International Orthopaedics (2020) 44:2211–2219
https://doi.org/10.1007/s00264-020-04567-0

ORIGINAL PAPER

Usefulness of inflammatory markers and clinical manifestation for an earlier method to diagnosis surgical site infection after spinal surgery

Shuai Zheng[1] · Zheng Wang[2] · Shuai Qin[3] · Jian-Ting Chen[1]

Received: 27 September 2019 / Accepted: 2 April 2020 / Published online: 21 May 2020

Abstract

Purpose To put forward a method for earlier diagnosis of surgical site infection (SSI) after spinal surgery and identify the best cut-offs of the selective signs.

Methods Ninety cases were prospectively collected in consecutive patients who underwent spinal surgery. The patients were divided into the SSI group and the normal group. White blood cell (WBC) count, lymphocyte count, serum amyloid A (SAA), procalcitonin (PCT) and C-reactive protein (CRP) were collected pre-operatively and at three andsix days post-operatively. Erythrocyte sedimentation rates (ESR) were acquired pre-operatively and at six days post-operatively. Body temperature (BT) was measured every day during hospitalisation. The conditions of the surgical sites were recorded at three and six days post-operatively. Differences of BT, the conditions of the wound and the values of the inflammatory markers between the two groups were studied. Finally, we used the receiver operating characteristic curve (ROC curve) to determine the best cut-offs of the selected signs.

Results Of the 90 patients, SSI occurred in seven and five of them reached a definite diagnosis of SSI as their bacterial cultures were positive. Significant differences were found in CRP levels at three and six days post-operatively with a cut-off of > 59.4 mg/L and > 34.9 mg/L, respectively; ESR level at six days post-operatively with a cut-off of > 51.5 mm/h; PCT at three days post-operatively with a cut-off of > 0.11 ng/mL; and BT at three days post-operatively with a cut-off of > 37 °C. Also, examination of the wound is also an important sign of SSI.

Conclusion CRP, ESR and PCT are considered useful markers for earlier diagnosis of SSI. Combining the above markers with BT and the wound condition yields more accurate results.

Keywords Surgical site infection · Inflammatory marker · Clinical manifestation · Earlier diagnosis · Post-operative infection

Shuai Zheng and Zheng Wang contributed equally to this work.

✉ Jian-Ting Chen
chenjt99@tom.com

Shuai Zheng
356428130@qq.com

Zheng Wang
475171907@qq.com

Shuai Qin
qszswan841176@163.com

[1] Division of Spine Surgery, Department of Orthopadics, Nanfang Hospital, Southern Medical University, 1838 North Guangzhou Avenue, Guangzhou, People's Republic of China

[2] Department of Orthopaedic Trauma & Joint Surgery, The Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, Guangdong, People's Republic of China

[3] Department of Ophthalmology, Zhuhai Hospital Affiliated with Jinan University, Zhuhai People's Hospital,, Zhuhai, Guangdong, People's Republic of China

Introduction

The development of spinal instrumentation and its ability to provide strong fixation has brought great advantages to spinal surgery, such as stabilising the spine, reducing the rate of post-operative pseudarthrosis and correcting spinal deformity. However, it is also associated with a higher risk of complications. Surgical site infection (SSI) is one of the most common complications that surgeons have to contend with. If a small number of bacteria adhere to the instrumentation, forming a glycoprotein biofilm on its surface, SSI may occur. In general, the glycoprotein biofilm is resistant to antibiotics and protects the bacteria from the body's immune system and the bactericidal effects of antibiotics [1]. According to previous studies, the incidence of SSI ranges from 0.3 to 11.1% after instrumented spinal fusion [2–7]. As one of the most serious complications, SSI results in worse clinical outcomes, including pseudarthrosis, sepsis and even death [8]. Also, patients may

have to accept prolonged hospitalisation and recovery time, more surgical site pain, increasing cost of management and even re-operation. Therefore, early detection and diagnosis of SSI is necessary for acquiring a better outcome.

Pathogens are the gold standard of diagnosing SSI, but sometimes, it is difficult to obtain positive results. Therefore, several studies have focused on the post-operative kinetics of inflammatory markers and various methods have been described to identify the onset of early infection according to their research [9–17]. However, there are still some limitations in their studies, as the majority of them only paid attention to C-creative protein (CRP), erythrocyte sedimentation rate (ESR), lymphocytes and white blood cell (WBC), but procalcitonin (PCT) and serum amyloid A (SAA), which were also significant inflammatory markers in spinal surgery, were seldom used [18, 19]. Also, clinical symptoms and the conditions of the wound were meaningful signs, which were often neglected in previous studies. What is more, the diagnosis of SSI in previous studies was also delayed until seven days or even later post-operatively [10, 12, 15]. Therefore, the aim of the present study was to put forward an earlier method for diagnose of SSI which depends on the selected useful inflammatory biomarkers in combination with other clinical symptoms and identify the best cut-offs of the selective signs. By combining meaningful inflammatory markers on days three and six after spinal surgery and the patients' clinical symptoms together, SSI could be diagnosed earlier.

