

Clinical Study of Procalcitonin Combined with C-reactive Protein in the Early Diagnosis of Infection after Lumbar Internal Fixation

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1. Abstract

Infection is a serious complication after lumbar internal fixation, and it is the focus of current spinal surgery research. Procalcitonin is sensitive and specific biomarker for identifying bacterial infection, but whether it can be used as a detection index for the early diagnosis of infection after lumbar internal fixation requires further research. Objective: To investigate the clinical significance of procalcitonin (PCT) combined with C-Reactive Protein (CRP) detection in the early diagnosis of infection after lumbar internal fixation. Methods: Patients who underwent lumbar internal fixation in our hospital from August 2019 to December 2021 were retrospectively studied. According to the results of wound secretion culture, they were divided into an infection group and a noninfection group. Venous blood was collected at different time points after the operation to detect and analyse serum PCT and serum CRP. The sensitivity and specificity of combined CRP and PCT for diagnosing surgical site infection were calculated. Results: There was no significant difference in preoperative indicators among all patients, and postoperative PCT and CRP indicators were significantly higher than those before surgery. The sensitivity of PCT combined with CRP to detect early postoperative infection was higher than that of single use. Conclusion: The combined detection of serum PCT and CRP can be used as a diagnostic index for early infection after lumbar internal fixation and has value in clinical application.

2. Keywords

procalcitonin; C-reactive protein; lumbar internal fixation; infection; early diagnosis

3. Introduction

Internal fixation is required for lumbar fusion, and for the treatment of lumbar fractures and degenerative diseases; but the internal fixation material, as a foreign body, has a high risk of postoperative infection [1]. Once infection occurs after lumbar internal fixation, it is often necessary to remove the internal fixation material and then reimplant it after controlling the infection. It is difficult to handle, has many complications, a long treatment cycle and high cost, which seriously affects the quality of life of patients and increases personal and social concerns. Economic burden, and the clinical efficacy of reoperation is far from ideal [2]. Therefore, how to provide effective and early diagnosis of postoperative lumbar spine infection is a difficult concern in spine surgery research.

Early and correct diagnosis of infection after lumbar internal fixation is a requirement for effective treatment and functional recovery of patients, but thus far, there is no rapid, reliable or highly accurate method for diagnosis [3, 4]. First, the symptoms and signs of infected patients after lumbar internal fixation are atypical, there is a lack of systemic inflammatory markers that can be used as diagnostic indicators, and bacterial culture results are often negative [5]. Second, there is still no unified definition and standard for infection after

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lumbar internal fixation, and different doctors and medical institutions have inconsistent reference values for diagnosis [6]. Current protocols for diagnosing infection after lumbar internal fixation combine serological testing, histological examination, local appearance of the lesion, the results obtained by culturing intraoperative specimens on solid medium, preoperative local aspirate examination results and so on [7]. To a large extent, however, current diagnostic protocols cannot provide the necessary and accurate information to demonstrate the presence and pathogenicity of pyogenic bacteria in an infected immobilizer. Since there is no standard method for detecting infections after posterior lumbar internal fixation, current diagnostic protocols can be complicated.

Serological examination is the most widely used method for monitoring infection after lumbar internal fixation. Commonly used serological indicators include C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and white blood cell (WBC) count. CRP is an acute phase reactive protein that occurs in various pathological conditions and is one of the commonly used indicators for the clinical evaluation of infection. It is elevated, not only in bacterial infections, but also in other noninfectious diseases, and remains high for days after the infection is controlled [8, 9]. Therefore, although CRP can be used as a diagnostic indicator of bacterial infection, it has low specificity and cannot reflect the severity and prognosis of infection. ESR is the sedimentation rate of red blood cells under certain conditions. It is a common manifestation during infection. The more severe the infection is, the faster the erythrocyte sedimentation rate is. However, its positive predictive value is low [10]. As a routine clinical detection index, it has certain significance in guiding care, especially in dynamically observing the changes in certain diseases and formulating treatment plans. However, ESR, like CRP, has low specificity and cannot accurately monitor the early stages of infection. WBC count and classification are traditional inflammatory markers. Clinically, in patients suspected of infection, white blood cell counts are usually used to make judgements and serve as the basis for antibiotic application. However, the WBC count is affected by many factors, such as the degree of infection and the immune status of the body, and its specificity and sensitivity for infection diagnosis have great limitations.

