Title: High risk clinical characteristics of pyogenic spinal infection presenting to a community emergency department

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ABSTRACT: (word count: 320)

Objective: To identify clinical characteristics associated with pyogenic spinal infection and describe the prevalence of these characteristics among adults presenting to a community emergency department (ED) with neck or back pain.

Methods: We conducted a prospective cohort study in a single community ED (2004 to 2018) of adults who presented to the ED with neck or back pain in whom the ED provider had a clinical concern for pyogenic spinal infection. Phase 1 of the study (2004- March 2010) included patients with and without pyogenic spinal infection. Phase 2 (March 2010-2018) included only patients with pyogenic spinal infection. We performed univariate and multivariate analyses for association of clinical characteristics with pyogenic spinal infection. We summarized the clinical presentation of spinal epidural abscess (SEA) versus non-SEA pyogenic spinal infection.

Results: We enrolled 232 patients, 89 of whom had pyogenic spinal infection. The median age was 55 years (interquartile range 41 to 66 years) and 102 patients (45.7%) were male. Study phase 1 analyzed 174 patients (40 with pyogenic spinal infection), and clinical characteristics with the strongest association with pyogenic spinal infection on multivariate analysis were recent soft tissue infection or bacteremia

(odds ratio [OR] 13.8, 95% confidence interval [CI] 3.5 to 54.3), male sex (OR 6.2, 95% CI 2.9 to 13.2), history of fever in the ED or prior to arrival (OR 4.9, 95% CI 2.2 to 10.6), and diabetes (OR 2.2, 95% CI 1.0 to 4.7). Among patients with SEA (n=61), 49 (80.3%) had at least one historical risk factor, 12 (19.7%) had fever in the ED, and 8 (13.1%) had a history of intravenous drug use.

Conclusion: In this prospective cohort of adults with pyogenic spinal infections presenting to a community ED, male sex, fever, and recent soft tissue infection or bacteremia had the strongest association with pyogenic spinal infection. The majority of patients with pyogenic spinal infection were afebrile on presentation to the ED.

Introduction

1.1. Background

Pyogenic spinal infections include spinal epidural abscess (SEA), vertebral osteomyelitis, septic facet joint, paravertebral abscess, and paraspinal abscess.[1–3] The incidence of spinal infections are increasing due to an aging population, greater use of spinal instrumentation, and larger burden of comorbidities.[4–6] Prospective data from the emergency department (ED) setting are limited to inform expert recommendations for ED diagnosis of pyogenic spinal infections.[7–10] The majority of studies include patients from primary care, intensive care unit, and other settings making it difficult to describe ED patients specifically. The largest ED specific study examined 86 cases of SEA at a single academic ED.[11] The generalizability of these data to other ED settings remain unclear as the 60% prevalence of prior intravenous drug use (IVDU) contrasts with the 8.8% prevalence of IVDU reported in a review of 915 SEA cases.[11,12]

1.2. Importance

Pyogenic spinal infections pose a diagnostic challenge to emergency providers. Previous authors have questioned the validity of the frequently cited historical risk factors for pyogenic spinal infection.[9,13] Despite this, current recommendations for evaluation of spinal infection in the ED recommend a risk factor and neurologic assessment coupled with inflammatory biomarkers to identify patients in need of urgent or emergent spinal MRI.[7,11] Delay in diagnosis of SEA is associated with increased risk of permanent neurologic deficits.[14] Yet, spinal magnetic resonance imaging (MRI), the diagnostic imaging modality of choice, is expensive and time consuming.[4,9,15] Additional data clarifying the characteristics of patients presenting with these deadly and elusive diagnoses may inform imaging protocols to help ED providers avoid missing this diagnosis and better target those patients requiring urgent MRI.[16,17] Such data will ideally encompass patients with any pyogenic spinal infection and not just SEA given the risk of permanent neurologic deficits (3-32%) from pyogenic vertebral osteomyelitis.[18–22] Data describing patients with pyogenic spinal infection in community ED settings are lacking.

1.3. Goals of this investigation

We identified high risk clinical characteristics for pyogenic spinal infection among adults presenting to a community ED with neck or back pain. We described the frequency of those characteristics among adults with SEA and non-SEA pyogenic spinal infection, which included any combination of vertebral osteomyelitis, septic facet joint, paravertebral abscess, and paraspinal abscess.

