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Risk factors for surgical intervention in patients with primary spinal infection on initial presentation

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OBJECTIVE Treatment of primary spinal infection includes medical management with or without surgical intervention. The objective of this study was to identify risk factors for the eventual need for surgery in patients with primary spinal infection on initial presentation.

METHODS From January 2010 to July 2019, 275 patients presented with primary spinal infection. Demographic, infectious, imaging, laboratory, treatment, and outcome data were retrospectively reviewed and collected. Thirty-three patients were excluded due to insufficient follow-up (≤ 90 days) or death prior to surgery.

RESULTS The mean age of the 242 patients was 58.8 ± 13.6 years. The majority of the patients were male (n = 130, 53.7%), White (n = 150, 62.0%), and never smokers (n = 132, 54.5%). Fifty-four patients (22.3%) were intravenous drug users. One hundred fifty-four patients (63.6%) ultimately required surgery while 88 (36.4%) never needed surgery during the duration of follow-up. There was no significant difference in age, gender, race, BMI, or comorbidities between the surgery and no-surgery groups. On univariate analysis, the presence of an epidural abscess (55.7% in the no-surgery group vs 82.5% in the surgery group, p < 0.0001), the median spinal levels involved (2 [interquartile range (IQR) 2–3] in the no-surgery group vs 3 [IQR 2–5] in the surgery group, p < 0.0001), and active bacteremia (20.5% in the no-surgery vs 35.1% in the surgery group, p = 0.02) were significantly different. The cultured organism and initial laboratory values (erythrocyte sedimentation rate, C-reactive protein, white blood cell count, creatinine, and albumin) were not significantly different between the groups. On multivariable analysis, the final model included epidural abscess, cervical or thoracic spine involvement, and number of involved levels. After adjusting for other variables, epidural abscess (odds ratio [OR] 3.04, 95% confidence interval [CI] 1.64–5.63), cervical or thoracic spine involvement (OR 2.03, 95% CI 1.15–3.61), and increasing number of involved levels (OR 1.16, 95% CI 1.01–1.35) were associated with greater odds of surgery. Fifty-two surgical patients (33.8%) underwent decompression alone while 102 (66.2%) underwent decompression with fusion. Of those who underwent decompression alone, 2 (3.8%) of 52 required subsequent fusion due to kyphosis. No patient required hardware removal due to persistent infection.

CONCLUSIONS At time of initial presentation of primary spinal infection, the presence of epidural abscess, cervical or thoracic spine involvement, as well as an increasing number of involved spinal levels were potential risk factors for the eventual need for surgery in this study. Additional studies are needed to assess for risk factors for surgery and antibiotic treatment failure.

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KEYWORDS spine infection; spinal infection; osteomyelitis; discitis; epidural abscess; surgical decompression

ABBREVIATIONS CAD = coronary artery disease; CI = confidence interval; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; ESRD = end-stage renal disease; IQR = interquartile range; IV = intravenous; MI = myocardial infarction; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *S. aureus*; UTI = urinary tract infection; WBC = white blood cell.

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Spinal infection comprises between 2% and 7% of all musculoskeletal infections each year[1] and has an estimated incidence of between 1 in 20,000 and 1 in 100,000, and up to a 2%–3% mortality rate.[2,3] The etiologies of spinal infection include postoperative infection after spinal surgery and primary infection from hematogenous seeding from bacteremia or adjacent spread of soft-tissue infection. The treatment paradigm for spinal infections in a neurologically intact patient without concern for instability consists of first-line treatment with broad spectrum intravenous antibiotics and identification of the causative organism through either blood cultures or needle biopsy cultures. A subset of patients may ultimately develop evidence of spinal instability, worsening neurological function, or failure of antibiotic treatment and require surgical management consisting of decompression only or decompression and fixation.[4] While previous studies have explored factors associated with failure of antibiotic therapy,[5] it remains difficult to predict which patients who present with primary spinal infection will ultimately require surgery. We retrospectively reviewed our 9.5-year institutional experience with treatment of primary spinal infections and identified which risk factors present at initial consultation may predict eventual need for surgical intervention.

Methods

Study Population and Data Collection

Approval to conduct the study was obtained from the IRB of the Johns Hopkins Hospital. A database of all patients who were evaluated by the Department of Neurosurgery at the Johns Hopkins Hospital from January 2010 to July 2019 was searched using the keywords "osteo," "discitis," "abscess," "epidural," and "infection." Patients who did not have a spinal infection or whose infection was secondary to surgical-site infection were excluded. Demographic factors collected included patient age, gender, race, and BMI. Comorbidities included intravenous (IV) drug use, diabetes mellitus, coronary artery disease (CAD), chronic heart failure, prior myocardial infarction (MI), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), end-stage renal disease (ESRD), immunosuppression, osteoporosis, prior cancer history, chronic steroid use, and prior smoking history. Infection history included recent spinal epidural steroid injections, history of bacteremia, active bacteremia, concurrent infection, and type of organism. Laboratory values included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC) count, platelet count, creatinine, and albumin. Treatment characteristics included antibiotic agents used, initial management decisions including attempts at percutaneous drainage, and eventual need and timing of surgery.

