MAJOR ARTICLE

Long-Term Outcome of Pyogenic Vertebral Osteomyelitis: A Cohort Study of 260 Patients

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Background. The long-term outcome of patients with pyogenic vertebral osteomyelitis (PVO) has not been fully assessed.

Methods. We conducted a retrospective cohort study to describe the long-term outcome of PVO and to assess risk factors for treatment failure in patients evaluated at our institution between 1994 and 2002. Patients were observed until July 1, 2013.

Results. Two hundred sixty patients with PVO were included in this study. Twenty-seven percent (70) of patients developed their infection after an invasive spinal procedure. *Staphylococcus aureus* accounted for 40% (103) of infections. Forty-nine percent (128) of patients underwent spinal surgery as part of their initial therapy. The median duration of parenteral antimicrobial therapy was 42 days (interquartile range, 38–53). The estimated 2-, 5-, and 10-year cumulative probability of treatment failure-free survival was 72%, 69%, and 69%, respectively. Seventy-five percent of patients who developed treatment failure did so within 4.7 months of diagnosis. Residual neurological defects and persistent back pain were seen in 16% and 32% of patients, respectively. In a multivariate analysis, longer duration of symptoms before diagnosis and having an infection with *S. aureus* were associated with increased risk of treatment failure.

Conclusions. Increasing duration of symptoms and infection with *S. aureus* were associated with treatment failure in patients with PVO. Most treatment failures occurred early after initiation of treatment. Pyogenic vertebral osteomyelitis is associated with a high 2-year failure rate. Persistent neurological deficits and back pain are common after therapy.

Keywords. outcome; spondylodiscitis; treatment failure; vertebral osteomyelitis.

Pyogenic vertebral osteomyelitis (PVO) has long been recognized as a challenging clinical problem with potential devastating sequelae on spine and neurologic functions [1]. Nonspecific symptoms and the relative infrequency of PVO amidst the ubiquitous complaints of back pain often impede a timely diagnosis [2, 3]. Modern imaging advances, including magnetic resonance imaging (MRI) [4] and computerized tomography (CT)-guided percutaneous aspiration [5], have substantially improved diagnostic capabilities.

Previous studies have identified several risk factors for poor outcomes among patients with spine infections, including age [2, 3], diabetes mellitus [2, 6], rheumatoid arthritis [2], immunocompromised status [2, 3], prolonged symptoms before diagnosis [6, 7], *Staphylococcus aureus* [2, 3], the presence of paravertebral extension [6], nonresponsive erythrocyte sedimentation rates (ESRs) [8], and the duration of antimicrobial therapy [9, 10].

Most cases of PVO can be managed successfully with antibiotics alone. Surgical management is typically reserved for patients with deformity, neurologic deficits, chronic unremitting pain, uncontrolled infection

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Table 1. Definitions Used in a Retrospective Cohort Study of Patients With Pyogenic Vertebral Osteomyelitis at the Mayo Clinic, Rochester

Term	Definition
Case definitions	Patients ≥18 years old with symptoms or signs consistent with spinal column infection ***PLUS:*** Positive spine site cultures [a] ***OR*** ≥2 sets of positive blood cultures ***OR*** Histopathology suggestive of infection ***OR*** Gross intraoperative purulence ***OR*** Presence of a sinus tract to bone ***OR*** A positive gram stain from tissue specimens ***OR*** Radiographic diagnosis without microbiologic or histopathologic confirmation
Epidural extension	Because of difficulties clearly delineating the distinction among epidural enhancement, phlegmon, and definite abscess, we used a broad definition of epidural involvement to be the presence of any of these findings [22, 23], as determined by MRI, CT, or intraoperative findings
Paravertebral extension	As determined by MRI, CT, or intraoperative findings
Psoas abscess	As determined by MRI, CT, or intraoperative findings
Improved follow-up inflammatory biomarkers	25% reduction in ESR (mm/h) or CRP (mg/dL) compared with baseline value during the period 4–8 weeks after diagnosis. If no baseline values were available but follow-up values were available, an ESR (mm/h) <40 and CRP (mg/dL) <1 were considered improved[b]
Treatment failure: Microbiologically defined or mechanically defined	Microbiologically defined failure included infection-related death, diagnosis of microbiologically confirmed relapse with same or different organism, developing acute neurological deficits, or having an unplanned surgical procedure with positive intraoperative microbiology. Mechanically defined failure included undergoing unplanned surgical procedures for purely mechanical reasons (pain/spinal instability/deformity) with negative intraoperative microbiology

Abbreviations: CRP, C-reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging.