Materials and methods

Patients

Ninety patients who underwent spinal surgery using internal fixation were prospectively collected from January 2016 to November 2017. The exclusion criteria were history of previous surgery, autoimmune disease, malignancy, recent infectious disease, acquired or inherited immunodeficiency and liver disease. Diagnosis of SSI was made according to the criteria of the Centers for Disease Control and Prevention [20], and at least one of the following was present:

1. Purulent drainage from the deep incision, but not from the organ/space component of the surgical site.
2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (> 38 °C), localised pain or tenderness, unless site is culture-negative.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

The follow-up in our study lasted for three months after surgery. In the meantime, we determined patients with SSI when they conformed to the above points. Informed consent was obtained from all individual participants included in the study, and approval was obtained from the Institutional Review Board of the Southern Medical University, China.

Assessment

Body temperature (BT) was measured and recorded every day during hospitalisation. WBC count, lymphocyte count, CRP, PCT and SAA were collected preoperatively and on days three and six after surgery. ESRs were detected preoperatively and on day six after surgery. The reference value of each marker was as follows in our hospital: CRP < 5 mg/L, ESR < 20 mm/1 h, PCT < 0.05 ng/L, SAA < 10 mg/L, $3.5 \times 10^9 \leq$ WBC count $\leq 9.5 \times 10^9$ and $1.10 \times 10^9 \leq$ lymphocyte count $\leq 3.20 \times 10^9$.

Antibiotic treatment

All of the patients received 1 g cefazolin intravenously within 15 minutes of skin incision. If the operation lasted for more than three hours, another 1 g was administered. After surgery, an additional 1 g cefazolin was given but limited to the first day post-operatively. If there existed an allergic reaction, clindamycin was considered as a secondary choice.

Culture of pathogenic bacteria

In the patients of SSI group, wound swabs were used to detect the wound drainage after spinal surgery. During debridement, both wound swabs and wound tissues were used for culture of pathogenic bacteria. Blood microbiological culture was required when body temperature was over 38.5 °C.

Statistical analysis

Student's *t* test was used to compare means of quantitative data between the SSI group and the normal group. Chi-squared test was used to compare the differences of qualitative data between the two groups. As the biologic markers may be influenced by surgical conditions, including the volume of blood loss during surgery, the operative time and range of surgical levels, partial correlation coefficient was performed to demonstrate their relationship. Finally, we used the receiver operating characteristic (ROC) curve to determine the best cut-offs of the effective inflammatory markers and BT in diagnosing SSI. All the statistical analyses were performed with SPSS 19.0. *P* value < 0.05 was considered to be statistically significant.

Results

Characteristics of the patients

Overall, 90 patients (48 male, 42 female) who met the inclusion criteria were included in the study. The mean age of the enrolled patients was 53.4 (± 12.4) years. The range of surgical levels was 1.9 (± 1.3). The mean volume of blood loss was 221.7 (± 151.8) mL, and the mean operative time lasted for 3.4 (± 1.2) hours (Table 1).

Of the 90 patients, SSI occurred in seven and five of them reached a definite diagnosis of SSI as their bacterial cultures were positive. We conducted debridement in four, two of whom had to have their instrumentation removed. The remaining patients were treated with antibiotics. However, in the other two patients in SSI group, they were diagnosed as SSI by two senior spinal surgeons according to the abnormally increased value of biomarkers in combination with clinical symptoms, including redness, swelling or abnormal drainage of the wound and abnormal body temperature that resulted in long-term intravenous antibiotic therapy or debridement though their bacterial cultures were negative (Table 2). All of the seven patients recovered with their inflammatory marker values returned to normal after therapy.

Comparison between the SSI group and the normal group

On comparing the demographic data between the two groups, no significant differences of the factors including sex, age, operative time, blood loss and comorbidities were found (Table 3).