Statistical Analyses

Patient characteristics at initial consult were assessed for association with surgery. Unadjusted associations between each characteristic and surgery were assessed using chi-square or Fisher's exact tests for categorical measures and t-tests or Wilcoxon rank-sum tests for continuous measures as appropriate. Variables associated with surgery at the $p < 0.20$ level in unadjusted analysis were considered for inclusion in a multivariable model of surgery. Candidate variables included age, IV drug use, history of bacteremia, outside hospital transfer, active bacteremia at time of initial consult, ESR > 20 mm/hr, epidural abscess, involvement of cervical or thoracic spine, and number of involved spinal levels. Although COPD was associated with surgery at the $p < 0.20$ level, it was not considered a candidate variable due to the low number of cases (n = 6, all in the surgery arm). The final model was selected using backward selection. All analyses were conducted using the SAS statistical program (version 9.4, SAS Institute).

Results

Baseline Characteristics and Comorbidities

From January 2010 to July 2019, 275 patients presented with and underwent neurosurgical consultation for a primary spinal infection (osteomyelitis, discitis, and/or epidural abscess). Thirty-one patients were excluded from the analysis because they underwent medical management but had insufficient follow-up duration (< 90 days). Two patients died shortly after neurosurgical consultation/intervention and prior to any surgery, and thus were also excluded. The final patient cohort consisted of 242 patients who either underwent medical management with at least 90 days of follow-up (n = 88, 36.4%) or required surgery (n = 154, 63.6%).

Demographic and baseline characteristics for the 242 patients are described in Table 1. The mean (± SD) patient age was 58.8 ± 13.6 years. One hundred thirty patients (53.7%) were male, and 112 (46.3%) were female. The majority of patients were White (n = 150, 62.0%) or Black (n = 79, 32.6%). The mean BMI was 28.8 ± 8.2 kg/m^2. The majority of patients had no smoking history (n = 132, 54.5%), while 56 patients (23.1%) were prior smokers and 54 (22.3%) were active smokers. The most common comorbidities were diabetes (n = 61, 25.2%), IV drug use (n = 54, 22.3%), history of cancer (n = 32, 13.2%), and CAD (n = 33, 13.6%). The majority of patients presented to our hospital system directly (n = 140, 57.9%) while 102 patients (42.1%) presented as transfers from another hospital. There were no significant differences in demographic characteristics or comorbidities between the no-surgery and surgery groups (Table 1).

Infection Characteristics

Seventy-two patients (29.8%) had active bacteremia at the time of initial neurosurgical consultation at our institution (Table 2). The presence of active bacteremia significantly differed between the surgery (54 of 154, 35.1%) and no-surgery (18 of 88, 20.5%) groups ($p = 0.02$). Eighty-seven patients (36.0%) had a history of bacteremia during preceding hospital encounters that was first diagnosed a median of 8.5 days (interquartile range [IQR] 4–48.3 days) prior to neurosurgical consultation at our institution. Seventy-two patients (29.8%) had an additional site of infection other than the spine: 55 patients (22.7%) had only one other location of infection while 17 patients (7.0%) had multiple. The most common locations for the infections were urinary tract infection (UTI)/pyelonephritis (n = 15, 6.2%), paraspinal/psoas (n = 13, 5.4%), soft tissue (n = 13,

TABLE 1. Demographic information

Variable	All, N = 242	No Surgery, n = 88	Surgery, n = 154	p Value
Mean age (SD), yrs	58.8 (13.6)	60.4 (14.6)	57.9 (12.9)	0.17
Male, n (%)	130 (53.7)	47 (53.4)	83 (53.9)	0.94
Race, n (%)				>0.99
White	150 (62.0)	55 (62.5)	95 (61.7)	
Black	79 (32.6)	29 (33.0)	50 (32.5)	
Other	7 (2.9)	2 (2.3)	5 (3.2)	
Hispanic	6 (2.5)	1 (1.1)	5 (3.2)	0.42
Comorbidities, n (%)				
Diabetes	61 (25.2)	19 (21.6)	42 (27.3)	0.33
IV drug use	54 (22.3)	15 (17.0)	39 (25.3)	0.14
CAD	33 (13.6)	11 (12.5)	22 (14.3)	0.70
Prior cancer history	32 (13.2)	11 (12.5)	21 (13.6)	0.80
Immunosuppression	22 (9.1)	9 (10.2)	13 (8.4)	0.64
ESRD	17 (7.0)	6 (6.8)	11 (7.1)	0.92
CKD	11 (4.5)	4 (4.5)	7 (4.5)	>0.99
MI	11 (4.5)	4 (4.5)	7 (4.5)	>0.99
CHF	10 (4.1)	2 (2.3)	8 (5.2)	0.33
Chronic steroid use	10 (4.1)	4 (4.5)	6 (3.9)	>0.99
COPD	6 (2.5)	0 (0.0)	6 (3.9)	0.09
Osteoporosis	2 (0.8)	1 (1.1)	1 (0.6)	>0.99
Mean BMI (SD), kg/m^2	28.8 (8.2)	28.7 (7.3)	28.9 (8.8)	0.88
Smoking history, n (%)				0.96
Never	132 (54.5)	49 (55.7)	83 (53.9)	
Prior	56 (23.1)	20 (22.7)	36 (23.4)	
Active	54 (22.3)	19 (21.6)	35 (22.7)	
Outside hospital transfer, n (%)	102 (42.1)	31 (35.2)	71 (46.1)	0.10

CHF = congestive heart failure.