[a] Common skin contaminants, such as coagulase-negative *Staphylococcus*, *Propionibacterium acnes*, and diphtheroids were not considered pathogenic unless growth occurred from ≥2 separate cultures.

[b] Based upon unpublished data and author experience.

(ie, clinically significant abscesses), failure to respond to conservative therapy, and requirement of an open biopsy [11, 12]. The goal of this study is to describe the long-term outcome and factors associated with treatment failure in patients with PVO using a retrospective cohort study design.

MATERIALS AND METHODS

Study Design

This is a single-center retrospective cohort study undertaken at the Mayo Clinic, Rochester. Medical and surgical therapies were not standardized. Subsets of this cohort were previously published in studies detailing specific MRI findings [13] and the association between follow-up imaging and outcomes [14].

Study Population and Case Ascertainment

Study patients were evaluated at our institution between January 1, 1994 and December 31, 2002. Cases were ascertained by searching our institution's medical and surgical indices, the interventional radiology database, and the microbiology database using multiple broad and specific terms to ensure capture of all potential cases. Patients were observed until July 1, 2013. Patients over 18 years of age that met our case definitions were included (Table 1). Patients with only soft tissue spinal infections, patients with tuberculosis and brucellosis, and patients with implant-associated spine infection were excluded. Only the first episode of PVO in a given patient was included. Abstracted characteristics included clinical features, results of laboratory and imaging studies, medical and surgical therapies used, and outcomes. Written informed consent was obtained from all subjects, and the study was approved by the Institutional Review Board of the Mayo Clinic.

Definitions

Definitions used in the study are outlined in Table 1. Patients were observed until the development of treatment failure, death, or loss to follow-up. Patients were either classified as having a good outcome or having failed treatment. Treatment failure was microbiologically or mechanically defined (Table 1).

Statistics

Descriptive statistics were used to summarize the demographic, clinical, and treatment details. Comparisons between categorical and continuous data were performed using the Fischer's exact test and Wilcoxon rank-sum test as appropriate. The rate of survival free of treatment failure was estimated using the Kaplan–Meier survival method. Univariate and multivariate assessments of selected risk factors were performed using a Cox proportional hazard model. Variables having P value <.20 in the univariate model were included in a multivariate model. All statistics were analyzed using JMP, version 9.0.1 (SAS Institute Inc.).

RESULTS

Two hundred sixty patients met our case definition and were included in the study. Demographic and clinical characteristics of the cohort are outlined in Table 2. The median duration of follow-up among patients that did not develop treatment failure was 4.4 years (interquartile range [IQR], 0.94–11.2). The median duration of symptoms before diagnosis was 32.5 days (IQR, 13–66).

Microbiological characteristics of the cohort are given in Table 3. *Staphylococcus aureus* was the most common pathogen accounting for 40% of infections (103 patients). Of the *S. aureus* isolates, 11% (11) were methicillin-resistant.

Epidural, paravertebral, and psoas extension was noted in 61% (158), 41% (106), and 10% (27) of patients, respectively. The combination of all 3 was present in 13 patients. Eighty-eight percent (229) and 6% (16) of patients underwent initial diagnostic MRI or CT, respectively.

Table 2. Characteristics of Patients With Pyogenic Vertebral Osteomyelitis at the Mayo Clinic, Rochester[a]

Patient Characteristic	Value
Age (years)	67 (55–75)
Male gender	163 (63)
Duration of follow-up (years)[b]	4.4 years (0.94–11.2)
Diabetes mellitus	39 (15)
Systemic malignancy	37 (14)
Hepatic failure	8 (3)
Use of immunocompromising medications	23 (9)
End-stage renal disease[c]	22 (8)
Prior spinal radiation therapy	14 (5)
Body mass index (kg/m^2)	27.6 (24.3–32.4)
Infection location[d]	
Cervical	39 (15)
Thoracic	88 (34)
Lumbosacral	133 (51)
Temperature (maximum) at diagnosis (ºC)	37.9 (37.4–38.6)
Sinus tract present	3 (1)
Epidural extension	158 (61)
Paravertebral extension	106 (41)
Psoas extension	28 (10)
ESR at diagnosis (mm/h)	61 (30–88)
CRP at diagnosis (mg/dL)	6.0 (1.5–13.1)
WBC at diagnosis (*10^9/mL)	9.4 (7.2–13.3)
Positive blood cultures	118 of 210 patients (55)

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell count.

