168 (42.0)	232 (58.0)	
	West	315 (23.7)	119 (37.8)	196 (62.2)	

Abbreviations: DoD, Department of Defense; VA, Veteran Affairs.

^aBy Pearson's chi-square test.

^bRegion: Midwest includes Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; Northeast includes states of Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; South includes Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West includes Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

with those with less ID experience (38%; $P < .001$). Response rates also varied significantly in relation to the respondent's primary hospital type ($P = .008$) and were highest for respondents from Veteran Affairs (VA)/Department of Defense (DoD) hospitals and nonuniversity teaching hospitals, as compared with respondents from other practice settings. By contrast, response rates did not vary depending on respondents' geographic location or hospital size.

Of the 558 respondents, 94 (17%) reported not having managed any patient with a stage 4 pressure ulcer during the prior year, and so they exited the survey, by design. Of the 464 remaining respondents, 62% (288/464) reported having managed >10 such patients during the prior year, 23% (107/464) had managed 6–10 patients, and 15% (69/464) had managed 1–5 patients.

Diagnosis of Osteomyelitis

We asked respondents about level of diagnostic confidence, physical findings that would indicate osteomyelitis, approach to testing, and specific tests they would prefer to assess for osteomyelitis. Overall, respondents expressed moderate confidence in their ability to confirm or exclude osteomyelitis under a stage 4 pressure ulcer based on physical findings, and laboratory or imaging results, with 60% (276/464) being usually confident and 37% (172/464) being sometimes confident. The proportion of respondents reporting being usually confident increased progressively with the number of stage 4 pressure ulcers seen in the last year, from 45% (31/69) for 1–5 to 59% (63/107) for 6–10, and to 63% (182/288) for >10 ($P = .03$ overall; $P = .01$ for <6 vs ≥6).

Of the 5 listed physical findings, the 2 that respondents considered most indicative of underlying osteomyelitis were (i)

visible bone and (ii) palpable or probe-detectable bone at the ulcer base (Figure 1). In a patient with such findings but no local or systemic signs of infection, respondents' reported approach to diagnosing osteomyelitis varied. Of the 457 respondents, 41% considered this presentation sufficiently indicative of osteomyelitis to obviate further diagnostic testing. By contrast, 27% would pursue laboratory and imaging testing for osteomyelitis only if the ulcer did not improve with a trial of wound care and pressure off-loading, 22% would pursue laboratory and imaging tests immediately, and 10% would pursue a strategy not listed.

Respondents' 5 most preferred tests to assess for osteomyelitis, in rank order (% of 464 respondents choosing the test among their preferred 5), were bone biopsy for culture (95%), magnetic resonance imaging (MRI; 89%), bone biopsy for histopathology (80%), C-reactive protein (55%), and erythrocyte sedimentation rate (43%) (Figure 2). Only 2% of respondents selected a superficial wound culture among their top 5 tests, and mostly as number 5.

Treatment of Osteomyelitis

We asked respondents about preferred route, criteria for stopping, duration, and adequacy of antimicrobial therapy for osteomyelitis underlying stage 4 pressure ulcers. Presuming pathogen susceptibility to both intravenous and highly bioavailable oral agents, respondents disagreed widely regarding favored routes of antimicrobial therapy (ie, intravenous only, oral only, or both), regardless of the presumed pathogen ($P < .001$ overall) (Figure 3). Even though for no pathogen category did >56% of respondents select a specific route, several significant trends suggested a favored route for a specific pathogen. Specifically,