2. Materials and methods

2.1. Study design and setting

This was a single-center, prospective, observational study at a community hospital located in the metropolitan area of a major southwestern U.S. city. The annual ED census was approximately 50,000 patients during the study period. The hospital institutional review board approved the study protocol. We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement in our research design, reporting, and analysis.[23]

2.2. Selection of participants

We enrolled a convenience sample of adult patients presenting to the ED from January 2004 to August 2018. Adults (≥17 years old) presenting to the ED with neck or back pain in whom the ED provider was clinically concerned for pyogenic spinal infection were potentially eligible for study inclusion. Possible prompts for patient enrollment included fever, recent spinal procedure, multiple recent visits for unexplained spinal pain, the presence of published risk factors for spinal infection, new neurologic deficits or clinical gestalt suggesting spinal infection. We excluded patients diagnosed with fungal or tuberculous spinal infection to allow comparison to other similar studies.[2,14] We excluded patients who underwent spinal surgery less than 5 days prior to ED presentation as inflammatory markers remain elevated during this period.[24–26]

ED providers received education regarding the study including inclusion and exclusion criteria and patient recruitment procedures through quarterly group communications. During phase 1 of the study

during January 2004 - February 2010, ED providers contacted the principal investigator (PI) whenever ordering a C-reactive protein (CRP) and/or spinal MRI for the express purpose of evaluation for spinal infection. Thus, study phase 1 entailed enrollment of patients with and without spinal infections. During study phase 2 from March 2010-August 2018, ED providers contacted the PI after making a diagnosis of spinal infection. PI availability determined enrollment times. The PI personally screened all patients for enrollment. All enrolled patients received routine care and provided verbal consent as per the wavier for documentation of informed consent.

2.3. Methods of measurement

The PI personally completed all data collection by interviewing each patient, performing a focused physical examination, and prospectively abstracting data from the patient's medical record. Historical data collected included demographics, history of measured fever (≥ 38 degrees Celsius), and pain characteristics. Additional history included the presence of historical risk factors as identified by a comprehensive review of the literature describing SEA: diabetes, IVDU, immunocompromise, dialysis, active malignancy, recent soft tissue infection or bacteremia (defined as positive blood culture or hospitalization with infection concerning for bacteremia within 2 weeks of presentation), indwelling vascular catheter, presence of spinal implant, cirrhosis, vertebral fracture within 2 weeks of presentation, and spinal spinal surgery injection (including epidural steroid injection or epidural catheter placement) within 3 months of presentation.[12,27–30] Data collected by physical exam included an examination of each patient's back and neurologic examination of strength, sensation, and reflexes of the perineum and all extremities. Data recorded from the medical record at the time of the initial ED visit included vital signs at presentation. Data prospectively collected from the medical record once available following the initial ED visit included operative findings, discharge diagnosis, and the results of any cultures of the blood, needle aspiration, or operative wounds. Additional data collected included formal written interpretations of all MRI studies by neuroradiologists. The PI recorded all collected data on a hard copy instrument.

2.4. Outcome measures

Pyogenic spinal infection diagnoses included SEA, vertebral osteomyelitis, paraspinal abscess, paravertebral abscess or septic facet joint.[2] Providers could reach these diagnoses in one of three ways: 1) MRI evidence of spinal infection as documented by a neuroradiologist, 2) surgical findings consistent with spinal infection as documented in an operative report, or 3) positive culture by needle aspiration of the spinal infection. Radiologists were provided with the usual clinical information at our institution and were blinded to the data collected specifically for the study. Two investigators independently reviewed all MRI reports for location and diagnosis of spinal infection.

We categorized patients as negative for infection if an MRI was negative for pyogenic spinal infection, spinal symptoms resolved without antibiotics on telephone follow up, or a follow up period of at least six months in the medical record did not reveal a diagnosis of spinal infection, new neurologic deficits, or death due to spinal infection. This extended follow up period was chosen as many patients have multiple months of symptoms prior to diagnosis of spinal infection.[3,31] All patients did not receive a spinal MRI due to the observational nature of the study. The PI placed a telephone call between 14 to 28 days after discharge to patients without a diagnosis of spinal infection. We reviewed available medical records for a period of up to 3 years following the index presentation for all patients without a diagnosis of spinal infection. The PI queried these sources for evidence of neurologic deficits or diagnosis of spinal infection. We reviewed death records looking for any patient that was lost to follow up through the above sources. Among patients not receiving a spinal MRI, we excluded patients who did not confirm resolution of spinal symptoms at the follow up telephone call and had less than six months of follow up data available in the medical record.