5.4%), pneumonia (n = 12, 5.0%), and septic arthritis (n = 9, 3.7%). Other less common locations are listed in Table 2. Common organisms isolated from these other areas of infection included methicillin-resistant *Staphylococcus aureus* (MRSA; n = 36, 14.9%), methicillin-sensitive *S. aureus* (MSSA; n = 26, 10.7%), *Streptococcus* species (n = 13, 5.4%), and other *Staphylococcus* species (n = 12, 5.0%).

Most patients presented with clinical signs of spinal infection, including pain or neurological deficit. Spinal infection was incidentally discovered on workup for other pathologies in only 11 patients (4.5%). Approximately half of the patients (n = 123, 50.8%) had already begun antibiotics at the time of initial consultation. One hundred thirty-five infections (55.8%) involved the lumbar spine, 98 (40.5%) involved the thoracic spine, 63 (26.0%) involved the cervical spine, and 42 (17.4%) involved the sacrum (Table 3). Few cases involved infections that spanned across junctional levels: 32 cases (13.2%) spanned the lumbosacral junction, 16 cases (6.6%) involved the thoracolumbar junction, and 11 cases (4.5%) involved the cervicothoracic junction. A small number of patients had distant surgery involving the infected level (n = 13, 5.4%). Only 1 patient had an unknown date of prior surgery; the remaining 12 had surgery over a year prior to presentation. Six patients (2.5%) had prior spine surgery at a neighboring level: 2 patients had surgery within a year of presentation, whereas the remaining patients had surgery several years prior.

Most cases involved infections of only 2 levels of the spine (n = 110, 45.5%), followed by those that involved 3 levels (n = 44, 18.2%) and 4 levels (n = 33, 13.6%). The median number of levels involved was 3 levels (IQR 2–4 levels). The median number of involved levels differed significantly between the surgery (median 3 levels, IQR 2–5 levels) and no-surgery (median 2 levels, IQR 2–3 levels) groups ($p < 0.0001$). The majority of patients (n = 176, 72.7%) had an associated epidural abscess or phlegmon. The presence of an epidural abscess or phlegmon was significantly different between the surgery (n = 127, 82.5%) and no-surgery (n = 49, 55.7%) groups ($p < 0.0001$).

The majority of patients had an elevated ESR > 20 mm/hr (209/221, 94.6%), elevated CRP > 0.5 mg/dl (219/228, 96.1%), and a low albumin < 3.5 g/dl (123/179, 68.7%; Table 4). Ninety-six (39.7%) of 242 patients had an elevated WBC count > 11 × 10^3/mm^3, 70 patients (28.9%) had an elevated platelet count > 350 × 10^3/mm^3, and 49 patients (20.2%) had an elevated creatinine level > 1.3 mg/dl. Mean or median values for each laboratory study are as follows: mean ESR 83.7 ± 36.5 mm/hr, median CRP 9.1 (IQR 4.0–16.5) mg/dl, mean WBC count 11.3 ± 5.4 × 10^3/mm^3, mean platelet count 298.4 ± 146.5 × 10^3/mm^3, median creatinine

TABLE 2. Infection history information

Variable	All	No Surgery	Surgery	p Value
Incidentally found, n (%)	11 (4.5)	6 (6.8)	5 (3.2)	0.21
History of epidural steroid injections, n (%)	13 (5.4)	6 (6.8)	7 (4.5)	0.56
History of bacteremia, n (%)	87 (36.0)	27 (30.7)	60 (39.0)	0.20
Median time from prior bacteremia to initial consult (IQR), days*	8.5 (4–48.3)			
Active bacteremia at time of initial consult, n (%)*	72 (29.8)	18 (20.5)	54 (35.1)	**0.02**
Other source of infection, n (%)	72 (29.8)	26 (29.5)	46 (29.9)	0.96
One source	55 (22.7)			
Multiple sources	17 (7.0)			
UTI/pyelonephritis	15 (6.2)			
Soft tissue	13 (5.4)			
Paraspinal	13 (5.4)			
Pneumonia	12 (5.0)			
Endocarditis	9 (3.7)			
Septic arthritis	9 (3.7)			
Meningitis	5 (2.1)			
Abdominal	4 (1.6)			
Line	3 (1.2)			
Arteriovenous graft	2 (0.8)			
S. aureus as source of infection, n (%)	67 (27.7)	24 (27.3)	43 (27.9)	0.91
Isolated organism, n (%)				
MRSA	36 (14.9)			
MSSA	26 (10.7)			
Streptococcus species	13 (5.4)			
Staphylococcus species	7 (2.9)			
S. aureus otherwise unspecified	5 (2.1)			
Enterococcus faecalis	4 (1.7)			
Klebsiella	4 (1.7)			
Escherichia coli	3 (1.2)			
Already on antibiotics at time of consult, n (%)	123 (50.8)	39 (44.3)	84 (54.5)	0.13