Procalcitonin (PCT) is an inactive prohormone, a propeptide of calcitonin, which can be secreted by neuroendocrine cells in the lung and small intestine and is not affected by hormone levels in the body. PCT has very low concentrations in healthy individuals and is a very stable protein *in vitro* and *in vivo* [11, 12]. Bacterial lipopolysaccharide induces the release of PCT. PCT is degraded by a specific protease with a half-life of approximately 24 h. PCT is significantly elevated in systemic bacterial or fungal infections but normal or slightly elevated in viral or local infections, which is of great significance for identifying bacterial or viral infections and judging the severity and prognosis of infection [13]. PCT can be used as a routine detection index of infection to guide clinicians in

early diagnosis and formulate reasonable treatment plans. It is stable in plasma and quick and easy to detect in the laboratory, which is conducive to wide clinical application. Studies have shown that PCT appears and peaks earlier than CRP, and because PCT has a short half-life and is not easily disrupted by surgery [14]. Therefore, we infer that serum PCT detection is helpful for the early diagnosis of infection after lumbar spinal fixation.

Because lumbar internal fixation is a deep operation, the early diagnosis of infection is very difficult. Although various methods have been applied to the diagnosis of infection after lumbar internal fixation, to date, there is no effective detection method or index that can accurately diagnose the lumbar spine. Infection after internal fixation and early detection of infection after lumbar spine surgery are crucial for determining treatment plans and the quality of the treatment's effects.

4. Materials and Methods

4.1 Subjects

From August 2019 to December 2021, 136 patients underwent lumbar internal fixation in our hospital, including 65 males and 71 females. Their ages ranged from 49 to 81 years, with an average of 65.8 ± 16.3 years, including 52 cases of lumbar fracture, 46 cases of lumbar spinal stenosis and 38 cases of lumbar disc herniation. Depending on the postoperative infection status (bacterial culture results), they were divided into an infection group (6 cases) and a noninfection group (130 cases).

The inclusion criteria were as follows: (1) at least 18 years old; (2) single segment and multisegment internal fixation of the lumbar spine were performed; (3) there was no systemic or surgical site infection before the operation; and (4) the postoperative hospital stay was ≥ 7 days.

The exclusion criteria were as follows: (1) acquired or hereditary immune deficiency; (2) systemic or local infection; (3) preoperative urinary tract or respiratory tract infection; (4) antibiotics or surgical treatment within 2 weeks before operation; and (5) severe systemic underlying diseases, such as severe diabetes; (6) Autoimmune diseases in the active stage, such as ankylosing spondylitis and rheumatoid arthritis; (7) No internal fixation materials were used during the operation.

4.2 Operation method

All included cases were operated on by the same surgical team from our hospital in strict accordance with the operation specifications and preoperative discussion plan. Imported or domestic instruments that can be used for a long time and are stable and reliable were selected for lumbar internal fixation. A prophylactic intravenous drip of 1 g of first-generation cephalosporin antibiotics was given 1 hour before the operation, and the antibiotic dose was increased if the exposure time in the operation field was more than 3 hours.

4.3 Observation indicators

The levels of serum PCT and CRP were measured on the 1st, 3rd and 7th days after the operation. At the same time, the sensitivity and specificity of indices between groups were compared to evaluate the diagnostic value of serum PCT and CRP in early infection after lumbar internal fixation.

4.3.1 PCT level detection: The serum PCT of all patients was detected by chemiluminescence at different time points, and the normal value was 0-0.5 ng/ml. Bacterial infection was considered when PCT was ≥ 0.5 ng/ml, and bacterial infection was excluded when PCT was < 0.5 ng/ml.

4.3.2 CRP level detection: Serum CRP of all patients was detected by immunoturbidimetry at different time points, and the normal value was 0-8 mg/L. When CRP was ≥ 8 mg/L indicates bacterial infection, and when CRP was < 8 mg/L, bacterial infection is excluded.

4.4 Statistical analysis

SPSS 17.0 statistical software was used to process the data. The measurement data are expressed as the mean \pm standard deviation ($\bar{x} \pm s$). One-way ANOVA was used for intergroup comparisons. The ROC curves of patients diagnosed with postoperative infection by PCT and CRP were drawn respectively, and the Z test was used to compare the area of the ROC curves under different tests. The combined diagnosis was fitted with a logistic regression model to fit the combined predictors. There was a significant difference ($p < 0.05$).