2.5. Data analysis

Two investigators double entered all hard-copy data collection forms into an Excel database (version 14; Microsoft, Redmond, WA). We exported all data into SPSS (version 22; IBM, Armonk, NY) for statistical analysis. We reported all collected data for each patient regardless of whether data were missing for some study variables.

We performed descriptive statistics for clinical characteristics of all patients in the cohort. For patients enrolled in phase 1 of the study prior to March 2010, we performed a univariate analysis to compare clinical characteristics among patients with and without pyogenic spinal infection. Next, we constructed a multivariate binary logistic regression model with pyogenic spinal infection as the dependent variable. We included history components and physical exam findings as co-variates. We repeated the univariate analysis including all patients in the cohort (see appendix). We performed descriptive statistics for the clinical characteristics in all enrolled patients with SEA versus non-SEA pyogenic spinal infections to allow comparison of our cohort to previous studies focusing solely on SEA. Non-SEA pyogenic spinal infections included patients with any combination of vertebral osteomyelitis, septic facet joint, paravertebral abscess, or paraspinal abscess.[2] We compared data among patients with pyogenic spinal infection enrolled before versus after March 1, 2010 to analyze possible effects from the change in study protocol enrollment process (see appendix).

3. Results

3.1. Characteristics of study subjects

We approached 261 patients and enrolled 232 patients during 2006-2018 (Figure 1). We excluded nine patients: three patients were lost to follow up after not receiving an MRI to exclude spinal infection, two patients were diagnosed with fungal spinal infections, and three patients enrolled in study phase 2 did not meet criteria for spinal infection on case adjudication. Another excluded patient died two weeks following ED presentation with a clinical diagnosis of pneumonia but never received a spinal MRI or autopsy to definitively rule out spinal infection. In study phase 1, we analyzed 174 patients, of whom 40 had spinal infection. In study phase 2, we analyzed 49 patients, all of whom had spinal infections. The median age was 55 years (interquartile range [IQR] 41 to 66 years). Approximately half of the patients were male (45.7%).

3.2. Main results

Final diagnoses included nonspecific back pain (40.8%), pyogenic spinal infection (39.9%), other emergent spinal conditions (11.7%) such as epidural hematoma or metastatic cancer, and non-spine diagnoses (7.6%) such as pyelonephritis or pneumonia (Table 1). SEA was present in the majority (68.5%) of pyogenic spinal infections. The majority of patients were evaluated with spinal MRI (84.3%) and were admitted to the hospital (70.9%).

The clinical characteristics most strongly associated with pyogenic spinal infection on univariate analysis of patients enrolled in study phase 1 (Table 2) were recent soft tissue infection or bacteremia (odds ratio [OR] 26.2, 95% confidence interval [CI] 7.1 to 97.2), male sex (OR 7.1, 95% CI 3.2 to 15.8), and having at least one historical risk factor (OR 7.1, 95% CI 2.1 to 24.3). Odds ratios for indwelling vascular catheter and IVDU history could not be calculated as no patient in the non-infection group had either risk factor. Notable characteristics which were not significantly associated with pyogenic spinal infection included recent spinal injection, radicular pain (OR 0.9) and midline spinal tenderness (OR 0.6). When the univariate analysis was repeated to include the patients with spinal infections enrolled during study phase 2 (Appendix table 1), the majority of these associations remained stable. Notable changes included weaker associations for recent spinal surgery (OR 1.3), having at least one historical risk factor (OR 2.8) and fever in the ED (OR 1.6) or measured prior to arrival (OR 2.5).