Boldface type indicates statistical significance.
* In 82 patients.

level 0.8 (IQR 0.6–1.2) mg/dl, and median albumin level 3.0 (IQR 2.4–3.6) g/dl. There were no significant differences in the mean/median values between the surgery and no-surgery groups (Table 4).

Overall Management of Spinal Infection

A summary of the management of all spinal infection patients is displayed in Fig. 1. Initial neurosurgical consultation occurred a median of 0 days (IQR 0–1 days) from the time of initial admission to our hospital or a median of 5 days (IQR 2–11 days) from the time of initial outside hospital admission. Management options included observation (n = 1, 0.4%), antibiotics alone (n = 61, 25.2%), antibiotics with image-guided biopsy (n = 67, 27.7%), and surgery (n = 113, 46.7%).

Of the patients who underwent image-guided biopsy, the median time to biopsy from consultation was 2 days (IQR 1–4 days). Forty (59.7%) of the patients were already taking antibiotics at the time of biopsy. Thirty-two (47.8%) of the 67 patients had cultures with no growth; 18 (56.3%) of these patients were already receiving antibiotics while 14 (43.8%) had antibiotics started after the biopsy was completed. Of the 17 patients who had prior culture data (from bacteremia or another foci of infection) and underwent image-guided biopsy, only 1 patient had a spinal biopsy that resulted in growth of a different organism (MRSA) from prior cultures (MSSA). Eight patients had biopsy cultures that matched their prior culture data. Eight patients had prior culture data that grew an organism with spinal biopsy demonstrating no growth, 6 of whom had already been started on antibiotics.

Of the 129 patients who underwent nonsurgical management at the time of initial consultation, 62 (48.1%) underwent a second neurosurgical consultation that occurred a median of 31 days (IQR 14–60.5 days) from the initial consultation. Blood culture data at the time of second consultation were available for 58 patients, 8 (13.8%) of which had active bacteremia. The majority (46/62, 74.2%) were already receiving antibiotics at the time of the second consultation. The

TABLE 3. Spine infection information

Infection Variable	All	No Surgery	Surgery	p Value
Prior spine surgery at infected level, n (%)	13 (5.4)			
Prior spine surgery at neighboring level, n (%)	6 (2.5)			
Epidural abscess or phlegmon, n (%)	176 (72.7)	49 (55.7)	127 (82.5)	**<0.0001**
Spinal levels involved				
Median (IQR)	3 (2–4)	2 (2–3)	3 (2–5)	**<0.0001**
1	3 (1.2%)			
2	110 (45.5%)			
3	44 (18.2%)			
4	33 (13.6%)			
5	10 (4.1%)			
6	15 (6.2%)			
7	6 (2.5%)			
8	5 (2.1%)			
9	3 (1.2%)			
10	6 (2.5%)			
>10	7 (2.9%)			
Location of spinal infection, n (%)				
C	38 (15.7)			
C, L	3 (1.2)			
C, L, S	3 (1.2)			
C, T	11 (4.5)			
C, T, L	8 (3.3)			
T	57 (23.6)			
T, L	16 (6.6)			
T, L, S	6 (2.5)			
L	67 (27.7)			
L, S	32 (13.2)			
S	1 (0.4)			

C = cervical; L = lumbar; S = sacral; T = thoracic.
Boldface type indicates statistical significance.

TABLE 4. Laboratory values

Laboratory Test	N	All	No Surgery	Surgery	p Value
Mean ESR (SD), mm/hr	221	83.7 (36.5)	80.5 (39.1)	85.5 (34.9)	0.33
>20, n (%)		209/221 (94.6)	74/81 (91.4)	135/140 (96.4)	0.13
Median CRP (IQR), mg/dl	228	9.1 (4.0–16.5)	8.0 (3.4–15.1)	10.0 (4.3–17.3)	0.13
>0.5, n (%)		219/228 (96.1)	81/85 (95.3)	138/143 (96.5)	0.73
Mean WBC count (SD), × 10^3/mm^3	242	11.3 (5.4)	10.7 (5.1)	11.7 (5.6)	0.15
>11, n (%)		96/242 (39.7)	33/88 (37.5)	63/154 (40.9)	0.60
Mean platelet count (SD), × 10^3/mm^3	242	298.4 (146.5)	317.1 (159.6)	287.8 (138.0)	0.13
>350, n (%)		70/242 (28.9)	26/88 (29.5)	44/154 (28.6)	0.87
Median creatinine (IQR), mg/dl	242	0.8 (0.6–1.2)	0.8 (0.7–1.1)	0.8 (0.6–1.2)	0.55
>1.3, n (%)		49/242 (20.2)	16/88 (18.2)	33/154 (21.4)	0.55
Median albumin (IQR), g/dl	179	3.0 (2.4–3.6)	3.0 (2.5–3.7)	3.0 (2.4–3.5)	0.42
<3.5, n (%)		123/179 (68.7)	44/66 (66.7)	79/113 (69.9)	0.65