The differences of inflammatory biomarkers, BT and examination of the wound are listed in Table 4. Significant differences were found in CRP levels at three and six days post-operatively (94.5 ± 45.2 mg/L for SSI group and 54.3 ± 42.6 mg/L for normal group on day three post-operatively, $P = 0.001$; 64.5 ± 32.9 mg/L for SSI group and 39.6 ± 34.0 mg/L for normal group at six days post-operatively, $P = 0.008$) and in PCT three days post-operatively (0.19 ± 0.13 ng/mL for SSI group and 0.12 ± 0.96 ng/mL for normal group, $P = 0.027$). Significant differences were also found in ESR at six days post-operatively (67.4 ± 27.5 mm/h for SSI group and 42.7 ± 30.7 mm/h for normal group, $P = 0.002$). In addition, significant differences were shown in BT three days and six days post-operatively (37.1 ± 0.7 °C for SSI group and 36.7 ± 0.4 °C for normal group on day three post-operatively, $P = 0.002$; 37.2 ± 0.8 °C for SSI group and 36.7 ± 0.7 °C for normal group on day six post-operatively, $P = 0.022$). We also used the correlation test to determine whether the values of these significant biomarkers were affected by the surgical condition, but no significant differences were found (Table 5). Redness, swelling or abnormal drainage appeared in seven patients in the SSI group and 2 in the normal group ($P < 0.001$). However, no significant differences were found in white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count and lymphocyte percentage. The change of these biomarkers and BT with significant differences is also shown in the figures (Fig. 1).

Table 1 Demographic and surgical data

Age, years (mean)	53.4 (± 12.4)
Sex	
Male	48 (53.3%)
Female	42 (46.7%)
Region	
Cervical	17 (18.9%)
Thoracic	5 (5.6%)
Thoracolumbar	5 (5.6%)
Lumbar	63 (70%)
Blood loss volume, ML (mean)	221.7 (± 151.8)
Operative time, hour (mean)	3.4 (± 1.2)

Standard deviation (±)

The best cut-offs of the selective signs

Finally, we used the ROC curve to identify the cut-offs for the above four biomarkers (Fig. 2). The cut-offs were as follows: > 59.4 mg/L for CRP at three days post-operatively (sensitivity 87.5%, specificity 62.5%, area under the curve [AUC] 0.76), 34.9 mg/L for CRP at six days post-operatively (sensitivity 94.1%, specificity 52.3%, AUC 0.73), 0.11 ng/mL for PCT at three days post-operatively (sensitivity 78.6%, specificity 61.1%, AUC 0.70), 51.5 mm/h for ESR at six days post-operatively (sensitivity 80.0%, specificity 68.5%, AUC 0.73), 37.0 °C for BT at three days post-operatively (sensitivity 58.8%, specificity 76.7%, AUC 0.71) and 37.2 °C for BT at six days post-operatively (sensitivity 52.9%, specificity 71.2%, AUC 0.59).

Discussion

Delayed diagnosis of SSI leads to prolonged hospitalisation and recovery time, increased surgical site pain, increased cost of management and even re-operation. Ishii et al. [21] reported that early diagnosis of SSI could reduce the chance of removing the implantation. Also, Tsubouchi et al. [22] found that early treatment of SSI improves implant survival after surgery. Therefore, earlier diagnosis of SSI is essential for patients to acquire a better clinical outcome.

CRP, the acute-phase protein produced by the liver in response to inflammatory and tissue damage, has been widely reported and used to diagnose SSI after spinal surgery due to

Table 2 Patient data in SSI group

Patient no.	Age (years)	Diagnosis	Approach	Region	Procedure	Segment	Method of diagnosis	Culture	Timing of diagnosis (days)	Treatment
1	58	Degenerative	Posterior	Lumbar	Laminectomy, discectomy, fusion, instrumentation	1	Debridement	MRSA	10	Debridement, implant removal
2	78	Degenerative	Anterior	Cervical	Discectomy, fusion, instrumentation	2	Wound drainage	MSSA	12	Antibiotic medication
3	63	Deformity	Posterior	Lumbar	Laminectomy, discectomy, fusion, instrumentation	1	Debridement	Unknown	7	Debridement
4	34	Degenerative	Posterior	Lumbar	Laminectomy, discectomy, fusion, instrumentation	1	Debridement	MRSA	20	Debridement, implant removal
5	54	Degenerative	Posterior	Lumbar	Laminectomy, discectomy, fusion, instrumentation	2	Blood culture	Unknown	15	Antibiotic medication
6	51	Deformity	Posterior	Thoracolumbar, lumbar	Osteotomy, deformity correction, instrumentation	4	Wound drainage	*Staphylococcus haemolyticus*	9	Antibiotic medication
7	67	Degenerative	Posterior	Lumbar	Laminectomy, discectomy, fusion, instrumentation	2	Debridement	MRSA	24	Debridement