The presence of new neurologic deficits had weak associations with pyogenic spinal infection (Table 2). The majority of patients (57.7%) with emergent spinal diagnoses other than pyogenic spinal infection (n=26) had a neurologic deficit on presentation to the ED. When excluding these 26 patients from the non-infection group, neurologic deficits had the following associations with pyogenic spinal infection: urinary incontinence (OR 5.2, 95% CI 1.6 to 16.9), extremity weakness (OR 3.6, 95% CI 1.3 to 10.2), extremity numbness (OR 3.6, 95% CI 1.0 to 12.7), abnormal reflex exam (OR 15.3, 95% CI 1.7 to 135.3), and any new neurologic deficit (OR 4.4, 95% CI 1.8 to 10.4).

Table 3 displays the output of the multivariate logistic regression model for the presence of pyogenic spinal infection. The predictor variables associated with pyogenic spinal infection included recent soft tissue infection or bacteremia, male sex, any fever in the ED or measured prior to arrival, and diabetes.

The clinical characteristics were similar between patients with SEA (n=61) and non-SEA (n=28) pyogenic spinal infections (Table 4). The most common historical risk factors among patients with SEA were diabetes mellitus (37.7%) or a recent soft tissue infection or bacteremia (36.1%). Among patients with SEA, a minority had a history of IVDU (13.1%) or fever either in the ED or measured prior to arrival (32.8%). Diabetes (46.4%) and recent spinal surgery (35.7%) were the most common historical risk factors among patients with non-SEA pyogenic spinal infection. An analysis comparing patients with spinal infections enrolled during study phase two versus phase one (Appendix Table 2) respectively found that patients enrolled after March 2010 were less likely to have a historical risk factor (75.5% versus 92.5%) or fever in the ED (16.3% versus 35.0%).

4. Discussion

In this single center, prospective, community ED cohort of adults in whom the ED provider had clinical concern for pyogenic spinal infection, the clinical characteristics most strongly associated with pyogenic spinal infection were male sex, fever, and recent soft tissue infection or bacteremia. Our study adds to the literature as a large prospective ED cohort evaluating which clinical characteristics are actually associated with spinal infection.

The majority of spinal infections occur due to hematogenous spread, so a recent infection complicated by bacteremia can increase a patient's risk of spinal infection.[4] The presence of another site of infection was strongly associated with SEA in a large ED-based cohort (OR 18.1) from University of California San Diego (UCSD) and a recent large single center retrospective study (OR 6.1).[11,32] Our study reinforces the findings of these previous studies that pyogenic spinal infection should be strongly

considered when back pain develops after soft tissue infection or any other infection possibly complicated by bacteremia.

Our study finding of male predominance (69.7%) among patients with pyogenic spinal infection is consistent with the largest review of SEA cases (64% male), the UCSD ED cohort (60% male), and a large RCT examining antibiotic regimens for pyogenic vertebral osteomyelitis (69% male). To our knowledge, our study is the first to show male sex as a risk factor for pyogenic spinal infection among ED patients. A possible explanation for this finding is that female patients were not identified by ED providers for study inclusion. Alternatively, males may be at higher risk due to having more risk factors than females. Further study is needed to characterize the presentation of pyogenic spinal infection among females and validate our finding of male sex as a risk factor in other ED settings.

New neurologic deficits were weakly associated with pyogenic spinal infection due to the high prevalence of neurologic deficits among patients with other emergent spinal diagnoses included in the non-infection group. Radicular pain or midline spinal tenderness were present in many cases of spinal infection, but these findings did not differentiate spinal infection from nonspecific back pain syndromes. Additional study is needed for patients presenting to the ED with spinal pain following epidural steroid injection or epidural catheter placement to determine whether patients are truly at increased risk for pyogenic spinal infection following these procedures. Pyogenic spinal infection is a rare complication as one prospective study found that SEA complicated one of every 1,930 epidural catheter procedures.[33]

All patients with SEA had at least one historical risk factor in the UCSD ED cohort.[11] The minority of SEA patients with no identifiable historical risk factor in our study (19.7%) is consistent with other cohorts.[12,34] The prevalence of IVDU in this UCSD cohort (60%) was much higher than the IVDU prevalence among patients with SEA in our study (13.1%), a review of 915 SEA cases (8.8%), and 162 SEA cases from a Boston academic hospital (20.4%).[11,12,32] Our data suggest that lack of historical risk factors does not definitively exclude SEA and many ED patients presenting with SEA lack IVDU as a risk factor.

