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Clinical Studies

Factors associated with the time required for CRP normalization in pyogenic spondylitis: A retrospective observational study

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ABSTRACT

Background: Treatment for pyogenic spondylitis tends to be prolonged; however, few studies have examined the factors associated with the time required for infection control. Therefore, we analyzed a consecutive cohort of patients to identify factors associated with the time required to control infection in pyogenic spondylitis. This study aimed to clarify the factors linked to the duration necessary for achieving infection control in cases of pyogenic spondylitis, using C-reactive protein (CRP) normalization as an indicator.

Methods: In this retrospective observational study, we investigated 108 patients diagnosed with pyogenic spondylitis. We evaluated the number of days from the first visit to CRP normalization; for cases wherein CRP did not normalize, the number of days to the date of final blood sampling was evaluated. In the present study, infection control in pyogenic spondylitis was defined as a CRP falling within the normal range (≤0.14 mg/dL). We performed univariate and multivariate Cox regression analyses to identify various factors associated with the time required for CRP normalization in pyogenic spondylitis.

Results: The mean time required for CRP normalization was 148 days. Univariate Cox regression analysis showed that the serum creatinine level, estimated glomerular filtration rate (eGFR), lymphocyte percentage, neutrophil percentage, CRP level, CRP-albumin ratio, and neutrophil-to-lymphocyte ratio were significantly associated with the time required to control infection. Multivariate Cox regression analysis showed that a higher neutrophil percentage, diabetes mellitus, and a lower eGFR were the independent factors associated with a longer infection control time.

Conclusions: We found that a higher neutrophil percentage, diabetes mellitus, and a lower eGFR were significantly associated with a longer time for CRP normalization in pyogenic spondylitis. These findings may help identify patients with pyogenic spondylitis who are at a high risk for an extended infection control period.

Introduction

Pyogenic spondylitis has been considered a rare condition [1]; however, its incidence has increased with aging of the society [1,2]. Pyogenic spondylitis is an intractable disease that requires prolonged and expensive treatment [3]. Therefore, it is vital to consider strategies to reduce the time required to control infection in pyogenic spondylitis and lower the cost of care.

C-reactive protein (CRP), an acute-phase protein released by hepatocytes to coactivate the complement system in response to antigenic and other stimuli, is commonly used as an indicator of the infection status [4,5]. Accordingly, it is also used as an indicator of infection control in

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pyogenic spondylitis [6,7]. Previous studies have focused on the time required for CRP to normalize during pyogenic spondylitis treatment [7–9].

To date, the following risk factors have been reported for refractory pyogenic spondylitis: lower hemoglobin count [8], higher CRP concentration [7,10,11], expansion of an abscess to the epidural spaces [8,10,12], expansion of an abscess to the paravertebral spaces [8,10], higher number of infected vertebral bodies [8,12], positive culture [11], resistant strains of pathogenic bacteria [8], prolonged duration of symptoms [7], antibiotic treatment time < 6 weeks [11], neurologic deficit [10], underlying diabetes [12], fever [11,12], and age [10]. However, to our knowledge, there have been few reports on the factors associated with the time required to control infection in pyogenic spondylitis. Thus, we aimed to identify these factors in the present study; we hypothesized that these factors would help plan future treatment strategies for reducing the duration of treatment for pyogenic spondylitis.

Methods

Study design and population

We conducted a retrospective observational study to investigate the factors associated with the time required to control infections in patients diagnosed with pyogenic spondylitis in the Department of Orthopedic Surgery at Tokyo Medical and Dental University Hospital in Japan. Consecutive patients who were diagnosed with pyogenic spondylitis between May 2010 and August 2021 were enrolled. We focused on the treatment course of pyogenic spondylitis rather than postoperative infections. According to Centres for Disease Control and Prevention definition, infections of the spine near the surgical site within 30 days after spinal decompression and within 1 year after spinal instrumentation surgery were considered postoperative infections and, thus, were excluded from this study [13]. In other words, this study focused on patients with pyogenic spondylitis resulting from nonsurgical causes of the spine. A total of 108 patients were included in the study.