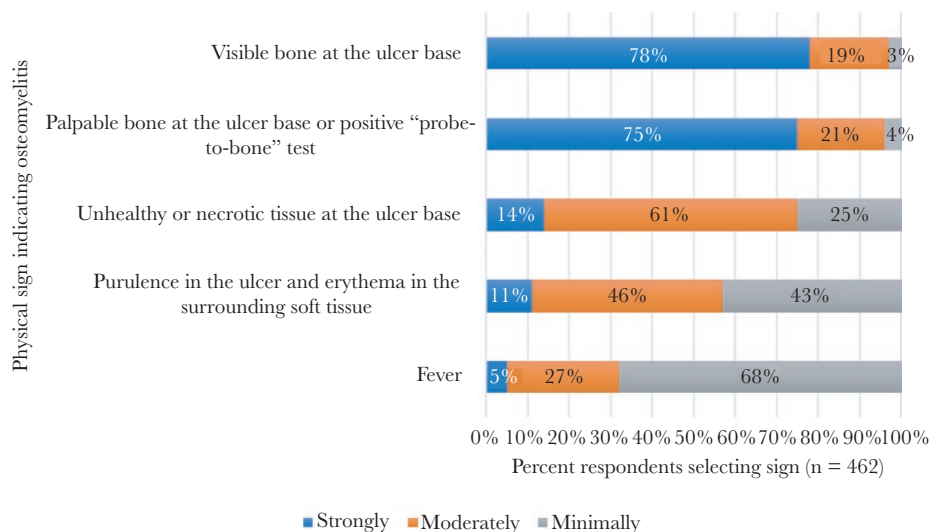


Figure 1. Physical signs that indicate osteomyelitis. Respondents rated each of the listed physical signs (y-axis) as indicators of osteomyelitis. Physical signs are listed in rank order according to what proportion of 462 total respondents selected that sign as strongly indicative of osteomyelitis (x-axis). Within each bar, the width of each colored segment and the corresponding number indicate the percentage of respondents who ranked that physical sign as strongly (dark blue), moderately (orange), or minimally (gray) indicative of osteomyelitis.

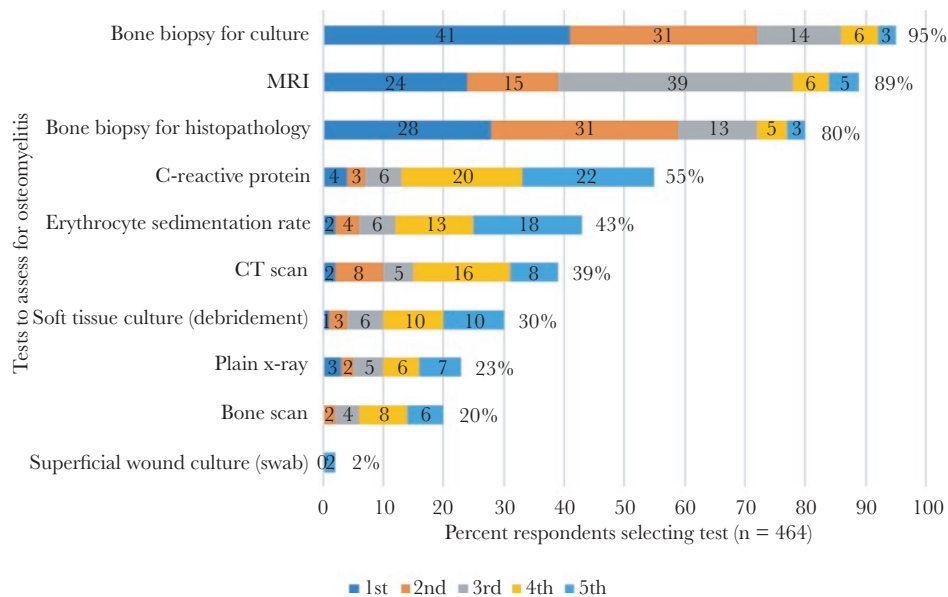


Figure 2. Preferred tests to assess for osteomyelitis. Respondents selected up to 5 of the 10 tests listed in the survey (y-axis). Tests are listed in rank order according to what proportion of respondents selected the test as their top 5 (x-axis). The total width of each bar reflects the percentage of 464 total respondents who chose that test among their preferred 5 (% values shown at end of the bar). Within each bar, the width of each colored segment and the corresponding number reflect the percentage of respondents that ranked that test as their first (dark blue), second (orange), third (gray), fourth (yellow), or fifth (light blue) choice. Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