Fever has been traditionally reported as present at the time of diagnosis in the majority of patients with SEA (66% of 915 SEA cases).[12] In contrast, a minority of patients (7.3%) presented with fever in the UCSD ED cohort, suggesting that fever may be less prevalent among patients with this disease process in the modern ED setting.[11] Indeed, the prevalence of fever in the ED among patients with SEA in our study was only 19.7% and only rose to 32.8% when including patients with fever measured prior to arrival. The lower prevalence of fever in more recent ED-based studies may represent identification of SEA earlier in the course of disease. Regardless, emergency physicians should maintain SEA on the differential diagnosis in afebrile patients.

4.1. Limitations

Initial medical evaluations frequently miss spinal infections,[4,14] and we were unable to include patients that did not undergo work up for this disease process in our study. Next, we collected our data at a single center, so the generalizability of our study to other ED settings is not known. We lack data describing patients when ED providers contacted the PI for enrollment during time periods when the PI was unavailable. Also, we collected data over an extended time period. Although this is common practice in SEA research given the rarity of the diagnosis, changing diagnostic, treatment, and epidemiologic patterns may have led to evolution of cohort characteristics over the course of the study.[6,11,27] Moreover, there was a change in study enrollment procedures during the study time period. Prior to March 2010, we collected data before the establishment of spinal infection diagnosis. After March 2010, we collected data after spinal infection was diagnosed. Univariate and multivariate analyses presented in the manuscript only included patients from phase 1 to eliminate this source of bias. The majority of associations remained stable when all cases were included (Appendix table 1).

Interpretation of the physical exam for patients with back pain requires clinical judgement. A specific example is whether midline spinal tenderness is present in the setting of diffuse, severe back pain. A single attending emergency physician made these assessments, so we are unable to assess interrater reliability across multiple ED providers. We lack data on post-void residuals as an objective

measurement for urinary retention, which is reported in 9-24% of SEA cases.[12,14,32] Finally, the diagnosis of spinal infection could be made in one of three ways: MRI, operative findings, or needle aspiration culture. Although our study lacked a single gold standard for diagnosis, we feel that these methods provided the most accurate categorization of subjects and reflection of clinical practice.

4.2. Conclusion

In conclusion, this prospective cohort of patients with pyogenic spinal infections presenting to a community ED found that the clinical characteristics most strongly associated with pyogenic spinal infection were male sex, having at least one historical risk factor, and recent soft tissue infection or bacteremia. Most patients with pyogenic spinal infection were afebrile on presentation.

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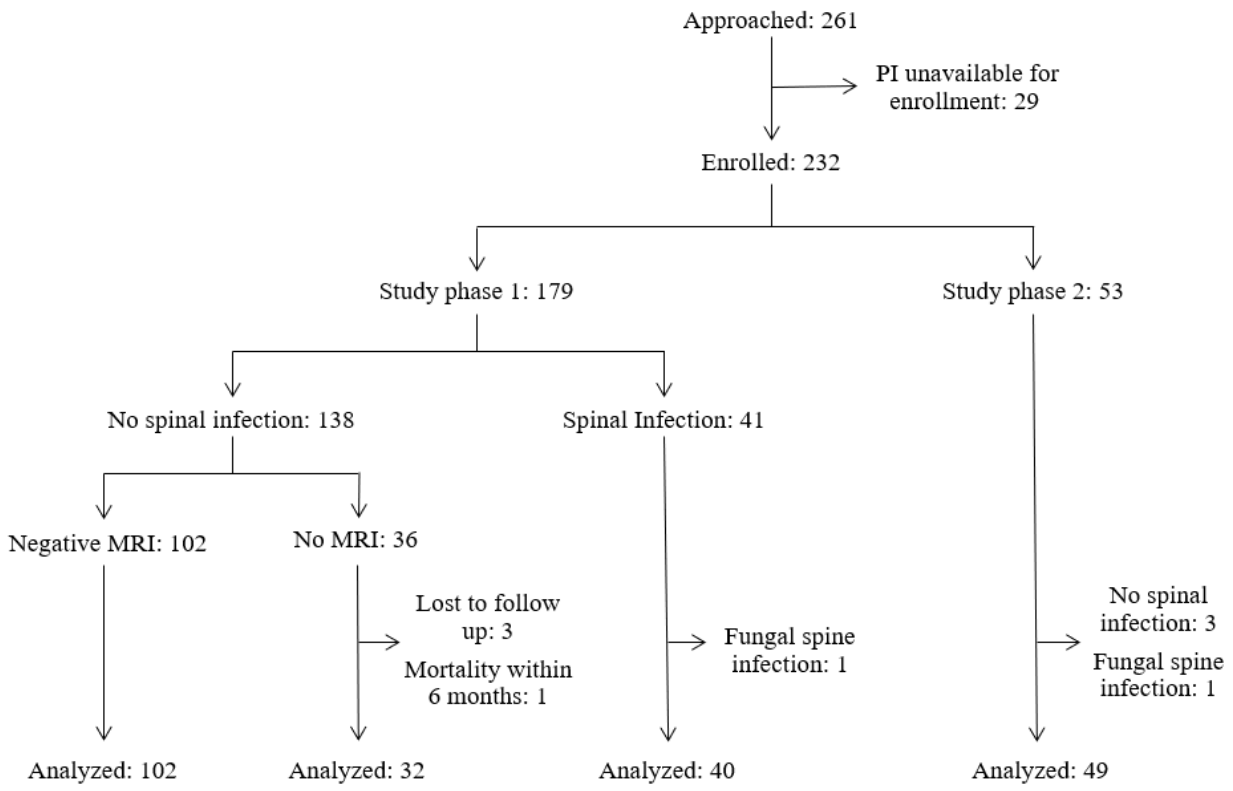
Figure 1. Patient flow diagram.