5. Results

5.1 Comparison of general data

There was no significant difference in sex, average age, surgical site, preoperative PCT or CRP between the observation group and the control group ($p > 0.05$).

5.2 Comparison of serum PCT and CRP levels after operation

Table 1 shows the changes in serum PCT and CRP levels at different time points in the infection and control groups. We found that the serum PCT and CRP levels at different time points after surgery were significantly higher than those before surgery. Compared with the first day after the operation, the levels of serum PCT and CRP in the infection group increased significantly on the third and seventh days after the operation ($p < 0.05$).

5.3. Sensitivity and specificity of serum PCT and CRP levels alone or in combination (Day 1 after operation)

Table 2 shows the sensitivity and specificity of serum PCT and CRP levels alone or in combination. It is obvious that the sensitivity of serum PCT and CRP levels alone is 76.9% and 84.6%, respectively. The sensitivity of the combined use of the two indicators was 92.3%. Compared with the single use of any index, the sensitivity of the combined use of the two indices was significantly improved, and the difference was statistically significant ($p < 0.05$). The specificity of the two indices used alone was 95.3% and 89.4%, respectively. The specificity of the combination of the two indices was 98.2%. Therefore, compared with the use of either index alone, the specificity of the combination of the two indices was significantly improved, and the difference was statistically significant ($p < 0.05$).

Table 1: Changes in serum PCT and CRP levels at different time points in the infection combination control group.

	Time after surgery (day)	PCT ($\mu\text{g/L}$)	CRP (mg/L)
Infection group	1	1.38 \pm 0.61	85.33 \pm 28.24
	3	3.27 \pm 1.26	124.40 \pm 30.13
	7	2.35 \pm 0.98	90.90 \pm 32.65
Noninfection group	1	0.85 \pm 0.45	43.22 \pm 16.92
	3	0.62 \pm 0.30	29.30 \pm 15.06
	7	0.35 \pm 0.13	18.03 \pm 9.77

Table 2: Sensitivity and specificity of serum PCT and CRP levels alone or in combination.

	Sensitivity (%)	Specificity (%)	AUC (95%CI)
PCT	76.9	89.4	0.763(0.556-0.971)
CRP	84.6	95.3	0.858(0.729-0.982)
PCT+CRP	92.3	98.2	0.985(0.959-1.000)

6. Discussion

Open lumbar surgery (fracture, severe degeneration of lumbar spine and tumour) mostly requires internal fixation. At present, it is the most important treatment for spinal diseases. The active prevention and treatment of postoperative complications also greatly affects the rehabilitation and prognosis of patients. Among them, lumbar postoperative infection is currently a more serious complication [15]. In the case of lumbar postoperative infection, subsequent nonsurgical treatment and surgical treatment will increase the economic burden and personal suffering of the patient's family. Sometimes it even requires repeated surgical treatment. It seriously affects the rehabilitation and quality of life of patients. In addition, antibiotic resistance presents new challenges for the prevention and treatment of postoperative surgical site infection. Therefore, timely detection, early diagnosis and early treatment of postoperative lumbar infection are very important to control infection and improve prognosis. If we can find and diagnose the infection in time, use thorough debridement and lavage in the early stage, and use antibiotics precisely and effectively, the general curative effect and prognosis are good. However, in clinical practice, routine prophylactic antibiotics are given to patients undergoing lumbar internal fixation during the perioperative period, which may lead to the concealment of early infection symptoms and atypical clinical manifestations, especially for patients with deep infection and with thick subcutaneous soft tissue. Clinically, there are often patients without obvious symptoms, such as fever, incision redness, swelling and pus, after surgery, but the healing of the surgical incision is delayed compared with ordinary patients, and patients have mild symptoms of lumbar discomfort, so it is difficult to make a clinical diagnosis of infection for these patients [16, 17]. The early diagnosis of lumbar postoperative infection is very difficult because of the atypical clinical manifestations and the lack of specific examination methods. X-ray, CT and MRI only have significant reference value during the middle and late stages of infection. These will add complexity to the timely diagnosis and treatment of postoperative infections.