[a] Data are number (%) of patients or median (interquartile range, 25th–75th percentile) unless otherwise indicated.

[b] Excluding patients who developed clinical failure.

[c] Creatinine >2.0 mg/dL.

[d] Categorized by the most superior segment involved.

Twenty-seven percent (70) of patients developed their infection after an invasive procedure to the spine. Fifty-seven of them had a major surgical procedure (eg, discectomy, laminectomy) performed for a mechanical reason before the PVO episode. Nine had epidural injections, 2 had a lumbar puncture, and 1 each had cervical discography and intradiscal electrothermal therapy performed.

Baseline ESR and C-reactive protein (CRP) values were available for 194 and 88 patients, respectively. Of these, 23% (45) and 19% (17) patients had normal ESR and CRP values at the time of diagnosis. The median ESR and CRP at diagnosis were 61 mm/1 h (IQR, 30–88) and 6.0 mg/dL (IQR, 1.5–13.1), respectively. Follow-up ESR and CRP (4–8 week) information was available for 20% and 10% of patients, respectively. Of the 53 patients with follow-up ESR information available, 3 of 31 patients (10%) with improved values failed treatment vs 6 of 22 patients (27%) with unimproved values ($P = .14$). The median 4- to 8-week ESR value was 40 (IQR, 16.5–73). Of the 25 patients with follow-up CRP information available, 2 of 12 (17%) patients with improved values failed treatment vs 3 of 13 patients (23%) with unimproved values ($P = .99$). The median 4- to 8-week CRP value was 1.1 (IQR, 0.5–5.0). (Treatment failure both microbiologically and mechanically defined.)

Table 4 summarizes the surgical and medical therapies. The initial therapy for 51% of patients (132) did not include surgical therapy; 128 were treated with antimicrobial therapy only, whereas 4 had a concomitant drain placed. The remaining 49% of patients (128) underwent spinal surgery as part of

Table 3. Microbiologic Findings in Patients With Pyogenic Vertebral Osteomyelitis at the Mayo Clinic, Rochester[a]

Microbiologic Findings	Number (%) of patients
Methicillin-sensitive *Staphylococcus aureus*	92 (35)
Methicillin-resistant *S. aureus*	11 (4)
Staphylococcus coagulase negative	26 (10)
Streptococci[b]	26 (10)
Enterococcus sp[c]	6 (2)
Gram-negative bacilli[d]	10 (4)
Anaerobes[e]	12 (5)
Polymicrobial infection	13 (5)
Fungi[f]	5 (2)
Culture negative	59 (23)

[a] Data are number (%) of patients.

[b] Viridans group streptococci (13), Group B streptococci (8), *Streptococcus bovis* (2), *Streptococcus pneumonia* (1), Group A streptococci (1), Group F streptococci (1).

[c] One of 6 was vancomycin-resistant.

[d] *Klebsiella* sp (3), *Enterobacter* sp (2), *Burkholderia* sp (1), *Cardiobacterium* sp (1), *Citrobacter* sp (1), *Pseudomonas* sp (1), *Serratia* sp (1).

[e] *Propionibacterium acnes* (9), *Peptostreptococcus* sp (3).

[f] *Aspergillus* sp (2), *Candida albicans* (1), *Candida parapsilosis* (1), *Candida glabrata* (1).

Table 4. Medical and Surgical Treatment Information in Patients With Pyogenic Vertebral Osteomyelitis at the Mayo Clinic, Rochester[a]

Therapy	Value
Main parenteral antimicrobial used (in 255 patients)[b]	
β-lactam	156 (61)
Vancomycin	62 (24)
Combination therapy	26 (10)
Other	11 (4)
Antimicrobial therapy duration (days)	
Parenteral therapy (255 patients)[b]	42 (38–53)
Adjunctive oral therapy (80 patients)[c]	40 (26–60)
Any surgery performed	128 (49)
Type of surgery by approach	
Biopsy (anterior or posterior)	18 (14)
Anterior debridement	24 (19)
Posterior debridement ± laminectomy	48 (38)
Anterior fusion (without implant placement)	26 (20)
Anterior fusion with implant placement	4 (3)
Percutaneous posterior fusion with implant placement	2 (1)
Anterior fusion with posterior implant placement	6 (5)

[a] Data are number (%) of patients or median (interquartile range, 25th–75th percentile) unless otherwise indicated.