the sequential intravenous-to-oral approach was the most frequently selected option for *Pseudomonas*, mixed cultures, and non-*Pseudomonas* gram-negative rods (GNRs). By contrast, the most frequently selected option for methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) was intravenous therapy throughout, and for anaerobes it was oral therapy throughout (for both, comparisons of index pathogen vs all other pathogen categories combined, $P < .001$). This yielded a decreasing gradient of preference for all-intravenous therapy from MRSA/MSSA (highest) to anaerobes (lowest) and an increasing gradient of preference for all-oral therapy across the same categories (Figure 3).

Preferred duration of antimicrobial therapy varied widely regardless of the presumed extent of surgical debridement but was associated significantly with extent of debridement ($P < .001$) (Figure 4). Specifically, of respondents who specified a treatment duration, 50% (169/338) would treat for >6 weeks after no/partial debridement, whereas only 19% (82/433) would do so after full debridement ($P < .001$).

As their preferred criterion for stopping antimicrobial therapy, respondents selected diverse indicators, none with majority approval. The most favored criteria (% first choice, % second choice) included debridement of all infected tissue (49%, 23%), followed by completion of a defined antimicrobial course (27%, 33%), normalization of inflammatory markers (13%, 26%), and stabilized/improved imaging results (4%, 8%). Respondents indicated that osteomyelitis is always (20%) or usually (41%) treated too broadly or for too long with antimicrobials.

Survey Responses in Relation to Provider Characteristics

We assessed for variation in responses by providers' (i) years of ID experience, (ii) hospital type, (iii) hospital size, and (iv) geographic area. Among ID physicians with <25 years' experience (<5 years, 5–14 years, and 15–24 years), approach did not vary with experience duration stratum. By contrast, as compared with respondents with ≥ 25 years of experience, less experienced respondents were significantly more likely to (i) consider local signs of soft tissue inflammation (purulence and erythema) moderately or strongly indicative of osteomyelitis ($P < .001$), (ii) assume presence of osteomyelitis under visible and palpable bone ($P = .005$), (iii) obtain bone biopsies for culture ($P = .03$), and (iv) use exclusively intravenous therapy to treat MRSA ($P < .001$), MSSA ($P < .001$), *Pseudomonas* ($P = .01$), and mixed-culture osteomyelitis ($P = .04$). Duration of ID experience was unassociated with other responses.

Hospital type corresponded significantly with a preference for all-intravenous antimicrobial therapy for all pathogen categories: MRSA ($P < .001$), MSSA ($P < .001$), *Pseudomonas* ($P = .002$), non-*Pseudomonas* GNRs ($P < .001$), mixed cultures ($P = .002$), and anaerobes ($P = .03$). Overall, preference for all-intravenous antimicrobial therapy was lowest for city/county (14.9%) and VA/DoD hospitals (20.5%), intermediate for nonuniversity teaching (26.6%) and university hospitals (28.3%), and highest for community hospitals (43.9%; $P < .001$). Hospital type was unassociated with other responses. By contrast, hospital size and geographic location were unassociated with responses generally.