MRSA methicillin-resistant *Staphylococcus aureus*, *MSSA* methicillin-susceptible *Staphylococcus aureus*

its rapid response time and high sensitivity [11, 16, 17]. Usually, the values of CRP peak on day three, post-operatively, rapidly decrease from days three to five after surgery and return to normal values for 14 to 21 days after surgery [11, 13, 14, 16, 17]. Takahashi J et al. [9] reported that renewed elevation of CRP at seven days after spinal surgery could be a significant signal for SSI. Mok et al. [16] reported that a second increase or failure to decrease of CRP after it reached its peak value may indicate the occurrence of SSI. Another study of Kang et al. [11] also concluded that an abnormal value of CRP on days five or seven post-operatively is useful for diagnosing SSI. However, in our study, the results were similar to previous articles. The value of CRP rapidly decreased from three to six days post-operatively in both groups. More importantly, significant differences were found between two groups on these two days. These results express that CRP is a useful and sensitive biomarker to differentiate SSI from normal surgical tissue damage at the early period after spinal surgery.

Another meaningful biomarker in our study is ESR because of its significantly higher values for the SSI group in comparison with the normal group. ESR is also an acute-phase biomarker that reflects an increased concentration of fibrinogen in the plasma due to inflammation [19, 24]. After spinal surgery, ESR usually peaks at five days post-operatively [11, 17]. However, it may take up to six weeks for the value of ESR to return to baseline [23]. Although several studies have demonstrated that ESR is not as sensitive as CRP [11, 16, 17, 25], the results in our study show that ESR is also a useful tool to identify SSI at six days post-operatively and its values do not correlate with surgical condition. However, ESR may not be a sensitive biomarker to reflect the recovery of SSI due to its slower decrease to baseline after spinal surgery. However, when SSI occurs in patients without previous infection or surgery, ESR is still an effective biomarker to screen them out.

PCT is another helpful marker in the detection of SSI in our study. PCT is the calcitonin precursor that reflects inflammation, and it is widely used in clinical medicine [26, 27]. Nevertheless, few studies have reported the function of PCT in the field of the spine. Nie et al. [19] demonstrated that PCT is a reliable biomarker in predicting early post-operative infectious complications, which was even more effective than CRP. The optimal cut-off value of 0.5 ng/mL had a sensitivity of 88% to identify SSI. In our study, the value of PCT at three days post-operatively showed significant differences between the SSI and normal group, but this condition did not occur at five days post-operatively. These results show that PCT is a meaningful detective biomarker in the diagnosis of SSI in the early post-operative period.

However, biomarkers may be influenced by not only the occurrence of inflammation but also the surgical conditions, including the volume of blood loss during surgery, the operative time and range of surgical levels [10, 16]. Therefore, we used the correlation test to determine whether the values of

Table 3 Difference of patient and surgical data between SSI and normal groups

	SSI group ($n = 7$)	Normal group ($n = 83$)	P
Age, years (mean)	51.1 (± 14.5)	53.9 (± 11.2)	0.402
Sex	Male 3, female 4	Male 45, female 38	0.565
Operative time, hour (mean)	3.8 (± 1.2)	3.3 (± 1.2)	0.136
Blood loss volume, ML (mean)	232.4 (± 159.0)	219.2 (± 151.1)	0.749
Number of surgical levels (mean)	1.7 (± 0.6)	1.9 (± 1.4)	0.567
Comorbidity			
Diabetes mellitus	4	10	0.13
Osteoporosis	5	8	0.13
Hypertension	4	17	1.000

SSI indicates surgical site infection

Statistically significant ($P < 0.05$)

these significant biomarkers were affected by the surgical condition, but no significant differences were found. These biomarkers are appropriate indicators to predict the diagnosis of SSI. Nonetheless, these biomarkers are not specific for predicting the infection of surgical site. For this reason, the diagnosis of SSI should be combined with the clinical symptoms of the patients. The results in our study showed that BT and examination of the surgical site were also important for diagnosing SSI. Some previous studies emphasised the importance of these two clinical indicators. Takahashi et al. [9] reported that renewed elevation of body temperature after post-operative days four to seven may be a critical sign of post-operative infection. However, the conclusion was based on only three patients with post-operative infection, which lacked sufficient strength. The average body temperature of patients in the SSI group in our study exceeded 37 °C, meaning that low fever was also a critical sign of SSI in the early period. The condition of surgical site was another meaningful indicator of SSI. Once redness, swelling of the wound or abnormal wound drainage from it is detected, close attention should be paid to determine whether SSI has occurred. In this way, we can prevent the occurrence of SSI before the formation of purulent drainage in the wound, which will decrease the probability of removing the implants.

