Original article

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Use of C reactive protein (CRP) and creatine kinase (CK) as predictors of early postoperative infection after minimally invasive transforaminal lumbar interbody fusion

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Introduction: Minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) is increasingly used for the treatment of degenerative lumbar spine disease. Despite reduced soft-tissue trauma, early postoperative infection remains a clinically relevant complication and may be difficult to recognize in the early phase. C-reactive protein (CRP) and creatine kinase (CK) are routinely available laboratory markers reflecting inflammatory response and muscle injury, respectively. This study aimed to evaluate the association between postoperative CRP and CK kinetics and early postoperative infection following MIS-TLIF.

Materials and methods: A retrospective study was conducted involving 60 patients who underwent percutaneous pedicle screw fixation and MIS-TLIF between May and November 2022 at Thong Nhat Hospital, Ho Chi Minh City. Serum CRP and CK levels were measured preoperatively and on postoperative days (PODs) 3, 5, 7, 10, and 14. Postoperative infection was diagnosed based on Centers for Disease Control and Prevention criteria and included both surgical site and extra-surgical site infections. Pain outcomes were evaluated using the Visual Analog Scale (VAS). Statistical comparisons were performed using paired *t*-tests or Wilcoxon tests, and Mann–Whitney *U* tests for independent samples.

Results: Six patients (10%) developed postoperative infections, including two deep infections, one superficial infection, and three extra-surgical site infections. In the overall cohort, CRP peaked on POD 3 and gradually declined, with 76% of patients returning to normal levels by POD 14. In infected patients, CRP showed a higher peak and a delayed decline, with a secondary elevation observed after POD 7. CRP levels differed significantly between infected and non-infected groups on POD 10 and POD 14 ($p < 0.05$). In contrast, CK peaked on POD 3 and normalized in most patients by POD 10, with no significant differences between groups. VAS scores for back and leg pain improved significantly one week after surgery.

Conclusion: Serial CRP is a useful supportive marker associated with early postoperative infection when interpreted serially and in conjunction with clinical findings after MIS-TLIF, particularly when CRP fails to decline or increases again after PODs 7–10. CK reflects postoperative muscle injury but does not provide additional diagnostic value for infection detection. CRP trends should be interpreted in conjunction with clinical findings to guide early diagnosis and management.

Keywords: *C-reactive protein; creatine kinase; postoperative infection; minimally invasive spine surgery; MIS-TLIF*

Introduction

Minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF), first described by Foley in 2003, has gained widespread acceptance due to reduced soft-tissue damage, less paravertebral muscle injury, and faster postoperative recovery compared with open techniques. Nevertheless, postoperative infection remains one of the most serious complications of spinal surgery, potentially leading to prolonged hospitalization, revision surgery, and increased healthcare costs [1, 2, 3].

Despite standard preventive measures, including perioperative antibiotic prophylaxis and meticulous surgical technique, reported infection rates after lumbar fusion range from 1.9% to 11.9%, while minimally invasive approaches demonstrate lower rates of approximately 0.6–2.7%. Early diagnosis of infection following MIS-TLIF is particularly challenging because clinical symptoms may be subtle or delayed [4, 5, 6].

C-reactive protein (CRP) is an acute-phase reactant synthesized by hepatocytes in response to inflammatory cytokines and typically rises within hours after tissue injury or infection. After uncomplicated spinal surgery, CRP levels usually peak around postoperative day 3 and subsequently decline. Deviation from this normal kinetic

pattern may indicate an infectious complication. Creatine kinase (CK), an enzyme released during muscle injury, also increases after spinal surgery but primarily reflects the extent of muscle trauma rather than infection. The clinical value of CK for detecting postoperative infection remains uncertain [7, 8, 9].

The aim of this study was to evaluate the association between serial postoperative CRP and CK measurements and early postoperative infection after MIS-TLIF, and to clarify their clinical usefulness in routine postoperative monitoring.

Materials and methods

Study Design and Patients

This retrospective study included 60 patients who underwent percutaneous pedicle screw fixation and MIS-TLIF at Thong Nhat Hospital, Ho Chi Minh City, between May and November 2022. Patients with evidence of infection before postoperative day 3 were excluded. All patients received prophylactic cefazolin (2 g intravenously) 30 minutes before skin incision, with a repeated dose if operative time exceeded 4 hours.

Laboratory Measurements

Serum CRP and CK levels were measured preoperatively and on PODs 3, 5, 7, 10, and 14. Normal CRP levels were defined as ≤5 mg/L. Pain severity was assessed using the Visual Analog Scale (VAS) for back and leg pain preoperatively and on postoperative day 7.