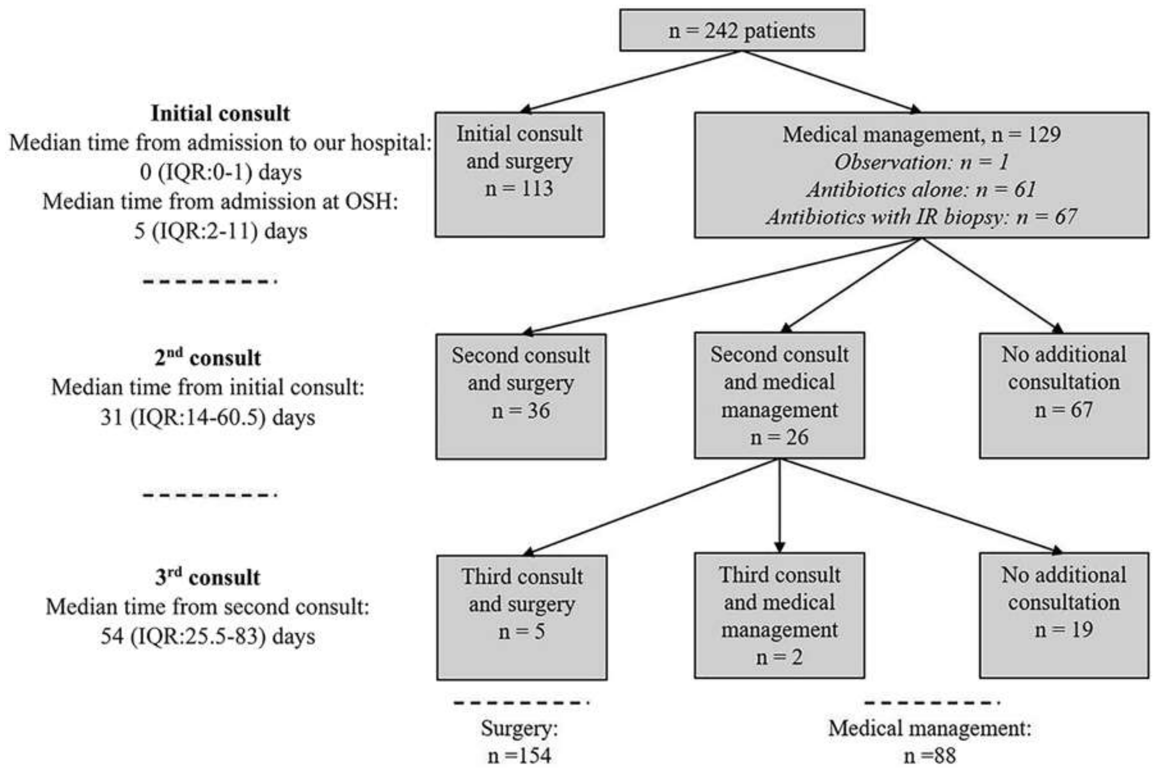

FIG. 1. Flow chart showing management of patients with spinal infection. IR = interventional radiology; OSH = outside hospital.

TABLE 5. Surgical management

Surgical Variable	Value
Surgery, n (%)	154 (63.6)
Failed medical management, n (%)	41 (16.9)
Median time to surgery (IQR), days	35 (12–64)
Indication, n (%)	
Weakness	81 (52.6)
Mechanical instability/kyphosis	33 (21.4)
Failed medical management w/o deficit or instability	16 (10.4)
Cauda equina syndrome	7 (4.5)
No. of surgeries, n (%)	
1	136 (88.3)
2	16 (10.4)
3	2 (1.3)
Decompression alone, n (%)	52 (33.8)
Median days to follow-up, days (IQR)	221 (53–1203.5)
No. requiring subsequent fusion, n (%)	2 (3.8)
Median days to fusion surgery (IQR)	132 (88.8–174.3)
Decompression & fusion, n (%)	102 (66.2)
Hardware removal due to persistent infection, n (%)	0 (0)
Intraop purulence, n (%)	73 (47.4)
Operative cultures, n (%)	
No growth	69 (44.8)
MRSA	26 (16.9)
MSSA	24 (15.6)

recommendations for management were antibiotics alone (n = 19, 30.6%), antibiotics with image-guided biopsy (n = 5, 8.1%), surgery (n = 36, 58.1%), and no additional treatment (n = 2, 3.2%). Seven patients (2.9% of the initial 242) had a third neurosurgical consultation that occurred a median of 54 days (IQR 25.5–83 days) from the second consultation. Five of these patients ultimately underwent surgery while 2 patients continued antibiotic therapy.