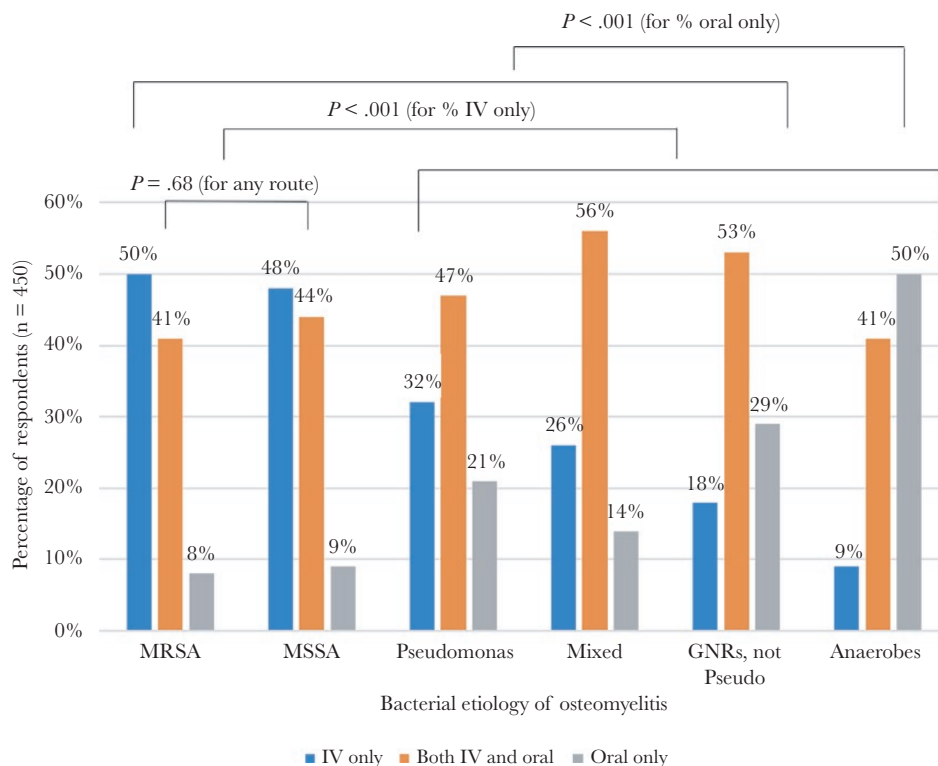


Figure 3. Preferred route of antimicrobial therapy for osteomyelitis in relation to pathogen. The question presumed pathogen susceptibility to intravenous (IV) and highly bioavailable oral agents. Percentage of 450 total respondents who favored the indicated route (y-axis) is plotted for various pathogens (x-axis): methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA), *Pseudomonas*, mixed cultures, gram-negative rods (GNRs), and anaerobes. Routes: IV only (blue bars); both IV and oral (orange bars); and oral only (gray bars). Preferred route(s) of therapy: no difference for MRSA vs MSSA ($P = .68$); for IV only, *S. aureus* vs all other pathogens ($P < .001$); for oral only, anaerobes vs all other pathogens ($P < .001$).

Knowledge Gaps and Future Research

Over half (59%) of respondents had questions regarding points of uncertainty and/or suggestions for future research (mean, 1.6 comments/respondent) (Table 2). Leading topics were antimicrobial duration (n = 100); when to attempt

antimicrobial treatment and the utility of antimicrobial therapy without debridement (n = 84); role, timing, and type of surgery, including debridement, muscle flap, and diverting colostomy (n = 55); and route of antimicrobial therapy (n = 51).

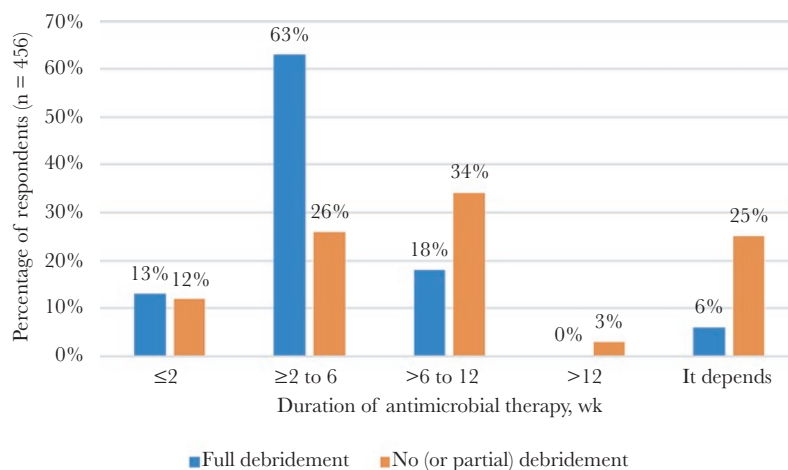


Figure 4. Preferred duration of antimicrobial therapy in relation to extent of debridement. Percentage of 456 total respondents (y-axis) who favored the indicated duration of antimicrobial therapy in weeks (x-axis), presuming full debridement (blue bars) vs no (or partial) debridement (orange bars).