Enrollment periods were 2004 – March 2010 for study phase 1 and March 2010 – 2018 for study phase 2.

Table 1. Final diagnosis of 223 analyzed patients.

Final diagnosis	No of patients (%)
Pyogenic spinal infection	89 (39.9)
Spinal epidural abscess	61 (27.4)
Vertebral osteomyelitis	54 (24.2)
Septic facet joint	15 (6.7)
Paraspinous abscess	37 (16.6)
Paravertebral abscess	11 (4.9)
Metastatic Cancer	7 (3.1)
Epidural hematoma	9 (4.0)
Central disc herniation	8 (3.6)
Meningitis or myelitis	2 (0.9)
Nonspecific back pain	91 (40.8)
Non-spine diagnosis	17 (7.6)

Table 2. Univariate analysis of clinical characteristics association with pyogenic spinal infection among patients enrolled in study phase 1.

	Pyogenic spinal infection (n = 40)	No spinal infection (n = 134)	Odds ratio (95% CI)
Median age (IQR), y	51.5 (41.8 to 59.3)	55.5 (38 to 69.8)	
Male sex	30 (75)	40 (29.9)	7.1 (3.2 to 15.8)
Historical risk factors			
≥1 risk factor present	37 (92.5)	85 (63.4)	7.1 (2.1 to 24.3)
Intravenous drug use history	3 (7.5)	0 (0)	-
Dialysis	3 (7.5)	4 (3.0)	2.6 (0.6 to 12.3)
Indwelling vascular catheter	4 (10)	0 (0)	-
Recent soft tissue infection or bacteremia*	15 (37.5)	3 (2.2)	26.2 (7.1 to 97.2)
Immunosuppression	2 (5)	4 (3.0)	1.7 (0.3 to 9.7)
Active malignancy	2 (5)	4 (3.0)	1.7 (0.3 to 9.7)
Diabetes	17 (42.5)	39 (29.1)	1.8 (0.9 to 3.7)
Cirrhosis	3 (7.5)	0 (0)	-
Spinal implant present	0 (0)	7 (5.2)	-
Recent vertebral fracture[†]	0 (0)	5 (3.7)	-
Recent spinal surgery[†]	14 (35)	24 (17.9)	2.5 (1.1 to 5.4)
Recent spinal injection[†]	0 (0)	21 (15.7)	-
Reported Symptoms			
Radicular pain	17 (42.5)	59 (44)	0.9 (0.5 to 1.9)
Urinary incontinence [§]	8 (20)	8 (6)	3.9 (1.4 to 11.3)
History of measured fever[‡]	19 (47.5)	21 (15.7)	4.9 (2.2 to 10.6)
Physical exam findings			
Fever in ED[‡]	14 (35)	23 (17.2)	2.6 (1.2 to 5.7)
Midline spine tenderness	11 (27.5)	50 (37.3)	0.6 (0.3 to 1.4)
Inability to sit independently	15 (37.5)	30 (22.4)	2.1 (1.0 to 4.4)
Extremity weakness[§]	9 (22.5)	21 (15.7)	1.6 (0.7 to 3.8)
Extremity numbness[§]	6 (15)	14 (10.4)	1.5 (0.5 to 4.2)
Abnormal reflex exam[§]	5 (12.5)	5 (3.7)	3.7 (1.0 to 13.5)
Any new neurologic deficit[‖]	15 (37.5)	28 (20.9)	2.3 (1.1 to 4.9)