Measured data

Data on the following parameters were extracted from the medical records: age; sex; body mass index (BMI); location of pyogenic spondylitis; body temperature; creatinine level; estimated glomerular filtration rate; blood urea nitrogen; serum albumin concentration; total cholesterol level; hemoglobin concentration; platelet; white blood cell count; lymphocyte %; neutrophil %; erythrocyte sedimentation rate; conventional serum CRP; number of operations; number of patients with positive culture (biopsies and blood), on dialysis, with diabetes mellitus, and treated with hyperbaric oxygen therapy; number of smokers; use of steroids; time from symptom onset to the first visit; time from the first visit to CRP normalization; and number of days to the date of final blood sampling in cases wherein CRP did not normalize.

The CRP was quantified by latex-coagulating nephelometry using a buffer solution and latex reagent solution (N-assay LA CRP-T, Nittobo Medical, Japan). The CRP assay had a detection limit of 0.03 mg/dL. The sample was assigned a value equivalent to the detection limit where activity was undetectable. The reference value of CRP was < 0.14 mg/dL. Blood test data were collected from the time of admission. The modified Glasgow prognostic score (mGPS), CRP-albumin ratio (CAR), prognostic nutrition index (PNI), controlling nutritional status, neutrophil-to-lymphocyte ratio (NLR), and platelet–lymphocyte ratio (PLR) were determined as follows: the mGPS score was calculated based on the CRP concentration (≤ 1 mg/dL: 0 point, > 1 mg/dL: 1 point) and albumin concentration (≥ 3.5 g/dL: 0 point, < 3.5 g/dL: 1 point); the CAR was obtained by dividing the CRP level (mg/dL) by the albumin concentration (g/dL); the PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (cells/μL); the controlling nutritional status score was calculated based on the albumin level (≥ 3.5 g/dL: 0 point, 3.00–3.49 g/dL: 2 points, 2.50–2.99 g/dL: 4 points, < 2.50 g/dL: 6 points), total cholesterol level (≥ 180 mg/dL: 0 point, 140–179 mg/dL: 1 point, 100–139 mg/dL: 2 points, < 100 mg/dL: 3 points), and total lymphocyte count (≥ 1,600/μL: 0 point, 1,200–1,599/μL: 1 point, 800–1,199/μL: 2 points, < 800/μL: 3 points); the NLR was obtained by dividing the neutrophil count (/μL) by the lymphocyte count (/μL); and the PLR was obtained by dividing the platelet count (/μL) by the lymphocyte count (/μL).

Regarding radiological examinations, plain radiographic images were categorized as per the Griffiths classification [14]. Magnetic resonance imaging (MRI) findings were classified into the following 5 stages [15]: stage I, endplate destruction; stage II, vertebral edema; stage III, a high signal area contiguous to the disc on the T2 vertebra; stage IV, an epidural abscess; and stage V, a paravertebral abscess. The number of infected vertebral bodies and the presence of epidural, psoas, and paraspinal abscesses were also investigated. The presented patient background data include the results of blood sampling and imaging findings obtained at the first visit.

Statistical analysis

This study aimed to investigate factors that contribute to the time required for controlling infections in pyogenic spondylitis. Thus, we analyzed the number of days from the initial visit to the normalization of CRP levels (since CRP serves as an infection control marker). For cases wherein the CRP level did not normalize, we examined the number of days until the date of final blood sampling. In the Cox regression analysis, the event was defined as CRP normalization. We first conducted a univariate Cox regression analysis to identify factors associated with the time until CRP normalization. Factors with p-values < .25 in the univariate analysis were then included in the multivariate Cox regression analysis as candidates for independent factors associated with the time required to control infection in pyogenic spondylitis [16,17]. Finally, a backward elimination method was used to construct the final multivariate Cox regression model, retaining only variables with a p-value < .05. The days from the first visit to CRP normalization was examined using Kaplan-Meier survival curve. For all statistical analyses, JMP software version 12 (SAS Institute) was used, and a p-value < .05 was considered statistically significant.

Results

Patient demographics

The study population included 67 men and 41 women. The mean age at the first visit was 68 (standard deviation [SD], 13) years, and the mean BMI was 22.4 (SD, 4.8) kg/m^2. The number of patients with CRP normalization during follow-up was 83 patients (77%), and the mean time from the first visit to CRP normalization was 148 (SD, 242) days (Table 1 and Figure 1). There were 94 inpatients and 14 outpatients (Table 2). Of the 108 patients, 25 continued to have elevated CRP levels during follow-up despite treatment for pyogenic spondylitis at our hospital, and their CRP levels did not normalize. Of these, 17 were transferred to other hospitals and 1 died. (Table 3).