Surgical Management

Of the 242 patients, 154 (63.6%) ultimately underwent surgery. Common indications for surgery included weakness (n = 81, 52.6%) and mechanical instability or kyphosis (n = 33, 21.4%; Table 5). Sixteen patients (10.4%) underwent surgery due to failed medical management without neurological deficit or mechanical instability. Forty-one patients (16.9%) experienced failure of initial antibiotic treatment and ultimately required surgery at a median of 35 days (IQR 12–64 days) from initial consultation. Time to surgery is displayed as a Kaplan-Meier plot in Fig. 2. Of the patients who underwent surgery, the majority had surgery within 3 months of initial consultation.

Fifty-two patients (33.8%) underwent a decompression alone, while 102 patients (66.2%) underwent decompression with fusion. Of those patients who underwent a decompression alone, the median time to follow-up was 221 days (IQR 53–1203.5 days), and only 2 (3.8%) of 52 patients required a subsequent fusion due to kyphosis. Fusion surgery occurred a median of 132 days (range 88.8–174.3 days) after the initial decompression surgery.

One hundred thirty-six patients (88.3%) underwent 1 surgery, 16 patients (10.4%) underwent a second surgery, and 2 patients (1.3%) underwent a third surgery. Reasons for a second surgery included pseudoarthrosis (6/154, 3.9%) and wound washout (5/154, 3.2%) No patients required removal of hardware due to persistent infection. Intraoperative purulence at the time of initial surgery was observed in 73 cases (47.4%). Operative culture results included no growth (n = 69, 44.8%), MRSA (n = 26, 16.9%), and MSSA (n = 24, 15.6%).

Risk Factors for Surgical Intervention

Of the 242 patients, 88 (36.4%) did not require surgery and had a median duration to follow-up of 24 months (IQR 11–45 months, range 3–114 months). On univariate analysis, the presence of an epidural abscess (55.7% in the no-surgery group vs 82.5% in the surgery group, $p < 0.0001$), the median levels involved (2 levels [IQR 2–3 levels] in the no-surgery group vs 3 levels [IQR 2–5 levels] in the surgery group, $p < 0.0001$), and active bacteremia (20.5% in the no-surgery group vs 35.1% in the surgery group, $p = 0.02$) were significantly different between the two groups.

On multivariable analysis, the final model included the presence of an epidural abscess, cervical or thoracic spine involvement, and number of involved levels. After adjusting for cervical or thoracic spine involvement and number of involved levels, epidural abscess was associated with 3.04 times greater odds of surgery (95% confidence interval [CI] 1.64–5.63). After adjusting for epidural abscess, involvement of the cervical or thoracic spine and increasing number of involved levels were also both associated with greater odds of surgery (odds ratio [OR] for cervical or thoracic spine involvement 2.03, 95% CI 1.15–3.61; OR for number of involved levels 1.16, 95% CI 1.01–1.35).

When comparing patients who had surgery on their initial encounter with those who underwent conservative treatment, univariate analysis demonstrated increased WBC count (median $10.6 \times 10^3/mm^3$ [IQR $8.0–15.5 \times 10^3/mm^3$] in the initial-surgery group vs $9.7 \times 10^3/mm^3$ [IQR $6.9–13.0 \times 10^3/mm^3$] in the no initial surgery group, $p = 0.04$), decreased creatinine (median 0.7 mg/dl [IQR 0.6–1.1 mg/dl] in the initial-surgery group vs 0.9 mg/dl [IQR 0.7–1.3 mg/dl] in the no initial surgery group, $p = 0.05$), and increased presence of an epidural abscess (83.2% in the initial-surgery group vs 63.6% in the no initial surgery group, $p = 0.0006$) in association with increased odds of surgery on initial encounter.

Of the 129 patients who did not undergo surgery on their initial encounter, univariate analysis comparing the 41 patients who eventually needed surgery to the 88 patients who were nonoperatively managed demonstrated that the presence of an epidural abscess (80.5% in the eventual-surgery group vs 55.7% in the nonoperative group, $p = 0.006$) was again associated with an eventual need for surgery. Notably, of the 129 patients initially managed nonoperatively, all 3 of the patients with COPD eventually underwent surgery ($p < 0.03$).