Table 2. Distribution of Comments From Respondents Regarding Key Clinical and Research Questions^a

Category	Subcategory	No.
Diagnosis	Guidelines re: how to diagnose osteomyelitis	24
	Role of surface swabs	2
	Role of bone biopsy, histopathology, and culture	11
	Role of biomarkers	6
	Role of imaging (CT and MRI)	6
	Correlation of clinical, laboratory, and imaging findings with bone histopathology and culture	3
Antimicrobials	When to attempt antimicrobial treatment; utility of antimicrobials without debridement	84
	Antimicrobial duration	100
	Antimicrobial spectrum	8
	Route of antimicrobial therapy: intravenous vs oral	51
	Criteria for stopping antimicrobials	11
	Role of suppressive antimicrobial therapy	7
Surgery	Role, timing, and type (debridement, flap, diverting colostomy)	55
Adjunctive	Topical wound care	7
	Rehabilitation	5
	Hyperbaric oxygen	6
	Vacuum-assisted closure	7
Approach	Role of a multidisciplinary team	11
	Role of a palliative care team	16
	Guidelines re: role and timing of antimicrobials, surgery, and topical treatment	14
	Management differences for acute vs chronic osteomyelitis	5
Other	Recurrent osteomyelitis	9
	Prevention	7

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; No., number of comments.

^aFifty-nine percent (273/464) of respondents had comments, most in more than 1 subcategory.

DISCUSSION

This Internet-based survey of EIN members, who are adult ID physicians practicing in North America [10], represents, to our knowledge, the first broad survey of ID specialists regarding management of osteomyelitis underlying stage 4 pressure ulcer. The relatively high response rate (42%) resembled that of prior EIN surveys [11]. The only indications of response bias were that, compared with nonrespondents, respondents were more likely to work at VA/DoD and nonuniversity teaching hospitals and to have ≥ 25 years in ID practice, characteristics noted on prior EIN surveys [11, 12]. The fact that 83% of respondents reported having cared for a patient with a stage 4 pressure ulcer in the past year supports the clinical relevance of stage 4 pressure ulcer-associated osteomyelitis.

Nonetheless, despite most respondents having managed >10 such patients in the past year, 40% reported being less than usually confident in diagnosing osteomyelitis. This limited level of diagnostic confidence is concerning but may be appropriate, considering the lack of evidence-based or consensus diagnostic criteria for this condition—a gap identified by several

respondents. In contrast, for osteomyelitis associated with diabetic foot ulcers, published consensus diagnostic criteria incorporate physical examination, laboratory, and imaging findings to categorize the likelihood of osteomyelitis as definite, probable, possible, or unlikely [13].

Although most respondents considered visible/palpable/probe-detectable bone to be the most indicative finding for osteomyelitis and 41% considered it sufficiently indicative to obviate further diagnostic testing, the available published evidence suggests otherwise. Specifically, in 3 small case series (14–36 patients each), bone biopsy showed histological evidence of osteomyelitis (leukocytic inflammatory infiltrate in bone) in only 17%–46% of patients who had exposed bone at the ulcer base [14–16]. Similarly, whereas most of our survey respondents regarded local signs of soft tissue infection as strongly or moderately predictive of underlying osteomyelitis, in the only relevant study (38 patients) neither presence nor duration of local signs of inflammation correlated significantly with histologically proven osteomyelitis [17]. Our observation that respondents' opinions regarding the predictive value of visible or palpable bone for diagnosing osteomyelitis varied in relation to years of ID experience may be due to less experienced respondents (<25 years in practice) being unfamiliar with the above studies, most of which were published ≥ 25 years ago.