Identification of factors associated with the time required to control infection

No significant association was found between the time required for CRP normalization and imaging findings as well as the presence or absence of positive cultures. However, univariate Cox regression analysis revealed that the time required for CRP normalization was associated with the serum creatinine level (p = .045), eGFR (p = .002), lymphocyte percentage (p = .005), neutrophil percentage (p = .002), CRP (p = .018), CAR (p = .013), and NLR (p = .016) (Table 4).

Table 1
Baseline characteristics of demographic data.

Characteristics	N = 108
Age, years	67.7 ± 13.2
Sex male/female (%)	67 (62) / 41 (38)
BMI, kg/m^2	22.4 ± 4.8
Location	Cervical 9 (8) / Thoracic 26 (24) / Lumbar 77 (71)
Number of days from symptom onset to the first visit to our hospital, day	38 ± 47
Number of days from the first visit to CRP normalization or to the final blood sampling date, day	148 ± 242
Number of patients with CRP normalization during follow-up (%)	83 (77)
Creatinine, mg/dL	1.5 ± 2.0
eGFR, mL/min/1.73m^2	73 ± 50
BUN mg/dL	23 ± 14
Albumin, g/dL	3.1 ± 0.7
Total cholesterol, mg/dL	158 ± 41
Hemoglobin, g/dL	11.2 ± 2.2
Platelet, 10^3/μL	26.5 ±12.5
White blood cell, 10^3/μL	8.7 ± 4.1
Lymphocyte %	17 ± 10
Neutrophil %	75 ± 12
ESR, mm/1h	75.1 ± 32.0
CRP, mg/dL	8.7 ± 10.0
CONUT	5.1 ± 3.3
mGPS	1.6 ± 0.6
CAR	3.2 ± 4.1
NLR	8.5 ± 11.8
PNI	37.2 ± 7.6
PLR	279 ± 239
Dialysis	8 (7)
Diabetes mellitus	34 (31)
Smoking	18 (17)
Use of steroids	6 (6)
Use of synthetic or biological disease-modifying anti-rheumatic drugs	1 (1)
Use of anticancer drug	6 (6)
Use of antibiotics at the time of the first visit to our hospital	33 (31)
Body temperature at first visit, ˚C	37.3 ± 0.8

BMI, body mass index; BUN, Blood urea nitrogen; CAR, CRP-albumin ratio; CONUT, controlling nutritional status; CRP, C-reactive protein; eGFR, estimate glomerular filtration rate; ESR, erythrocyte sedimentation rate; JOA, Japanese Orthopaedic Association; mGPS, modified Glasgow prognostic score; NLR, neutrophil–lymphocyte ratio; PLR, platelet–lymphocyte ratio; PNI, prognostic nutrition index.
Data are presented as mean ± standard deviation or n (%).