Data are presented as No. (%) unless otherwise indicated. * Defined as a soft tissue infection, positive blood culture, or infection requiring hospitalization within 2 weeks of presentation. [†] Recent was defined as within 2 weeks for vertebral fracture and within 3 months for recent spinal surgery or injection. [‡]Temperature ≥38 degrees Celsius. [§]Developed within the last two weeks per assessment by principal investigator. [‖]Neurologic deficits included motor weakness, urinary retention, numbness, or abnormal reflexes.

Table 3- Multivariable analysis of association between clinical characteristics and pyogenic spinal infection (n = 174).

Variable	Adjusted odds ratio	95% CI
Age	1.0	1.0 to 1.0
Male Sex	6.2	2.9 to 13.2
ESRF	0.5	0.1 to 3.8
Recent infection	13.8	3.5 to 54.3
Immunocompromised	0.9	0.1 to 5.4
Cancer	0.3	0 to 2.6
Diabetes	2.2	1.0 to 4.7
Spinal surgery	1.8	0.7 to 4.4
Radicular pain	2.0	0.9 to 4.2
Fever in ED or measured prior to arrival	1.9	0.7 to 5.0
Midline spinal tenderness	1.5	0.7 to 3.1
Inability to sit upright independently	1.9	0.9 to 4.3
Any new neurologic deficit	1.2	0.5 to 3.3

382 Table 4. Clinical characteristics of all patients with pyogenic spinal infection stratified by the presence of
383 spinal epidural abscess (SEA).

	Spinal epidural abscess, n = 61 (%)	Non-SEA spinal infection, n = 28 (%)
Median age (IQR), y	55 (46 to 61)	57 (48.5 to 68.3)
Male sex	44 (72.1)	18 (64.3)
Historical risk factors		
≥1 risk factor present	49 (80.3)	25 (89.3)
Intravenous drug use history	8 (13.1)	0 (0)
Dialysis	2 (3.3)	3 (10.7)
Indwelling vascular catheter	8 (13.1)	3 (10.7)
Recent soft tissue infection or bacteremia	22 (36.1)	6 (21.4)
Immunosuppression	3 (4.9)	1 (3.6)
Active malignancy	1 (1.6)	2 (7.1)
Diabetes	23 (37.7)	13 (46.4)
Cirrhosis	3 (4.9)	4 (14.3)
Spinal implant present	1 (1.6)	1 (3.6)
Recent vertebral fracture	0 (0)	0 (0)
Recent spinal surgery	10 (16.4)	10 (35.7)
Recent spinal injection	5 (8.2)	4 (14.3)
Reported Symptoms		
Radicular pain	33 (54.1)	12 (42.9)
Urinary incontinence	12 (19.7)	3 (10.7)
History of measured fever	14 (23.0)	14 (50.0)
Physical exam findings		
Fever in ED	12 (19.7)	10 (35.7)
Midline spine tenderness	19 (31.1)	11 (39.3)
Inability to sit upright independently	30 (49.2)	8 (28.6)
Extremity weakness	11 (18.0)	6 (21.4)
Extremity numbness	6 (9.8)	4 (14.3)
Abnormal reflex exam	8 (13.1)	1 (3.6)
Any new neurologic deficit	22 (36.1)	8 (28.6)

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Appendix Table 1- Univariate analysis of clinical characteristics association with pyogenic spinal infection among entire cohort.