To assess for osteomyelitis, respondents preferred bone biopsy (for histopathology and culture) and MRI. Obtaining a bone biopsy requires special expertise, irrespective of whether it is done at the bedside, in the operating room, or in the interventional radiology suite, and bone biopsy may be difficult to obtain at some institutions. Additional limitations of bone biopsy include (i) possible sampling error and false-negative culture, given the small amount of bone obtained; (ii) uncertainty regarding the optimal approach to obtaining bone for culture (ie, through intact skin to avoid contamination, vs through the ulcer base); and (iii) insufficient bone for both histopathology and culture (many interventional radiology-obtained biopsies) [18]. A hypothetical (but undocumented) risk also exists of the biopsy procedure itself paradoxically introducing bacteria into uninfected bone [19]. Furthermore, biopsies are most useful for culture if obtained before starting antimicrobial therapy, which can be challenging. By contrast, only 2% of respondents preferred superficial wound cultures, which any physician or nurse can obtain promptly at the bedside. The results of the largest relevant study (220 patients) show that $>50\%$ of patients suspected of having osteomyelitis under a stage 4 pressure ulcer and who undergo any pressure ulcer-related microbiology test get a wound swab culture [20]. Prior studies have shown variable correspondence between culture results from soft-tissue drainage vs bone biopsy [18, 21–24].

The optimal diagnostic role of MRI, which here was the second most popular test for suspected stage 4 pressure

ulcer-associated osteomyelitis, is also unclear. An autopsy study of 28 patients found histological evidence of pressure-induced fibrotic changes, medullary edema, and/or reactive bone formation in all patients with a stage 4 pressure ulcer, including those without histological evidence of osteomyelitis [14]. As MRI cannot distinguish such (presumably) pressure-induced changes from infectious bone marrow edema, it exhibits poor specificity for osteomyelitis in this setting [25].

Survey respondents disagreed regarding the preferred route of antimicrobial therapy for osteomyelitis underlying stage 4 pressure ulcers. Their degree of preference for all-intravenous therapy corresponded to their hospital type, being highest for community hospitals, intermediate for nonuniversity teaching and university hospitals, and lowest for city/county and VA/DoD hospitals, suggesting a practice-related bias. Historically, in the absence of high-quality evidence, intravenous antimicrobial therapy has been favored for osteomyelitis [23]. However, a recent large randomized controlled trial (1054 patients) showing that oral therapy is noninferior to intravenous therapy for bone and joint infections may shift this preference in the future [26].

Fifty percent of respondents would treat osteomyelitis for >6 weeks after no/partial debridement. This reported practice is contrary to the conclusions of the authors of a systematic review, who found no evidence to support either (i) a role for antimicrobials in the absence of debridement and wound coverage—except short-term therapy (<2 weeks) for acute soft tissue infection around the ulcer (if present)—or (ii) >6 weeks of antimicrobial therapy after debridement and wound closure [9]. Respondents' preference for extended antimicrobial therapy may derive from uncertainty as to sufficient treatment durations (as reflected in their multiple questions regarding duration and utility of antimicrobial therapy). It also may paradoxically promote the practice patterns that underlie respondents' impression that osteomyelitis underlying stage 4 pressure ulcers is always or usually treated overly broadly or for too long.

Study limitations include the incomplete (albeit relatively high) response rate; reliance on self-report, which may be subject to recall bias; inadequate capture of all factors that affect decision-making for these very complex patients; and uncertain generalizability of the results to non-EIN members and to other geographic locations. Additionally, the use of multiple comparisons without prior hypotheses risked finding spurious associations. Study strengths include the large number of respondents, broad representation of geographical areas and hospital types and sizes, detailed attention to strategies for diagnosing and treating such patients (including liberal use of open-text fields and "other" option), and assessment for response variation by practice characteristics.