[b] Five patients that received highly bioavailable oral therapy are not included.

[c] Patients that received oral adjunctive antimicrobial therapy in addition to parenteral therapy.

their initial management. Of the patients who underwent specific surgical procedures such as posterior debridement with or without laminectomy; anterior fusion (without implant placement); and combined anterior fusion followed by posterior fixation with implants, 15 of 48 (31%), 9 of 26 (35%), and 1 of 6 (17%) developed treatment failure, respectively.

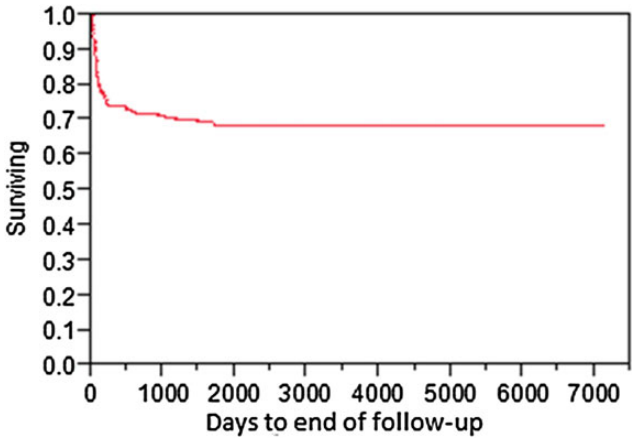

Figure 1. Kaplan–Meier free of treatment-failure survival curve in patients with pyogenic vertebral osteomyelitis at the Mayo Clinic, Rochester.

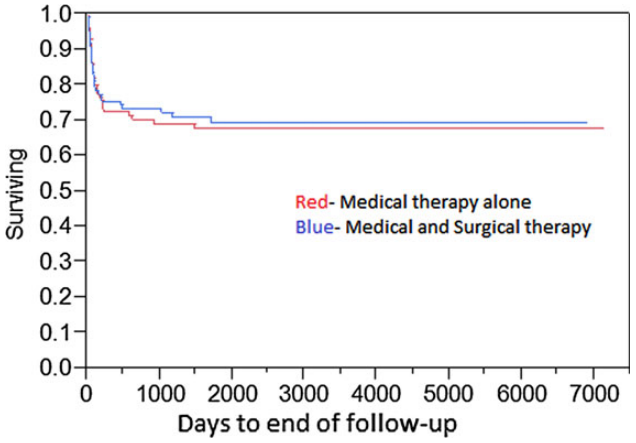

Figure 2. Kaplan–Meier free of treatment-failure survival curve by primary medical vs surgical therapy in patients with pyogenic vertebral osteomyelitis at the Mayo Clinic, Rochester.

The median duration of parenteral antimicrobial therapy was 42 days (IQR, 38–53). Twenty-seven percent of patients (71) developed treatment failure in the entire cohort. There was no significant difference in the median duration of combined parenteral and oral antimicrobial therapy between the 48 patients that developed failure after discontinuation of antimicrobial therapy and 189 patients who did not develop failure (46 days [IQR, 37–74] vs 47 days [IQR, 42–79]; $P = .98$). Five patients were treated with highly bioavailable oral antimicrobial therapy without any parenteral therapy. Thirty-one percent of patients (80 of 255) received adjunctive oral antimicrobial therapy after parenteral therapy for a median duration of 41 days (IQR, 26–60). When considering patients who had the opportunity to receive adjunctive oral antimicrobial therapy (ie, excluding patients that developed treatment failure on parenteral antimicrobial therapy), there was no significant difference in the treatment failure rates between patients that received oral antimicrobial therapy vs the ones that did not (17 of 85 [20%] vs 34 of 155 [20%]; $P = .87$).