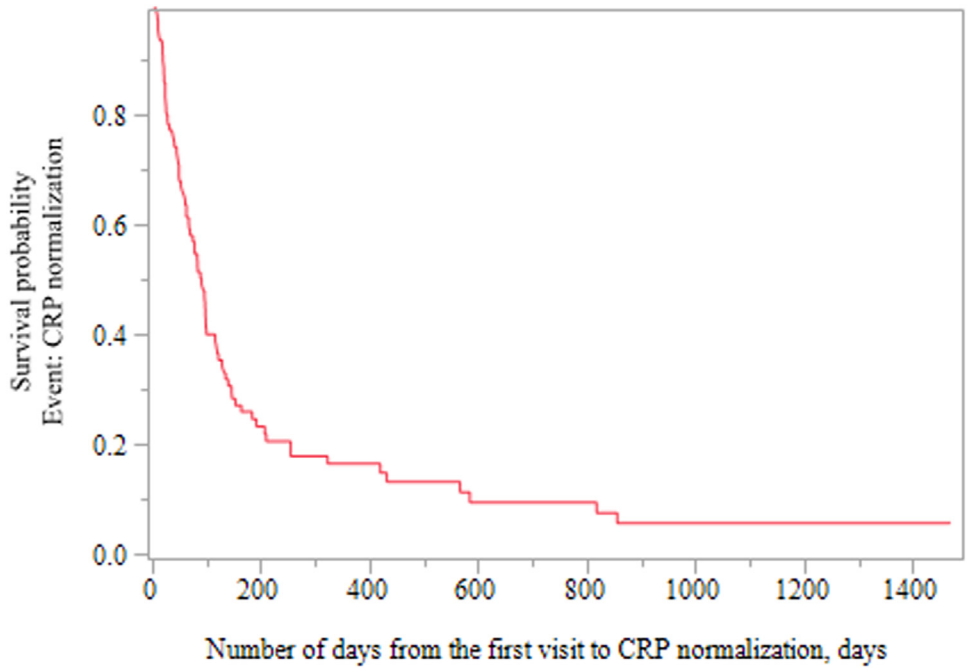

Figure 1. Kaplan-Meier survival curve demonstrating days from the first visit to CRP normalization.

Table 2
Baseline radiographic characteristics and operative data.

Characteristics	N = 108
Griffith early/destructive/sclerotic	55 (51)/52 (48)/1 (1)
MRI stage I/II/III/IV/V	1 (1)/10 (9)/67 (63)/23 (22)/5 (5)
No. of infected vertebral bodies	2.2 ± 0.8
Epidural abscess	28 (26)
Psoas abscess	22 (21)
Paraspinal abscess	7 (4)
Inpatient/Outpatient	94 (87)/14 (13)
HBO	47 (44)
Only biopsy	19 (18)
Open operation	41 (38)
Posterior decompression/Posterior fusion/Posterior decompression and fusion/Anterior fusion/Anterior and posterior fusion	4 (10)/2 (5)/10 (24)/2 (5)/23 (56)
Number of operations	0.9 ± 1.0
Culture positive/ Biopsy culture positive / Blood culture positive	50 (58)/ 16 (29)/ 38 (58)

HBO, hyperbaric oxygen therapy; MRI, magnetic resonance imaging.
Data are presented as mean ± standard deviation or n (%).

Next, we investigated independent factors associated with the time required for CRP normalization by conducting a multivariate Cox regression analysis. Based on the univariate Cox analysis findings, the dependent variable was defined as creatinine level, eGFR, blood urea nitrogen (BUN) level, hemoglobin level, platelet count, lymphocyte percentage, neutrophil percentage, CRP level, mGPS, CAR, NLR, PLR, dialysis, presence of diabetes mellitus, steroid usage, and presence of epidural abscess. Then, we used a backward elimination method to create the final multivariate model. As a result, neutrophil percentage (hazard ratio [HR] = 1.023, 95% confidence interval [CI] 1.002–1.043, p = .034), diabetes mellitus (HR= 1.703, 95% CI 1.011–2.973, p = .045), and eGFR (HR= 0.994, 95% CI 0.989–0.99994, p = .048) were identified as the independent factors associated with the time required for CRP normalization in pyogenic spondylitis (Table 5). Judging from the hazard ratios of the final model, a higher neutrophil percentage, diabetes mellitus, and a lower eGFR were significantly associated with a longer time for CRP normalization in pyogenic spondylitis.

Discussion

This study investigated the factors associated with the time required to achieve infection control in pyogenic spondylitis, using CRP normalization as an infection control marker. Univariate Cox regression analysis showed that creatinine level, eGFR, lymphocyte percentage, neutrophil percentage, CRP level, CAR, and NLR were associated with the time required for CRP normalization. Furthermore, multivariate Cox regression analysis identified neutrophil percentage, diabetes mellitus, and eGFR as the independent factors associated with the time required for CRP normalization in pyogenic spondylitis.

We found that a higher neutrophil percentage was independently associated with the time required for CRP normalization. Furthermore, in univariate Cox analysis, NLR and lymphocyte percentage were significantly associated with the time required for CRP normalization in pyogenic spondylitis. PLR also tended to be associated with the time. While previous studies showed that neutrophil, lymphocyte, NLR, and PLR were effective markers of systemic inflammation [18,19], predictors in surgical site infection [20–22], and associated with the progression and prognosis of viral hepatitis-related hepatocellular carcinoma [23], to our knowledge, this study is the first to identify neutrophil percentage, lymphocyte percentage, and NLR as factors associated with the time required for CRP normalization in pyogenic spondylitis. Neutrophils and lymphocytes are well-known to play important roles in the immune response to bacterial infections [21], and platelets also interact with bacterial pathogens by stimulating the release of neutrophil extracellular traps [24]. Based on the findings of this study, if a patient presents with an elevated neutrophil percentage at initial diagnosis of pyogenic spondylitis, it may be advisable to obtain blood and tissue cultures as soon as possible to identify the causative organism, and to initiate empiric antibiotic therapy promptly after culture collection.