Final Patient Outcomes

Of the 242 patients included, 28 (11.6%) were deceased at the time of chart review. The most common causes of death included septic shock (28.6%), cancer (10.8%), and

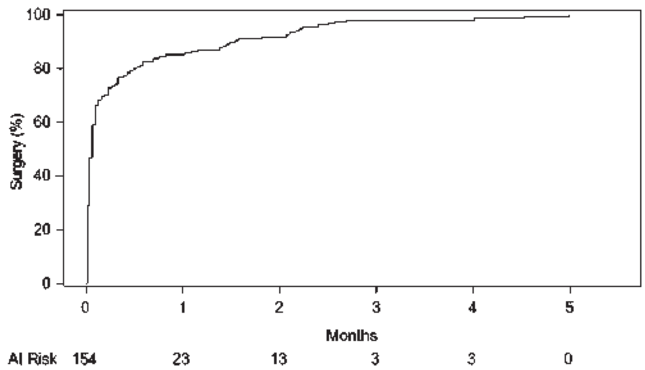

FIG. 2. Kaplan-Meier plot of time to surgery for patients who underwent surgery.

kidney failure (7.1%). Of the 88 patients who never underwent surgery, 13 (14.8%) were deceased (3 of whom [3.4%] died secondary to sepsis), 4 (4.5%) were receiving chronic antibiotic suppression therapy, and 3 (3.4%) left against medical advice in subsequent hospitalizations and were lost to follow up. The remaining 68 patients (77.3%) had complete resolution of their infections on follow-up.

Discussion

In our study of 242 patients with primary spinal infection, 63.6% of patients ultimately required surgery. We sought to determine risk factors at the time of initial presentation that are associated with the need for surgery, either acutely or in a delayed fashion, and found that potential risk factors include the presence of epidural abscess, cervical or thoracic spine involvement, and an increasing number of affected levels.

Studies on the predictors for the need for surgery in patients with primary spinal infection are very limited. The only study to date by Appalanaidu et al.[6] attempted to develop a scoring system to help predict the need for surgery. From a small cohort of 65 patients, 6 predictors were identified: distant site infection, medical comorbidities, immunocompromised state, MRI findings, anatomical location, and neurological deficit on presentation. Using these 6 factors, the authors developed the Brighton Spondylodiscitis Score, with a higher score indicating a higher risk of requiring surgery. More recently however, Hunter et al. and Urrutia et al. were unable to externally validate the Brighton Spondylodiscitis Score in their respective cohorts, which they hypothesized may be due to heterogeneity of the different study populations.[7,8]

Risk factors for failure of antibiotic treatment, which is often the first-line treatment, have also been minimally studied. In one of the largest studies to date, de Graeff et al. found that risk factors for antibiotic treatment failure (which they defined as the need for surgery or death due to infection) included diabetes, fever, osteomyelitis at an additional site, and the presence of an epidural abscess.[5] In their cohort of 215 patients, the mean age was 58 ± 15 years, 62% of patients were male, and mean BMI was 29 ± 6.8 kg/m^2. Our cohort of 242 patients had very similar demographics with a mean age of 58.8 ± 13.6 years, 53.7% male, and a mean BMI of 28.8 ± 8.2 kg/m^2. The rate of diabetes was higher in their study than in ours (33% vs 25.2%), and notably, they did not report their rate of IV drug use (although it was included in their statistical analysis), which was 22.3% in our cohort. Their cohort had a higher rate of active bacteremia as compared to ours (54% vs 29.8%), while their rate of epidural abscess was lower (54% vs 72.7%). As in our study, in their study the most common region affected by infection was the lumbar spine (49%). de Graeff et al. found an antibiotic treatment failure rate of 27% (59 patients) after a median duration of 25 days. Our cohort similarly had a failure rate of 16.9% after a median duration of 35 days. In another study of patients who underwent early spinal instrumentation with at least 4 weeks of follow up, Arnold et al. found that treatment failure occurred in 23% of their patients at a median of 4 months after surgery. Risk factors included cervical and thoracic infection sites, and the presence of negative cultures.[9] Our study similarly found that presence of infection at the cervical or thoracic levels was associated with surgical intervention.

One category of risk factors associated with treatment failure that is of particular interest is abnormal laboratory values. Few prior studies have explored whether laboratory values can be used to predict treatment success in spinal infections. Carragee notably found that in their retrospective analysis of 111 patients, having a stable or rising ESR was predictive of antibiotic treatment failure.[10] Conversely, de Graeff and colleagues did not find a significant correlation between serum albumin, alkaline phosphatase, calcium, CRP, sedimentation rate, hemoglobin, WBC count, or platelet count with failure of antibiotic therapy.[5] We also analyzed ESR, CRP, WBC count, platelet count, creatinine, and albumin at initial consultation for our patients and similarly did not find that they were associated with surgical intervention. Univariate analysis comparing patients who required surgery on their initial encounter to those who underwent nonsurgical management found that increased WBC count and decreased creatinine were associated with initial surgical intervention; however, the median laboratory values of each group (WBC count 9.7 vs $10.6 \times 10^3/mm^3$, and creatinine 0.9 vs 0.7 mg/dl) are too similar to be useful in a clinical setting.