The estimated cumulative 2-, 5-, and 10-year survival free of treatment failure rates were 72%, 69%, and 69% (Figure 1). The estimated cumulative 2-year survival free of treatment failure inpatients that received medical therapy alone and combination medical/surgical therapy was 70%, 69%, 68%, and 73%, 69%, 69%, respectively ($P = .85$) (Figure 2). Patients who did not develop treatment failure had a median duration of follow-up of 4.4 years (IQR, 0.94–11.2). The median duration to treatment failure from diagnosis was 67 days (IQR, 37–140). Seventy-five percent of patients who developed treatment failure did so within 4.7 months of diagnosis, and 90% within 19 months (Figure 1).

Of the 71 patients that failed treatment, 56 had microbiologically and 15 had mechanically defined failure. Eleven patients

(11 of 260 = 4.2%) died from initial infection-related causes and sepsis. Median time to death for these patients was 20 days (IQR, 15–25). Another 45 patients (45 of 260 = 17%) suffered a microbiologically confirmed relapse or reinfection. Of these 45 patients, 27 had the same, 15 had a different, and 3 had both the same and a different organism identified at time of treatment failure. Median duration to relapse/reinfection was 68 days (IQR, 39–121). Of these 45 patients, 10 patients presented with acute neurologic deficits at the time of treatment failure, a median of 51 days (IQR, 33–164) after treatment initiation. All of them had an unplanned surgical procedure performed at this time with intraoperative microbiology positive in all. Nine of these presented with acute paresis of lower extremities alone, whereas one had paresis accompanied by bladder incontinence. Nine of these 10 patients had been initially managed nonoperatively.

In the mechanically defined failure group, 15 patients underwent an unplanned surgical procedure of the spine for pain/disability. No evidence of an active infection was found during surgery. The median time to failure was 63 days (IQR, 35–106) in the microbiologically defined failure group and 116 days (IQR, 67–196) in the mechanically defined failure group. Sixteen percent (42) of patients had a residual neurologic deficit at the time of last contact; 50% of them (21) had paresis alone; 40% (17) of them had bowel and/or bladder incontinence in addition to paresis; the remaining 4 patients had isolated bowel and/or bladder incontinence or persistent sensory deficits. Thirty-two percent (82) of patients were receiving prescription pain relief medications for back pain at the time of last follow-up.

Univariate and multivariate analysis of factors that were associated with treatment failure in the entire cohort are shown in Tables 5 and 6 respectively. Having a combination of epidural, psoas, and paravertebral extension, *S. aureus* infection, and increased symptom duration before diagnosis were associated with an increased risk of failure in the univariate analysis. In a multivariate analysis, increasing duration of symptoms before diagnosis and infection with *S. aureus* were associated with increased risk of treatment failure.

Table 5. Univariate Analysis of Risk Factors for Treatment Failure in Patients With Pyogenic Vertebral Osteomyelitis at the Mayo Clinic, Rochester

Variable	Hazard Ratio	(95% Confidence Intervals)	*P* Value
Age	0.99	0.98–1.01	.50
Gender	1.25	0.77–2.02	.36
Diabetes mellitus	1.41	0.74–2.50	.27
Immunocompromised	1.35	0.56–2.75	.47
Systemic malignancy	0.49	0.19–1.05	.07
Epidural extension alone	0.91	0.56–1.46	.69
Psoas, paravertebral, and epidural extension	2.54	0.98–5.42	.05
Staphylococcus aureus	1.36	0.85–2.18	.19
Days of effective parenteral antimicrobials	1.00	0.99–1.01	.63
Culture positive vs Culture negative	0.89	0.53–1.61	.71
History of spinal procedure	1.40	0.84–2.60	.20

DISCUSSION

This retrospective cohort study demonstrates that PVO is still associated with a high relapse rate early in the course of disease, and treatment failure is uncommon after the first few months of being disease free. The 5- and 10-year failure rates were almost identical to the 2-year failure rate. However, residual neurologic defects and back pain were common even years after initial infection. In our cohort, increasing symptom duration before diagnosis and infection with *S. aureus* were identified as risk factors for treatment failure in patients with PVO. It is interesting to note that there was no difference in (1) treatment failure rates based on medical versus surgical management or (2) the duration of parenteral antimicrobial therapy.

The incidence of PVO is widely believed to be increasing [15, 16], and the demographics are shifting to an increasingly elderly population with attendant comorbid diseases [3, 6]. The age and demographics of our cohort confirm these findings. Our study was not designed to calculate PVO incidence over time because it is a single-center cohort study. A significant number of patients developed their infection after invasive procedures involving the spine. This finding represents a change from historic cohorts and likely reflects current medical practice, because dramatic increases in diagnostic and therapeutic spine procedures are occurring [17, 18]. Even relatively less invasive procedures such as lumbar punctures and epidural injections were followed by PVO. This highlights the importance of procedural precautions during the procedure and vigilance for signs and symptoms of PVO after the procedure.