At present, inflammatory indices commonly used in the clinic, such as CRP and WBC, cannot accurately distinguish between postoperative infection and postoperative systemic inflammatory response. Bacterial culture of incision secretions or deep puncture fluid is an important source for the diagnosis of infection after surgery and can be regarded as the gold standard for diagnosis. However, in clinical practice, the pathogen replication cycle is long, the positive rate of the detection results are low, and contamination may occur in the process of specimen retention, resulting in a some false-positive results. At the same time, it is difficult to isolate and culture some pathogens, which increases the economic burden on patients, so it is difficult to use for the early diagnosis of infection. WBC count is a traditional inflammatory marker. Its value is affected by many factors, such as the degree of infection and the immune status of the patient. It may be related to surgical trauma, the body's stress re-

sponse and the application of antibiotics, which affect WBC count, so that it cannot well reflect the progress of infection. Its specificity and sensitivity in the diagnosis of infection have great limitations.

CRP is a signalling protein in humans that is released during the acute stage of infections. It is induced by IL-6 and produced in the liver. It will rise after the body receives trauma. It is a nonspecific marker reflecting the systemic inflammatory response. CRP can trigger the immunomodulatory effect and phagocytosis of invasive cells. The combined complex can activate the complement system and induce an inflammatory response. It is a widely used diagnostic marker of bacterial infection in the clinic, with a sensitive response and low cost. However, as an acute phase reactive protein, it is affected by many factors (antibodies, drugs, tissue injury, radiation, trauma, surgery, noninfectious inflammatory response, the body's stress response, basic value, etc. and has large individual differences and a wide normal range. Therefore, the detection of plasma CRP levels alone has certain limitations in identifying infections and pathogen infections. This study suggests that the sensitivity of CRP alone in the diagnosis of infection is relatively high, but it lacks specificity, and its value in the early diagnosis of infection is limited. Infection caused by various pathogens, trauma, surgery, acute rejection and cardiovascular and cerebrovascular diseases can cause its increase, and studies have shown that the increase in CRP has nothing to do with the prognosis [18].

Procalcitonin (PCT), as a marker with good sensitivity and specificity, is increasingly used in the early diagnosis of infection and sepsis, infectious and noninfectious systemic inflammatory response syndrome, suppurative arthritis, acute osteomyelitis, and other postoperative complications [19]. However, the accuracy of PCT in the diagnosis of postoperative infection of lumbar fracture is still controversial. The purpose of this study was to compare PCT with other inflammatory markers and to explore the diagnostic value of PCT in fracture surgical site infection.

In this study, the postoperative PCT concentration in the infected group and the uninfected group was significantly higher than that in the preoperative control group ($P < 0.05$). This result may be related to trauma and surgical stress, which is consistent with relevant foreign reports. PCT can be increased in the early stage of the infectious inflammatory response and, therefore, has early diagnostic value. Our results are consistent with the relevant literature [20]. PCT is an ideal inflammatory marker. It is convenient and fast for clinical detection of infection and the results are accurate and stable. It is suitable for patients in emergency situations or undergoing hospitalization and meets the routine needs of clinical application.

This study confirmed that both PCT and CRP had high sensitivity for the diagnosis of lumbar postoperative infections. In terms of specificity, PCT was significantly higher than CRP. CRP is a reactive protein in the acute phase, and trauma will also cause an increase in CRP. Although CRP has high sensitivity, its specificity is poor, and it only has predictive value for infection when the acute stress

state is weakened. Therefore, it is not suitable to be used as an early predictor of infection alone. PCT has higher specificity and rises earlier than CRP, so it can be used as an early predictor of lumbar postoperative infection alone, and the combined detection of PCT + CRP improves the specificity and sensitivity of the detection.

However, this study still has the following deficiencies. First, this study is a retrospective study, the number of cases is relatively small, and there are differences in the mastery of various evaluation criteria in the process of data collection, which makes the research results have a certain deviation. Due to the small sample size, we included patients with incision infection and deep tissue infection in the same group for analysis, although there were significant differences in serum PCT levels between the two types of infection. These factors may affect the final results of this study. Therefore, it is necessary to further study the diagnostic value of serum PCT in surgical site infection of lumbar fracture in the next large sample prospective multicentre randomized control study to provide a stronger basis for clinical work.

In conclusion, after lumbar internal fixation, combined monitoring of plasma PCT and CRP levels and dynamic observation of the changes in PCT and CRP levels can guide rapid determination of the presence of infection and expedite treatment measures.

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