Spinal epidural abscess has been a well-studied entity.[11–14] At our institution, the presence of epidural abscess alone is not an indication for surgery, but we did find that epidural abscess was a risk factor for ultimately requiring surgery (both in patients who were taken to surgery on initial encounter as well as patients who initially attempted an antibiotic trial but eventually required surgery). This is unsurprising as the rates of neurological deficits associated with spinal epidural abscess have been reported to be as high as 76%.[14,15] Treatment failure for spinal epidural abscess has also been examined. Kim et al. found that in their cohort of 355 patients with spontaneous spinal epidural abscess, the most significant risk factor for failure of medical management was incomplete or complete spinal cord deficits. Other risk factors included age older than 65 years, diabetes, and MRSA.[16] In a cohort of 128 patients with spontaneous spinal epidural abscess, Patel et al. found that positive blood cultures, diabetes, WBC count $> 12.5 \times 10^3/mm^3$, and CRP > 115 mg/dl were associated with failure of medical management.[17]

When surgery is needed, the surgical approach and the need for instrumentation remains controversial. Options include decompression alone, decompression with instrumentation, and the use of intervertebral graft material for fusion. In cases without instability or deformity, the risk of needing fusion with decompression alone in the future has not been well-defined. Verla et al.[18] studied 16 patients with osteomyelitis-discitis at the thoracolumbar junction who underwent initial laminectomy (n = 4) or medical management alone (n = 12). All 4 patients who underwent initial laminectomy ultimately developed progressive kyphosis, which required instrumented fixation and fusion. After laminectomy, the average time to fusion was 2.6 months. In another large cohort study using data from MarketScan, Dietz et al.[19] examined the outcomes of 1452 patients who underwent decompression alone for spinal infection and had not undergone prior surgery within 12 months. In this group, the rate of a new fusion within a year of decompression was 6.6%, although the indications for surgery are unknown. In contrast, for our patients who underwent decompression only, the majority did not develop subsequent deformity or instability. Only 3.8% (2/52) patients required a fusion surgery due to kyphosis, suggesting that initial decompression surgery alone may be sufficient and durable in select cases without evidence of instability.

Another topic related to the use of instrumentation in the treatment of primary spinal infections is whether there is an associated risk of persistent infection. Bydon and colleagues demonstrated that in 118 patients who were surgically treated for primary spinal infections, there was no significant difference in reoperation or recurrent infection between the decompression only versus decompression and fusion groups.[4] Wang et al., in a meta-analysis of 24 studies and 239 patients, similarly demonstrated that placement of cervical instrumentation in primary spinal infections had comparable wound complication and hardware failure rates as those of elective cervical spine procedures.[20] In our study, we similarly found that the rate of reoperation for wound washout in the instrumented fusion group was 3.2%, which is comparable to prior published data on elective procedures.[21,22]

In addition to the risk factors for surgery, we found that our failure rate for antibiotic treatment was 16.9% after a median of 35 days. With decompression surgery alone, our rate of subsequent fusion was 3.8% and lower than other rates that have been reported in the literature. In patients who underwent fusion surgery, no patients required removal of hardware due to persistent infection.

Our study has several limitations. First, because this was a retrospective review of patients who underwent inpatient neurosurgical consultation, our study did not include patients who may have been evaluated on an outpatient basis or who never underwent neurosurgical consultation. Additionally, it can be argued that our study only captures those patients who have more severe symptoms or who were believed to be likely surgical candidates. Similarly, due to this inherent sample bias toward patients with more extensive disease, all patients in our review had concurrent osteomyelitis and discitis, making separation of the two entities impossible. Second, the decision to offer surgical intervention was also not governed by a strict algorithm or criteria, but rather was based on assessment of neurological deficit, mechanical instability or deformity, or perceived failure of medical management. Ultimately, the decision for surgery was based, at least in part, on individual surgeon clinical judgment. Our results may be difficult to extrapolate to other institutions who may have different criteria for proceeding with surgical treatment. Finally, our patient population may differ from others, although our demographic data do seem to be similar to what has been previously reported in the literature.

Conclusions

At the time of initial presentation of primary spinal infection, the presence of epidural abscess, cervical or thoracic spine involvement, as well as an increasing number of involved levels are potential risk factors for surgical intervention. Initial laboratory values (ESR, CRP, WBC, creatinine, and albumin) were not associated with the need for surgery. Additional studies are needed to assess for risk factors for surgical intervention as well as antibiotic treatment failure.

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Disclosures

Dr. Theodore reports being a consultant for Globus Medical, having direct stock ownership in Globus Medical, and receiving royalties from Globus Medical and DePuy Synthes. Dr. Bydon reports being a consultant for NuVasive Spine. Dr. Sciubba reports being a consultant for DePuy Synthes, Medtronic, Stryker, and Baxter, and having ownership in BioPhy.

Author Contributions

Conception and design: Lo, Jin, Liu, Witham. Acquisition of data: Jin, Liu, Medikonda, Ishida, Pairojboriboon. Analysis and interpretation of data: Lo, Jin, Liu, Overbey, Medikonda, Feghali, Krishnan, Ishida, Gokaslan, Wolinsky, Theodore, Bydon, Sciubba, Witham. Drafting the article: Lo, Jin, Liu. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Overbey, Feghali. Administrative/technical/material support: Lo. Study supervision: Lo.

Supplemental Information

Previous Presentations

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