We expected that identification of the causative organism by culture would lead to shorter treatment times, but no such association was found in this study. We believe that identification of the causative bac-

Table 3
Characteristics of patients who failed to achieve CRP normalization.

Age	sex	number of days from the first visit to the final blood sampling date, day	CRP at the final blood sampling, mg/dL	outcome
62	female	1,469	0.65	lost to follow-up
67	male	36	0.22	hospital transfer
70	female	44	0.88	hospital transfer
73	female	330	0.28	hospital transfer
84	male	56	0.4	hospital transfer
68	male	33	4.5	hospital transfer
62	male	119	0.72	hospital transfer
85	female	155	0.64	hospital transfer
83	male	172	1.82	hospital transfer
83	female	57	0.73	hospital transfer
67	male	94	0.64	hospital transfer
77	male	23	0.72	hospital transfer
93	male	38	3.2	hospital transfer
59	male	29	2.46	hospital transfer
80	female	13	0.6	hospital transfer
75	female	58	0.64	hospital transfer
80	male	14	5.84	hospital transfer
69	female	7	2.95	hospital transfer
76	male	56	0.47	follow-up in progress without blood sampling
72	female	406	0.4	follow-up in progress
60	female	1,137	0.2	follow-up in progress
69	male	433	2.91	Exacerbation of other diseases (cancer pleurisy)
66	male	45	1.51	end of follow-up
70	male	1,155	0.55	end of follow-up
70	male	187	17.15	death by aspiration pneumonia and pyogenic spondylitis

CRP, C-reactive protein.

Table 4
Univariate Cox regression analysis of demographic and radiographic data.

Characteristics	HR	95% CI	p
Sex male/female	1.085	0.687–1.685	.72
Age, years	1.007	0.990–1.022	.43
BMI, kg/m^2	1.015	0.978–1.055	.44
disease duration, day	1.000	0.997–1.004	.96
Creatinine, mg/dL	1.143	1.003–1.354	.045*
eGFR, mL/min/1.73m^2	0.992	0.988–0.997	.002*
BUN mg/dL	1.015	0.999–1.033	.060
Albumin, g/dL	0.907	0.665–1.254	.55
Total cholesterol, mg/dL	0.999	0.991–1.007	.77
Hemoglobin, g/dL	0.942	0.862–1.030	.19
Platelet, 103/μL	0.989	0.971–1.007	.21
White blood cell, 103/μL	1.026	0.976–1.085	.33
Lymphocyte %	0.969	0.949–0.990	.005*
Neutrophil %	1.029	1.011–1.048	.002*
ESR, mm/1h	1.001	0.992–1.010	.86
CRP, mg/dL	1.026	1.004–1.051	.018*
CONUT	0.980	0.894–1.075	.67
mGPS	1.347	0.937–1.897	.11
CAR	1.073	1.014–1.147	.013*
NLR	1.026	1.004–1.057	.016*
PNI	0.986	0.959–1.014	.32
PLR	1.001	1.000–1.002	.072
Dialysis	1.964	0.814–6.453	.15
Diabetes mellitus	1.507	0.950–2.460	.082
Smoking	1.231	0.689–2.402	.50
Use of steroids	1.815	0.729–6.096	.22
Use of anticancer drug	1.525	0.631–5.010	.38
Use of antibiotics at the time of the first visit to our hospital	0.978	0.615–1.604	.93
Body temperature	1.007	0.821–1.245	.95
Griffith early/destructive and sclerotic	1.041	0.675–1.604	.85
No. of infected vertebral bodies	0.958	0.734–1.278	.77
Epidural abscess	1.613	0.985–2.758	.058
Psoas abscess	0.984	0.592–1.720	.95
Paraspinal abscess	0.700	0.327–1.820	.43
Inpatient/Outpatient	1.294	0.666–2.301	.42
No. of operations	0.998	0.809–1.247	.99
Biopsy	0.971	0.629–1.497	.89
Open surgery	1.246	0.804–1.960	.33
Anterior surgery	0.945	0.585–1.589	.82
HBO	0.918	0.596–1.428	.70
Culture positive (Biopsy and/or Blood)	1.324	0.791–2.182	.28
Biopsy culture positive	0.802	0.423–1.605	.52
Blood culture positive	1.368	0.748–2.451	.30