Finally, we used the ROC curve to identify the cut-offs for the above four biomarkers. All the AUC of these biomarkers, except BT, at six days post-operatively exceeded 0.7, which indicated that the cut-offs were valuable for diagnosing SSI. However, the sensitivity and specificity of CRP in our study are lower than those of previous studies [10]. Iwata et al. [10] reported that the sensitivity and specificity of CRP were 90.0% and 89.2%, respectively. We believe that the different

Table 4 Difference of biomarkers between SSI and normal groups

	Pre-operatively	3 days - postoperatively	6 days - postoperatively
C-reactive protein	0.327	0.001 *	0.008*
White blood cell count	0.148	0.211	0.995
Neutrophil count	0.370	0.359	0.938
Neutrophil percentage	0.915	0.626	0.333
Lymphocyte count	0.089	0.962	0.671
Lymphocyte percentage	0.442	0.335	0.409
PCT	N	0.027*	0.383
ESR	0.867	N	0.006*
SAA	N	0.176	0.389
Body temperature	N	0.002*	0.022*
Examination of the wound (redness, swelling or abnormal drainage)	N	< 0.001*	< 0.001*

N indicates that the biomarker was not detected on the day

SSI indicates surgical site infection

*Statistically significant ($P < 0.05$)

Table 5 Statistical results of the correlation test in the normal group

	Blood loss	Operative time	Surgical levels
C-reactive protein at 3 days post-operatively	0.300	0.351	0.108
C-reactive protein at 6 days post-operatively	0.200	0.331	0.057
PCT at 3 days post-operatively	0.650	0.418	0.565
ESR at 6 days post-operatively	0.354	0.862	0.410
BT at 3 days post-operatively	0.808	0.315	0.502
BT at 6 days post-operatively	0.665	0.217	0.847

*Statistically significant ($P < 0.05$)

time to detect the value of CRP may be one of the reasons. Iwata et al. detected the value of CRP at seven days post-operatively, which was later than that of our study. As the CRP peaks at three days post-operatively and then begins to decrease to baseline, its value in the normal group at seven days post-operatively will be lower than that measured three and six days post-operatively. Because of this, the differences of value of CRP are larger between the SSI group and the normal group in Iwata's study. Consequently, it improved the sensitivity and specificity for CRP in his research. Otherwise, it should also be noted that the sensitivity and specificity of PCT in our study were lower than that in the study of Nie et al. [19]. These differences may be attributed to the following causes: firstly, the inclusion criteria of patients in his study were patients with acute traumatic spinal cord injury. As is known, PCT is also an acute-phase biomarker in response to proinflammatory stimulus. Acute trauma of the spinal cord may increase the inflammatory cytokines in tissue and blood, which affects the concentration of PCT. Secondly, the post-operative infections in his study included urinary tract infection, deep wound infection and pneumonia, while we only investigated SSI in our study. Therefore, different infectious complications might also influence the concentration of PCT. For this reason, the differences of PCT at three days post-operatively between the SSI group and the normal group might be smaller. This would decrease the sensitivity and specificity of PCT in our study.

Although the WBC count and differential had been thought to be useful in several studies [9, 10], its effect to diagnose SSI remains controversial. Hadjipavlou et al. [28] reported that WBC was elevated in less than 50% of SSI cases, which was found to be an unreliable diagnostic biomarker. In our study, no differences of WBC were found between the SSI group and the normal group. In our opinion, WBC is not a stable and reliable biomarker in diagnosing SSI after spinal surgery. In addition, SAA was meaningless in our study and