The difficulties with prompt diagnosis of spine infections are well documented. With readily available imaging, the time from symptom onset to diagnosis seems to be diminishing. Historically, an average delay of 6 weeks to 7 months has been observed

Table 6. Multivariate Analysis of Risk Factors for Treatment Failure in Patients With Pyogenic Vertebral Osteomyelitis at the Mayo Clinic, Rochester

Variable	Hazard Ratio	95% Confidence Interval	*P* Value
Staphylococcus aureus	1.74	1.02–2.98	.04
Duration of symptoms before diagnosis	1.004	1.002–1.007	.03

[6]. In our cohort, the median duration of symptoms before diagnosis was 32.5 days. This shortened duration may be due to the increased utilization of MRI scans (88%) in our cohort. Newer diagnostic modalities with high accuracy are also being tested [19]. In both this and earlier cohorts of patients with PVO [6, 20], increased symptom duration was independently associated with a poor outcome.

Of the patients in our cohort with available baseline ESR and CRP values, almost one quarter had normal values at diagnosis. The utility of following inflammatory biomarkers such as ESR and CRP to assess response to therapy is widely cited [8]. The lack of reduction in inflammatory biomarkers on therapy was not used to define treatment failure in our study. We assessed variation in biomarker levels on therapy to assess the association with treatment failure. Unfortunately, only a fraction of patients in our cohort had follow-up bioinflammatory markers performed, which precluded our ability to detect an association between these values and outcome. Previous reports using subsets of this cohort have shown that follow-up imaging is not helpful in assessing treatment failure for the majority of patients. For a long period of time, patients may have persistently abnormal imaging studies associated with clinical improvement and normalization of inflammatory markers.

Surgical management of PVO is associated with better pain control in patients with disabling back pain, although only one fifth of patients recovered completely from paralysis caused by frank epidural abscesses even after surgical intervention, as previously illustrated in a large retrospective study [21]. A similar percentage of patients in our cohort underwent surgery, compared with other reports [3, 6, 21]. There were no striking differences in treatment failure rates by the type of surgical procedure performed or in patients who developed infection after prior procedures to the spine.

Most data on the duration and choice of antibiotic treatment are based on PVO case series and studies of osteoarticular infections in general; no randomized controlled trials have been conducted in patients with PVO. At the authors' institution, parenteral antibiotic therapy is usually initiated with a goal of at least 6 weeks of therapy. In our cohort, effective antimicrobial therapy was promptly initiated against the offending microorganism(s) once the diagnosis was confirmed. Some studies indicate that therapy for PVO can be safely shortened to 6 weeks [22]. Others recommend treatment for at least 8 weeks [10] and report that it is the only factor associated with cure [23]. Patients in our cohort typically received 42 days of parenteral antimicrobial therapy.

A subsequent switch to an oral agent (chaser) is considered if an oral agent is available and compliance is not an issue. Parenteral therapy can be extended in patients with extensive soft tissue involvement or who do not show complete clinical response to therapy with continuing back pain/elevated biomarkers after 6 weeks. Imaging is not routinely performed to follow-up radiological response unless complications are suspected. In these cases, parenteral therapy can be continued for >6 weeks. Oral therapy (chaser) was often added in patients thought to be at high risk of treatment failure based on the judgment of the treating physician. Most patients who received oral therapy did not have distinguishing clinic-pathological feature(s). One third of patients in our study received adjunctive oral therapy for a median duration of ∼6 weeks after parenteral therapy. Our study only focused on patients with native PVO where chronic suppression therapy is often not needed. There was no difference in the duration of antimicrobials received by failure status. We also did not observe a beneficial effect of adjunctive oral antimicrobial therapy on the failure rate. On performing a microorganism specific analysis (eg, *S. aureus*), the duration of adjunctive oral therapy was not associated with an altered outcome in any subgroup of microorganisms; possibly due to the small sample size of each subgroup.