BMI, body mass index; BUN, blood urea nitrogen; CAR, CRP-albumin ratio; CI, confidence intervals; CONUT, controlling nutritional status; CRP, C-reactive protein; eGFR, estimate glomerular filtration rate; ESR, erythrocyte sedimentation rate; HBO, hyperbaric oxygen therapy; HR, hazard ratio; JOA, Japanese Orthopaedic Association; mGPS, modified Glasgow prognostic score; NLR, neutrophil–lymphocyte ratio; PLR, platelet–lymphocyte ratio; PNI, prognostic nutrition index, MRI, magnetic resonance imaging.
* $p<0.05$.

Table 5
Multivariate Cox regression analysis of demographic and radiographic data.

Characteristics	HR	95% CI	p
Neutrophil %	1.023	1.002–1.043	.034*
Diabetes mellitus	1.703	1.011–2.973	.045*
eGFR, mL/min/1.73m^2	0.994	0.989–0.99994	.048*

eGFR, estimate glomerular filtration rate; CI, confidence intervals; HR, hazard ratio.
* $p < .05$.

teria is important in determining treatment strategies. Interestingly, a recent meta-analysis showed that short time to positivity of blood culture was a significant predictor of mortality and septic shock in gram-positive and gram-negative–related bloodstream infections [25]. Thus, a positive culture may indicate a higher abundance of bacteria in the sample compared to a negative culture. Therefore, our research results may be interpreted to mean that even in cases of severe infection, identifying the causative bacteria through culture resulted in a treatment period similar to cases with unidentified causative bacteria due to a low bacterial count.

In this study, we found that diabetes mellitus was an independent risk factor for a longer time required for CRP normalization in pyogenic spondylitis. Previous studies showed that diabetes mellitus was associated with an increased risk of surgical site infection (SSI) following spinal surgery [26,27]. In an observational study of diabetic patients undergoing surgery, any postoperative 1-day blood glucose level above 220 mg/dL resulted in a 5.7-fold increase in the relative risk for serious postoperative infection [28]. In addition, a large primary care cohort study found that within diabetic patients, the incident rate ratio was 8.71 times higher in patients with poor glycemic control (glycated hemoglobin >11%) than in those with good glycemic control [29]. Furthermore, randomized controlled trials showed that intensive glycemic control resulted in a reduced incidence of infection [30,31]. Therefore, appropriate blood glucose management may enhance the therapeutic effect against infection in patients with pyogenic spondylitis complicated by diabetes.

We also found that a lower eGFR was independently associated with the time required for CRP normalization. Furthermore, in univariate Cox

analysis, the serum creatinine level was significantly associated with the time required for CRP normalization in pyogenic spondylitis. Previous studies showed that the eGFR and creatinine levels were predictors for SSI [32,33]. Our results indicate that pyogenic spondylitis takes a longer time to control when renal function is impaired. Patients with impaired renal function should have their antibiotic doses adjusted; however, our findings suggest that the effectiveness of antibiotics may be reduced in such cases when compared to patients with adequate renal function. The findings of this study suggest that the traditional approach to antibiotic selection may not be appropriate for patients with pyogenic spondylitis and impaired renal function. Instead of the standard first-line choice, such as cefazolin, it may be prudent to consider using an antibiotic that is not metabolized by the kidneys and does not require dosage adjustment due to decreased renal function, such as linezolid. However, further investigation is required to determine the efficacy of this treatment approach and the selection of the appropriate first-line antibiotic in such cases.