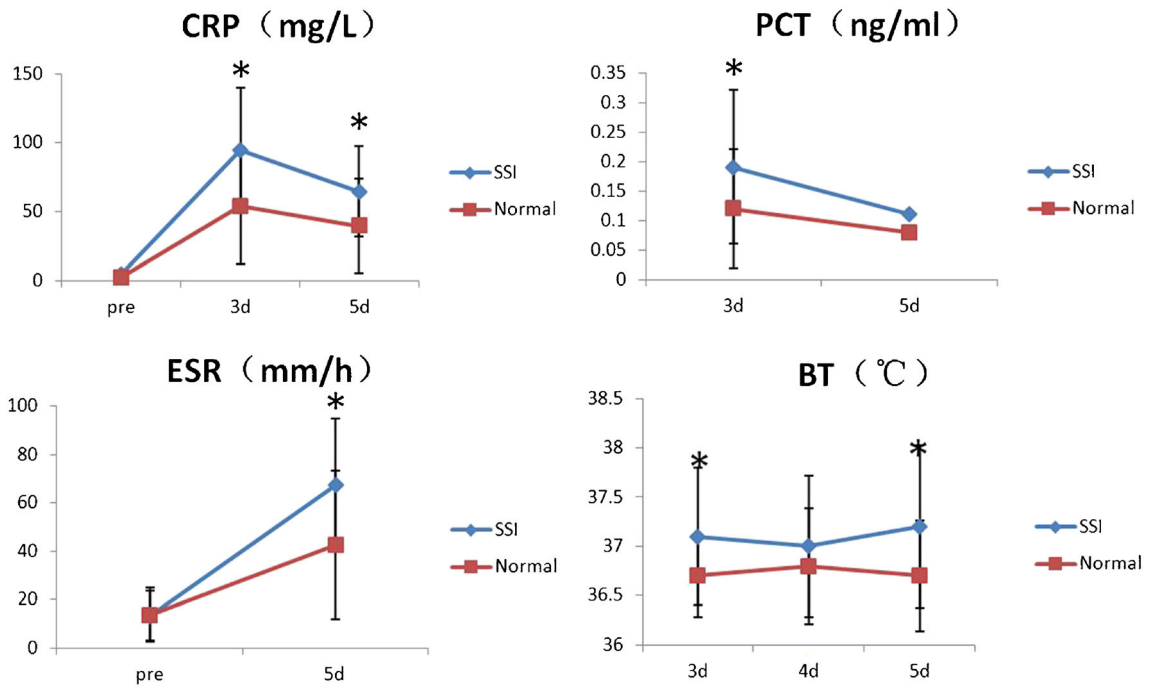

Fig. 1 Changes and differences of CRP, PCT, ESR and BT between the SSI group and the normal group. *Significant difference ($P < 0.05$)