Our results show substantial variation in ID physicians' diagnostic and therapeutic approaches to patients with pressure

ulcer-associated osteomyelitis. Most of the reported practice is not supported by current evidence. This disconnect may be due to physicians' (i) lack of confidence in the results of the limited and low-quality evidence (based on case series, with no prospective randomized trials); (ii) ignorance of the literature; (iii) commission bias, that is, a preference for active intervention (diagnostic studies and antimicrobial treatment) over watchful waiting; (iv) practice habits; and/or (v) belief in myths. Furthermore, pressure ulcer care is time-consuming, progress (if achieved) is often slow, and healing may not occur despite multimodality treatments and prolonged hospitalizations. This can be frustrating for both patients and physicians, possibly promoting non-evidence-based practices.

However, excessive antimicrobial therapy poses well-documented potential harms not only to individual patients (eg, drug side effects, vascular access complications, *Clostridioides difficile* infection, superinfections, and drug–drug interactions), but also to society (eg, antimicrobial resistance and treatment costs). Evidence from prospective studies, ideally randomized controlled trials to inform diagnostic and treatment approaches to such patients, would improve individual patient outcomes and antimicrobial stewardship.

CONCLUSIONS

We found that, regarding osteomyelitis underlying stage 4 pressure ulcers, ID physicians (i) report widely divergent diagnostic and treatment approaches, (ii) treat with longer duration of antimicrobial therapy than the literature supports, (iii) are concerned about excessive antimicrobial use, and (iv) perceive a need for additional research in this area. Most of the reported practice is not supported by the available evidence, which is quite limited and of low quality. These findings urge the performance of well-designed clinical trials or prospective observational studies to answer key questions regarding optimal management of stage 4 pressure ulcer-associated osteomyelitis.

Acknowledgments

We thank Aaron DeVries (Minneapolis VA Health Care System, Minneapolis, MN, USA) for piloting the survey and providing feedback. We thank Dimitri Drekonja (Minneapolis VA Health Care System, Minneapolis, MN, USA) for reviewing and providing feedback on the survey and manuscript.

Financial support. This work was supported by the Cooperative Agreement 1 U50 CK000477, funded by the Centers for Disease Control and Prevention (S.E.B., P.M.P.) and the Office of Research and Development, Department of Veterans Affairs (A.S.K., J.R.J.).

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Disclaimer. The contents of this work are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention (CDC), the Department of Health and Human Services, the Department of Veterans Affairs, or the authors' respective institutions.