This study has several limitations. First, the data were obtained from a single institution and relied on information recorded in the medical records. Second, the study included a mix of patients who underwent surgery and those who were treated conservatively in an outpatient setting. However, pyogenic spondylitis is a complex and intractable condition, and excluding mild cases by limiting the study to surgical cases would not be appropriate. Therefore, we analyzed both types of cases together. Finally, although the CRP level is commonly used as an indicator of infection, the use of normalized CRP as an indicator of infection control may be a study limitation. This is because the resolution of infection should be based not only on laboratory data, but also on clinical symptoms. However, none of the patients in this study experienced a relapse after their CRP decreased to less than 0.14, and none resumed treatments (such as with antibiotics). In addition, the 2015 Infectious Diseases Society of America Clinical Practice Guidelines recommend using CRP levels to assess the response to treatment in pyogenic spondylitis [34]. Nevertheless, prospective studies are needed to overcome these limitations and validate our findings.

Conclusions

In conclusion, the present study demonstrated that a higher neutrophil percentage, diabetes mellitus, and a lower eGFR were significantly associated with a longer time required for CRP normalization in pyogenic spondylitis. Therefore, clinicians should be cautious when treating patients with these factors, as more time may be required to control their infections.

IRB approval

The study was approved by the Medical Research Ethics Committee of the Tokyo Medical and Dental University (Approval number: M2022-335) and conducted in accordance with the Declaration of Helsinki. Informed consent was waived, owing to the retrospective, anonymized nature of the study.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

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References

[1] Cheung WY, Luk KD. Pyogenic spondylitis. Int Orthop 2012;36(2):397–404.
[2] Hopkinson N, Stevenson J, Benjamin S. A case ascertainment study of septic discitis: clinical, microbiological and radiological features. QJM 2001;94(9):465–70.
[3] Kim YS, Kim JG, Yi J, et al. Changes in the medical burden of pyogenic and tuberculous spondylitis between 2007 and 2016: a nationwide cohort study. J Clin Neurosci 2020;73:89–93.
[4] Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis 2004;39(2):206–17.
[5] von Dach E, Albrich WC, Brunel AS, et al. Effect of C-reactive protein-guided antibiotic treatment duration, 7-day treatment, or 14-day treatment on 30-day clinical failure rate in patients with uncomplicated gram-negative bacteremia: a randomized clinical trial. JAMA 2020;323(21):2160–9.
[6] Grados F, Lescure FX, Senneville E, Flipo RM, Schmit JL, Fardellone P. Suggestions for managing pyogenic (non-tuberculous) discitis in adults. Joint Bone Spine 2007;74(2):133–9.
[7] Fukuda K, Miyamoto H, Uno K, Okada Y. Indications and limitations of conservative treatment for pyogenic spondylitis. J Spinal Disord Tech 2014;27(6):316–20.
[8] Kugimiya F, Muraki S, Nagakura D, Umekoji H, Oda H, Takahashi K. Predictors of conservative treatment for pyogenic spondylitis. Spine Surg Relat Res 2017;1(3):135–9.
[9] Yoon SH, Chung SK, Kim KJ, Kim HJ, Jin YJ, Kim HB. Pyogenic vertebral osteomyelitis: identification of microorganism and laboratory markers used to predict clinical outcome. Eur Spine J 2010;19(4):575–82.
[10] Lee YM, Cho OH, Park SY, et al. Factors associated with sequelae after treatment of hematogenous pyogenic vertebral osteomyelitis. Diagn Microbiol Infect Dis 2019;94(1):66–72.
[11] Dai G, Li S, Yin C, et al. Culture-negative versus culture-positive in pyogenic spondylitis and analysis of risk factors for relapse. Br J Neurosurg 2021;8:1–5.
[12] de Graeff JJ, Paulino Pereira NR, van Wulfften Palthe OD, Nelson SB, Schwab JH. Prognostic factors for failure of antibiotic treatment in patients with osteomyelitis of the spine. Spine (Phila Pa 1976) 2017;42(17):1339–46.
[13] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control 1999;27(2):97–132 quiz 3-4; discussion 96.