	Pyogenic spinal infection (n = 89)	No spinal infection (n = 134)	Odds ratio (95% CI)
Median age (IQR), y	55 (47 to 62)	55.5 (38 to 69.8)	
Male sex	62 (69.7)	40 (29.9)	5.4 (3.0 to 9.7)
Historical risk factors			
≥1 risk factor present	74 (83.1)	85 (63.4)	2.8 (1.5 to 5.5)
Intravenous drug use history	8 (9.0)	0 (0)	-
Dialysis	5 (5.6)	4 (3.0)	1.9 (0.5 to 7.4)
Indwelling vascular catheter	11 (12.4)	0 (0)	-
Recent soft tissue infection or bacteremia	28 (31.5)	3 (2.2)	20.0 (5.9 to 68.5)
Immunosuppression	4 (4.5)	4 (3.0)	1.5 (0.4 to 6.3)
Active malignancy	3 (3.4)	4 (3.0)	1.1 (0.2 to 5.2)
Diabetes	36 (40.4)	39 (29.1)	1.7 (0.9 to 2.9)
Cirrhosis	7 (7.9)	0 (0)	-
Spinal implant present	2 (2.2)	7 (5.2)	0.4 (0.1 to 2.1)
Recent vertebral fracture	0 (0)	5 (3.7)	-
Recent spinal surgery	20 (22.5)	24 (17.9)	1.3 (0.7 to 2.6)
Recent spinal injection	9 (10.1)	21 (15.7)	0.6 (0.3 to 1.4)
Reported Symptoms			
Radicular pain	45 (50.6)	59 (44)	1.3 (0.8 to 2.2)
Urinary incontinence	15 (16.9)	8 (6)	3.2 (1.3 to 7.9)
History of measured fever	28 (31.5)	21 (15.7)	2.5 (1.3 to 4.7)
Physical exam findings			
Fever in ED	22 (24.7)	23 (17.2)	1.6 (0.8 to 3.1)
Midline spine tenderness	30 (33.7)	50 (37.3)	0.9 (0.5 to 1.5)
Inability to sit upright independently	38 (42.7)	30 (22.4)	2.6 (1.4 to 4.6)
Extremity weakness	17 (19.1)	21 (15.7)	1.3 (0.6 to 2.6)
Extremity numbness	10 (11.2)	14 (10.4)	1.1 (0.5 to 2.6)
Abnormal reflex exam	9 (10.1)	5 (3.7)	2.9 (0.9 to 9.0)
Any new neurologic deficit	30 (33.7)	28 (20.9)	1.9 (1.1 to 3.5)

Appendix Table 2. Comparison of patients with pyogenic spinal infection enrolled before and after March 2010 change in study protocol.

	Data collected Jan 2004 to Feb 2010 (n = 40)	Data collected Mar 2010 to Aug 2018, (n = 49)
Spinal epidural abscess present	27 (67.5)	34 (69.4)
Median age (IQR), y	51.5 (41.8 to 59.3)	57 (51 to 64)
Male sex	30 (75)	32 (65.3)
Historical risk factors		
≥1 risk factor present	37 (92.5)	37 (75.5)
Intravenous drug use history	3 (7.5)	5 (10.2)
Dialysis	3 (7.5)	2 (4.1)
Indwelling vascular catheter	4 (10.0)	7 (14.3)
Recent soft tissue infection or bacteremia	15 (37.5)	13 (26.5)
Immunosuppression	2 (5.0)	2 (4.1)
Active malignancy	2 (5.0)	1 (2.0)
Diabetes	17 (42.5)	19 (38.8)
Cirrhosis	3 (7.5)	4 (8.2)
Spinal implant present	0 (0)	2 (4.1)
Recent vertebral fracture	0 (0)	0 (0)
Recent spinal surgery	14 (35.0)	6 (12.2)
Recent spinal injection	0 (0)	9 (18.4)
Reported Symptoms		
Radicular pain	17 (42.5)	28 (57.1)
Urinary incontinence	8 (20.0)	7 (14.3)
History of measured fever	19 (47.5)	9 (18.4)
Physical exam findings		
Fever in ED	14 (35.0)	8 (16.3)
Midline spine tenderness	11 (27.5)	19 (38.8)
Inability to sit upright independently	15 (37.5)	23 (46.9)
Extremity weakness	9 (22.5)	8 (16.3)
Extremity numbness	6 (15.0)	4 (8.2)
Abnormal reflex exam	5 (12.5)	4 (8.2)
Any new neurologic deficit	15 (37.5)	15 (30.6)