References

- Whiteneck GG, Charlifue SW, Frankel HL, et al. Mortality, morbidity, and psychosocial outcomes of persons spinal cord injured more than 20 years ago. *Paraplegia* **1992**; 30:617–30.
- Johnson RL, Gerhart KA, McCray J, et al. Secondary conditions following spinal cord injury in a population-based sample. *Spinal Cord* **1998**; 36:45–50.
- Scheel-Sailer A, Wyss A, Boldt C, et al. Prevalence, location, grade of pressure ulcers and association with specific patient characteristics in adult spinal cord injury patients during the hospital stay: a prospective cohort study. *Spinal Cord* **2013**; 51:828–33.
- Charlifue S, Jha A, Lammertse D. Aging with spinal cord injury. *Phys Med Rehabil Clin N Am* **2010**; 21:383–402.
- Chen Y, Devivo MJ, Jackson AB. Pressure ulcer prevalence in people with spinal cord injury: age-period-duration effects. *Arch Phys Med Rehabil* **2005**; 86:1208–13.
- National Pressure Ulcer Advisory Panel EPUAPaPPPIA. Prevention and Treatment of Pressure Ulcers: Quick Reference Guide. Perth, Australia: Cambridge Media; **2014**.
- Rennert R, Golinko M, Yan A, et al. Developing and evaluating outcomes of an evidence-based protocol for the treatment of osteomyelitis in stage IV pressure ulcers: a literature and wound electronic medical record database review. *Ostomy Wound Manage* **2009**; 55:42–53.
- Brem H, Maggi J, Nierman D, et al. High cost of stage IV pressure ulcers. *Am J Surg* **2010**; 200:473–7.
- Wong D, Holtom P, Spellberg B. Osteomyelitis complicating sacral pressure ulcers: whether or not to treat with antibiotic therapy. *Clin Infect Dis* **2019**; 68:338–42.
- Pillai SK, Beekmann SE, Santibanez S, Polgreen PM. The Infectious Diseases Society of America Emerging Infections Network: bridging the gap between clinical infectious diseases and public health. *Clin Infect Dis* **2014**; 58:991–6.
- Johnson JR, Polgreen PM, Beekmann SE. Transrectal prostate biopsy-associated prophylaxis and infectious complications: report of a query to the Emerging Infections Network of the Infectious Diseases Society of America. *Open Forum Infect Dis* **2015**; 2(X):XXX–XX.
- Rapoport AB, Fischer LS, Santibanez S, et al. Infectious diseases physicians' perspectives regarding injection drug use and related infections, United States, 2017. *Open Forum Infect Dis* **2018**; 5(X):XXX–XX.
- Berendt AR, Peters EJ, Bakker K, et al. Diabetic foot osteomyelitis: a progress report on diagnosis and a systematic review of treatment. *Diabetes Metab Res Rev* **2008**; 24(Suppl 1):S145–61.
- Türk EE, Tsokos M, Dellling G. Autopsy-based assessment of extent and type of osteomyelitis in advanced-grade sacral decubitus ulcers: a histopathologic study. *Arch Pathol Lab Med* **2003**; 127:1599–602.
- Darouiche RO, Landon GC, Klima M, et al. Osteomyelitis associated with pressure sores. *Arch Intern Med* **1994**; 154:753–8.
- Sugarman B, Hawes S, Musher DM, et al. Osteomyelitis beneath pressure sores. *Arch Intern Med* **1983**; 143:683–8.
- Thornhill-Joynes M, Gonzales F, Stewart CA, et al. Osteomyelitis associated with pressure ulcers. *Arch Phys Med Rehabil* **1986**; 67:314–8.
- Ang MT, Wong GR, Wong DR, et al. Diagnostic yield of computed tomography-guided biopsy and aspiration for vertebral osteomyelitis. *J Med Imaging Radiat Oncol* **2019**; 63:589–95. PMID: 31301094. doi: 10.1111/1754-9485.12923
- Aslangul E, M'bemba J, Caillat-Vigneron N, et al. Diagnosing diabetic foot osteomyelitis in patients without signs of soft tissue infection by coupling hybrid 67Ga SPECT/CT with bedside percutaneous bone puncture. *Diabetes Care* **2013**; 36:2203–10.
- Bodavula P, Liang SY, Wu J, et al. Pressure ulcer-related pelvic osteomyelitis: a neglected disease? *Open Forum Infect Dis* **2015**; 2(X):XXX–XX.
- Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects. 3. Osteomyelitis associated with vascular insufficiency. *N Engl J Med* **1970**; 282:316–22.
- Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects (second of three parts). *N Engl J Med* **1970**; 282:260–6.
- Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects. *N Engl J Med* **1970**; 282:198–206.
- Mackowiak PA, Jones SR, Smith JW. Diagnostic value of sinus-tract cultures in chronic osteomyelitis. *JAMA* **1978**; 239:2772–5.
- Brunel AS, Lamy B, Cyteval C, et al; OSTEAR Study Group. Diagnosing pelvic osteomyelitis beneath pressure ulcers in spinal cord injured patients: a prospective study. *Clin Microbiol Infect* **2016**; 22:267.e1–8.
- Li HK, Rombach I, Zambellas R, et al; OVIVA Trial Collaborators. Oral versus intravenous antibiotics for bone and joint infection. *N Engl J Med* **2019**; 380:425–36.