More than 40% of cases in our cohort were caused by *S. aureus,* whereas other organisms such as other Gram-positive cocci, Gram-negative bacilli, anaerobes, and fungi were responsible for the remaining infections in the cohort. This allowed us to examine the role of microorganisms on the outcome of patients with PVO. We did observe that *S. aureus* was associated with a higher treatment failure in both univariate and multivariate models, although methicillin-resistant *S. aureus* did not have a worse outcome compared with methicillin-sensitive *S. aureus*. No significant difference in outcome was observed between any other microbiological group, including culture-negative versus culture-positive patients.

Median duration of follow-up in patients that did not develop failure was 4.4 years. The majority of patients who developed treatment failure in our cohort did so within 4.7 months of diagnosis, and the 2-year failure rate was strikingly similar to the 5- and 10-year failure rates. Seventeen percent of patients in our cohort suffered relapse, which is similar to the rate seen in other cohorts [6, 23, 24]. Median duration to infection-related complications was 2 months. Median duration to infection-associated death was <3 weeks. These findings support the conclusion that most serious complications in PVO occur early in the course of disease. Of the 71 patients who failed treatment overall, 56 had an infectious etiology identified at the time of treatment failure, whereas 15 cases of mechanically defined treatment failure could have had failure due to other unrelated noninfectious causes; however, an infection was not identified during the unplanned surgical procedure at the time of failure in these 15 patients. The chronology (unremitting pain/spinal deformity prompting a surgical procedure a median of 4 months after treatment initiation) and absence of alternate clinical explanations does support the idea that the treatment failure was mechanical in nature.

One third of patients with microbiological failure had a different organism identified at time of failure. Structural changes

in the spine caused by the initial infection could place the spine at risk for subsequent hematogenous seeding. Patients' characteristics associated with an increased risk of infection (eg, baseline immunocompromised status) may continue to place these patients at higher risk of reinfection with new infections. Some organisms may be more fastidious and slow to grow in culture than others. These organisms may be present in a polymicrobial setting in the original infection. Only one of them may be identified initially and antimicrobial therapy promptly initiated. Initial therapy may clear the identified organism, but it will allow the more fastidious organism to establish infection. Two take-home points emerge from these data: (1) patients with an episode of PVO may be at risk for new episodes of PVO, and (2) proper microbe identification at the time of first episode of PVO is crucial so that appropriate therapy can be initiated.

Some patients manifested new neurologic deficits despite appropriate initial therapy.

Nine of the 10 patients who developed acute new neurological deficits had initially been managed nonoperatively. Intraoperative microbiology was positive in all the above patients during the unplanned surgical procedure, indicating insufficient initial treatment. Median duration to these events was just over 7 weeks, highlighting the importance of vigilance for neurologic deficits by patients and providers.

Long-term sequelae were common, as suggested by the use of prescription pain relievers for back pain and residual neurologic deficits in a substantial number of patients. The high rate of neurologic sequelae is similar to other large reported series [3, 6, 21] and highlights the continued high morbidity of this disease even with advances in medical and surgical therapy.

This study's strengths include its large size and long-term follow-up. Major limitations in our study are those inherent to the retrospective study design that lends itself to studying a disease with such low incidence. Many patients did not have follow-up ESR or CRP values performed, which limited the power to analyze nonimprovement of inflammatory markers as predictive of failure. Treatment strategies, including the type of surgical procedure performed, were decided by the treating clinician (s), so selection bias may have impacted results. A large number of infections were postprocedural, and their results may be difficult to generalize to a population-based PVO cohort. Because this is a retrospective cohort, follow-up was determined by the treating physician and the patient. Electronic medical records were reviewed to check the date and the status at the last follow-up date. Death is recorded as reported. This passive follow-up is inherent to any retrospective study. Prospective follow-up may be warranted to overcome this limitation.

CONCLUSSIONS

In conclusion, PVO is typically a disease of elderly patients with other comorbidities, often times occurring after invasive procedures of the spine. Most treatment failures occurred soon after initiation of treatment. We did not observe differences in treatment failure between patients treated medically versus surgically or patients who received adjunctive oral antimicrobial therapy. Increased symptom duration before diagnosis, and infection with *S. aureus* were independent predictors of treatment failure and worse long-term outcome in our cohort. Future challenges include improving early diagnosis, standardizing measures to assess response to therapy, and clarifying the appropriate duration of antimicrobial therapy and the role for surgical intervention. Given the low incidence of this disease, these challenges will be best met through multicenter trials and well matched cohort studies.

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