[14] Griffiths HE, Jones DM. Pyogenic infection of the spine. A review of twenty-eight cases. J Bone Joint Surg Br 1971;53(3):383–91.
[15] Uchida K, Nakajima H, Yayama T, et al. Epidural abscess associated with pyogenic spondylodiscitis of the lumbar spine; evaluation of a new MRI staging classification and imaging findings as indicators of surgical management: a retrospective study of 37 patients. Arch Orthop Trauma Surg 2010;130(1):111–18.
[16] van Heijl M, Sprangers MA, de Boer AG, et al. Preoperative and early postoperative quality of life predict survival in potentially curable patients with esophageal cancer. Ann Surg Oncol 2010;17(1):23–30.
[17] Wierichs RJ, Kramer EJ, Reiss B, et al. A prospective, multi-center, practice-based cohort study on all-ceramic crowns. Dent Mater 2021;37(8):1273–82.
[18] Yao C, Liu X, Tang Z. Prognostic role of neutrophil-lymphocyte ratio and platelet–lymphocyte ratio for hospital mortality in patients with AECOPD. Int J Chron Obstruct Pulmon Dis 2017;12:2285–90.
[19] Demirdal T, Sen P. The significance of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and lymphocyte-monocyte ratio in predicting peripheral arterial disease, peripheral neuropathy, osteomyelitis and amputation in diabetic foot infection. Diabetes Res Clin Pract 2018;144:118–25.
[20] Zhuo Y, Cai Chen J, Zhang Q, Li X. Pre-surgical peripheral blood inflammation markers predict surgical site infection following mesh repair of groin hernia. Medicine (Baltimore) 2021;100(9):e25007.
[21] Inose H, Kobayashi Y, Yuasa M, Hirai T, Yoshii T, Okawa A. Procalcitonin and neutrophil lymphocyte ratio after spinal instrumentation surgery. Spine (Phila Pa 1976) 2019;44(23):E1356–E1e61.
[22] Inose H, Kobayashi Y, Yuasa M, Hirai T, Yoshii T, Okawa A. Postoperative lymphocyte percentage and neutrophil-lymphocyte ratio are useful markers for the early prediction of surgical site infection in spinal decompression surgery. J Orthop Surg (Hong Kong) 2020;28(2):2309499020918402.
[23] Meng X, Wei G, Chang Q, et al. The platelet-to-lymphocyte ratio, superior to the neutrophil-to-lymphocyte ratio, correlates with hepatitis C virus infection. Int J Infect Dis 2016;45:72–7.
[24] Yeaman MR. Platelets in defense against bacterial pathogens. Cell Mol Life Sci 2010;67(4):525–44.
[25] Hsieh YC, Chen HL, Lin SY, Chen TC, Lu PL. Short time to positivity of blood culture predicts mortality and septic shock in bacteremic patients: a systematic review and meta-analysis. BMC Infect Dis 2022;22(1):142.
[26] Xing D, Ma JX, Ma XL, et al. A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery. Eur Spine J 2013;22(3):605–15.
[27] Guzman JZ, Iatridis JC, Skovrlj B, et al. Outcomes and complications of diabetes mellitus on patients undergoing degenerative lumbar spine surgery. Spine (Phila Pa 1976) 2014;39(19):1596–604.
[28] Pomposelli JJ, Baxter JK 3rd, Babineau TJ, et al. Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. JPEN J Parenter Enteral Nutr 1998;22(2):77–81.
[29] Critchley JA, Carey IM, Harris T, DeWilde S, Hosking FJ, Cook DG. Glycemic control and risk of infections among people with type 1 or type 2 diabetes in a large primary care cohort study. Diabetes Care 2018;41(10):2127–35.

[30] Bilotta F, Spinelli A, Giovannini F, Doronzio A, Delfini R, Rosa G. The effect of intensive insulin therapy on infection rate, vasospasm, neurologic outcome, and mortality in neurointensive care unit after intracranial aneurysm clipping in patients with acute subarachnoid hemorrhage: a randomized prospective pilot trial. J Neurosurg Anesthesiol 2007;19(3):156–60.
[31] Wallia A, Schmidt K, Oakes DJ, et al. Glycemic control reduces infections in post-liver transplant patients: results of a prospective, randomized study. J Clin Endocrinol Metab 2017;102(2):451–9.
[32] Mujagic E, Marti WR, Coslovsky M, et al. The role of preoperative blood parameters to predict the risk of surgical site infection. Am J Surg 2018;215(4):651–7.
[33] Ishigami J, Trevisan M, Xu H, Coresh J, Matsushita K, Carrero JJ. Estimated GFR and hospital-acquired infections following major surgery. Am J Kidney Dis 2019;73(1):11–20.
[34] Berbari EF, Kanj SS, Kowalski TJ, et al. 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. Clin Infect Dis 2015;61(6):e26–46.