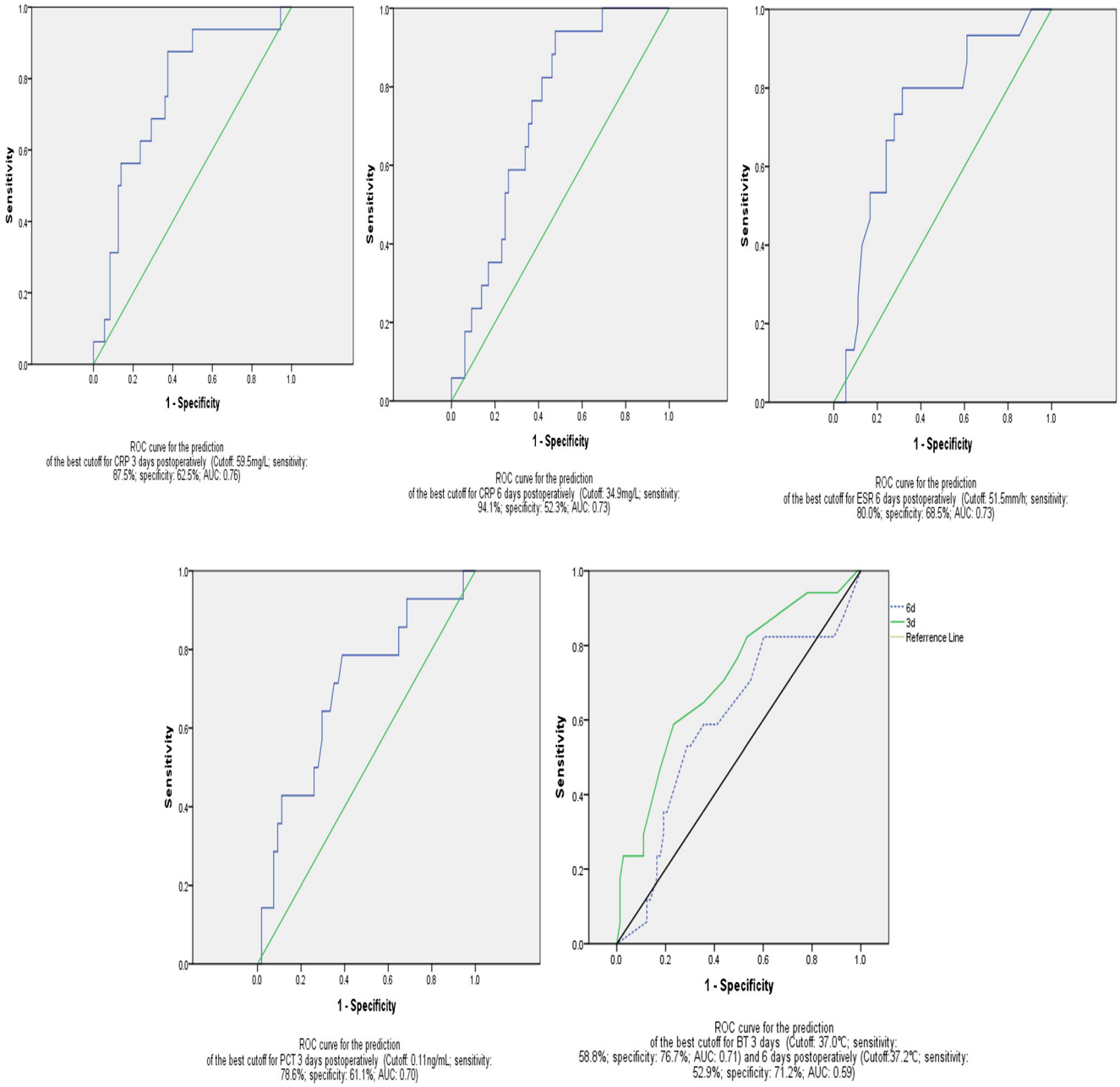

Fig. 2 ROC curve of CRP, PCT, ESR and BT

was also seldom used in previous studies. SAA is present as the precursor of AA amyloid fibrils in response to inflammation [29]. Although Deguchi et al. [18] reported that SAA was a better post-operative inflammatory marker than CRP, its function to diagnose SSI after spinal surgery remains unclear. Our study did not find SAA to be as useful as the other meaningful biomarkers, and routine detection of SAA after spinal surgery is unnecessary. On the other hand, reducing such dispensable examination can alleviate the patients' economic burden.

In our study, the incidence of SSI was 7.7% while five of which (5.5%) were proven to be exactly infected. According to previous studies, the incidence of SSI ranges from 0.3 to 11.1% after spinal surgery [2–7]. Nevertheless, majority of them were less than 5% except those who mainly focused on spinal deformity. In our opinion, the little higher rate of SSI in our study could be attributed to several points: (1) The inclusive criterion was patients who underwent spinal surgery using internal fixation in our study. We excluded others cases with merely decompression or removal of instrumentation. In addition, the sample of our study contained those who underwent spinal deformity correction. As we know, the rates of SSI among different spinal surgeries are not consistent. Low invasive interventions, such as discectomy, have a lower

rate of SSI while more invasive techniques, such as fusion with instrumentation are more liable to SSI. Besides, the SSI rates of deformity correction procedures are higher than procedures of degenerative aetiology [3, 23]; (2) occurrence of SSI is also relevant to patients' own factors including subcutaneous fat thickness, higher preoperative ASA score, lower pre-operative serum albumin and so on; (3) the small sample in our study may also influence the rate of patients with SSI. Furthermore, in our study, 2 patients in the SSI group were diagnosed as SSI while their bacterial cultures were negative. This also may increase the infectious rate in our patients.

Some limitations exist in our study. Like other studies [18, 30], partial patients lacked aetiological evidence, which may affect the inclusion of patients in the SSI group. A larger sample is needed in the follow-up studies.

Conclusions

The effect of each inflammatory biomarker is defective as different studies concluded different results, and none of these biomarkers could predict the occurrence of SSI with 100% accuracy. The patients' clinical symptoms, including body temperature and the condition of the wound, should not be ignored. Therefore, the earlier diagnosis of SSI after spinal surgery should depend on the combination of meaningful inflammatory markers and the patients' clinical symptoms, but not these factors individually.

Funding information This work was funded by the National Natural Science Foundation of China (No. 81601944), Guangdong Natural Science Foundation (No. 2015A030310481) and Guangdong Science and Technology Program key projects (No. 2016A020215100).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Approval was obtained from the Institutional Review Board of the Southern Medical University of China.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Dougherty SH, Simmons RL (1982) Infections in bionic man: the pathobiology of infections in prosthetic devices-part II. Curr Probl Surg 19(6):265–319
2. Liu J.M., Deng H.L., (2017) Risk factors for surgical site infection after posterior lumbar spinal surgery. Spine (Phila Pa 1976),
3. Kabirian N, Akbarnia BA (2014) Deep surgical site infection following 2344 growing-rod procedures for early-onset scoliosis: risk factors and clinical consequences. J Bone Joint Surg Am 96(15): e128
4. Pull TGA, Mohamed AS (2010) The presentation, incidence, etiology, and treatment of surgical site infections after spinal surgery. Spine (Phila Pa 1976) 35(13):1323–1328
5. Collins I, Wilson-MacDonald J (2008) The diagnosis and management of infection following instrumented spinal fusion. Eur Spine J 17(3):445–450
6. Okuda S, Miyauchi A (2006) Surgical complications of posterior lumbar interbody fusion with total facetectomy in 251 patients. J Neurosurg Spine 4(4):304–309
7. Moe JH (1967) Complications of scoliosis treatment. Clin Orthop Relat Res 53:21–30
8. Radcliff KE, Neusner AD (2015) What is new in the diagnosis and prevention of spine surgical site infections. Spine J 15(2):336–347
9. Takahashi J, Ebara S (2001) Early-phase enhanced inflammatory reaction after spinal instrumentation surgery. Spine (Phila Pa 1976) 26(15):1698–1704
10. Iwata E, Shigematsu H (2016) Lymphocyte count at 4 days postoperatively and CRP level at 7 days postoperatively. SPINE 41(14): 1173–1178
11. Kang BU, Lee SH (2010) Surgical site infection in spinal surgery: detection and management based on serial C-reactive protein measurements. J Neurosurg Spine 13(2):158–164
12. Lee J, Lee JH (2012) Normal range of the inflammation related laboratory findings and predictors of the postoperative infection in spinal posterior fusion surgery. Clinics in Orthopedic Surgery 4(4): 269
13. Kraft CN, Krüger T (2011) CRP and leukocyte-count after lumbar spine surgery: fusion vs. nucleotomy. Acta Orthop 82(4):489–493
14. Aono H, Ohwada T (2007) The post-operative changes in the level of inflammatory markers after posterior lumbar interbody fusion. J Bone Joint Surg Br 89(11):1478–1481
15. Takahashi J, Shono Y (2006) Usefulness of white blood cell differential for early diagnosis of surgical wound infection following spinal instrumentation surgery. Spine (Phila Pa 1976) 31(9):1020–1025
16. Mok JM, Pekmezci M (2008) Use of C-reactive protein after spinal surgery: comparison with erythrocyte sedimentation rate as predictor of early postoperative infectious complications. Spine (Phila Pa 1976) 33(4):415–421
17. Thelander U, Larsson S (1992) Quantitation of C-reactive protein levels and erythrocyte sedimentation rate after spinal surgery. Spine (Phila Pa 1976) 17(4):400–404
18. Deguchi M, Shinjo R (2010) The usefulness of serum amyloid a as a postoperative inflammatory marker after posterior lumbar interbody fusion. J Bone Joint Surg Br 92(4):555–559
19. Nie H, Jiang D (2011) Procalcitonin as an early predictor of postoperative infectious complications in patients with acute traumatic spinal cord injury. Spinal Cord 49(6):715–720
20. Mangram AJ, Horan TC (1999) 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 27(2):97–132 133-134, 96
21. Ishii M, Iwasaki M (2013) Postoperative deep surgical-site infection after instrumented spinal surgery: a multicenter study. Global Spine J 3(2):95–102
22. Tsubouchi N, Fujibayashi S (2017) Risk factors for implant removal after spinal surgical site infection. Eur Spine J 27:2481
23. Boody BS, Jenkins TJ (2015) Surgical site infections in spinal surgery. J Spinal Disord Tech 28(10):352
24. Olshaker JS, Jerrard DA (1997) The erythrocyte sedimentation rate. J EMERG MED 15(6):869–874
25. Larsson S, Thelander U (1992) C-reactive protein (CRP) levels after elective orthopedic surgery. Clin Orthop Relat Res (275): 237–242

26. Assicot M, Gendrel D (1993) High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 341(8844):515–518
27. Hunziker S, Hügle T (2010) The value of serum procalcitonin level for differentiation of infectious from noninfectious causes of fever after orthopaedic surgery. J Bone Joint Surg Am 92(1):138–148
28. Hadjipavlou AG, Mader JT (2000) Hematogenous pyogenic spinal infections and their surgical management. Spine (Phila Pa 1976) 25(13):1668–1679
29. Wilkins J, Gallimore JR (1994) Rapid automated enzyme immunoassay of serum amyloid A. Clin Chem 40(7 Pt 1):1284–1290
30. Iwata E, Shigematsu H (2016) Lymphopenia and elevated blood C-reactive protein levels at four days postoperatively are useful markers for early detection of surgical site infection following posterior lumbar instrumentation surgery. Asian Spine J 10(2):220