Definition of Infection

Postoperative infections, including surgical site infections and extra-surgical site infections, were defined according to Centers for Disease Control and Prevention criteria. [10] Patients were considered recovered when clinical improvement was accompanied by two consecutive negative CRP measurements obtained at least 15 days apart.

Statistical Analysis

Statistical analysis was performed using SPSS version 29.0. Normality was assessed using the Kolmogorov–Smirnov or Shapiro–Wilk tests as appropriate. Paired *t*-tests or Wilcoxon tests were used for within-group comparisons, and Mann–Whitney *U* tests were applied for comparisons between infected and non-infected groups. A p-value ≤0.05 was considered statistically significant.

Results

Among the 60 patients, 25 were male and 35 female. The mean age was 58.8±1.4 years. The average number of surgical levels was 2.12±0.1. The average surgery time was 226.75±5.6 minutes. There were 6 recorded cases of infection, including 1 superficial infection, 2 deep infections and 3 extra-incision infections as uninary tract infection (***Table 1***).

Postoperative CRP levels increased in all patients reaching a peak on postoperative day 3, followed by a gradual decline over time. In patients who developed infection, CRP demonstrated a higher peak and a slower decrease compared with the non-infected group. In addition, a secondary elevation or persistent plateau after postoperative day 7 was observed in infected cases, whereas CRP values in non-infected patients continued to decrease steadily. Differences between the two groups became more evident in the later postoperative period, particularly after postoperative day 10. Detailed numerical values are presented in ***Table 2***.

Fig. 1 illustrates the overall trend of CRP changes over time in both groups, highlighting the higher peak and delayed decline observed in infected patients.

Postoperative CK levels peaked on day 3 (1081±99 U/L) and then gradually decreased, with 81% of patients returning to normal CK levels after 10 days. No statistically significant differences in CK levels were observed between the infected and non-infected groups (***Fig. 2***).

Table 1. Patients demographic and surgical profile

Demographic data	Mean±SD
Age	58.8±1.4
Sex	
Male	25
Female	35
Number of surgical levels	2.12±0.1
1 level	13
2 levels	30
3 levels	14
4 levels	3
Surgical time (min)	226.75±5.6
Number of infections	6
Superficial infection	1
Deep infection	2
Extra-incision infection	3

Table 2. Comparison of CRP values between two groups

CRP values	No infection	Infection	*P*-value
Preoperative	3.5±0.4	4.67±1.64	0.306
Postoperative day 3	97.35±8.48	141.86±43.03	0.289
Postoperative day 5	38±3.63	54.55±11.18	0.121
Postoperative day 7	13.5±1.37	19.8±3.83	0.091
Postoperative day 10	7.1±0.93	23.2±7.36	0.002*
Postoperative day 14	3.67±0.38	25.58±2.56	<0.001*

Note. * Statistically significant

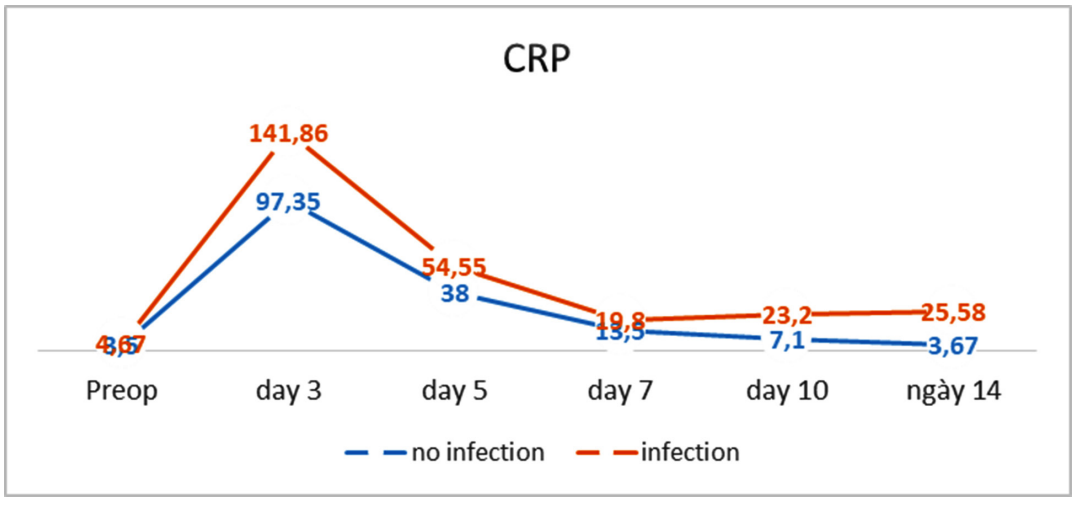

Fig. 1. Mean CRP values between the infected and non-infected patients, measured preoperatively and on PODs 3,5,7,10,14, respectively

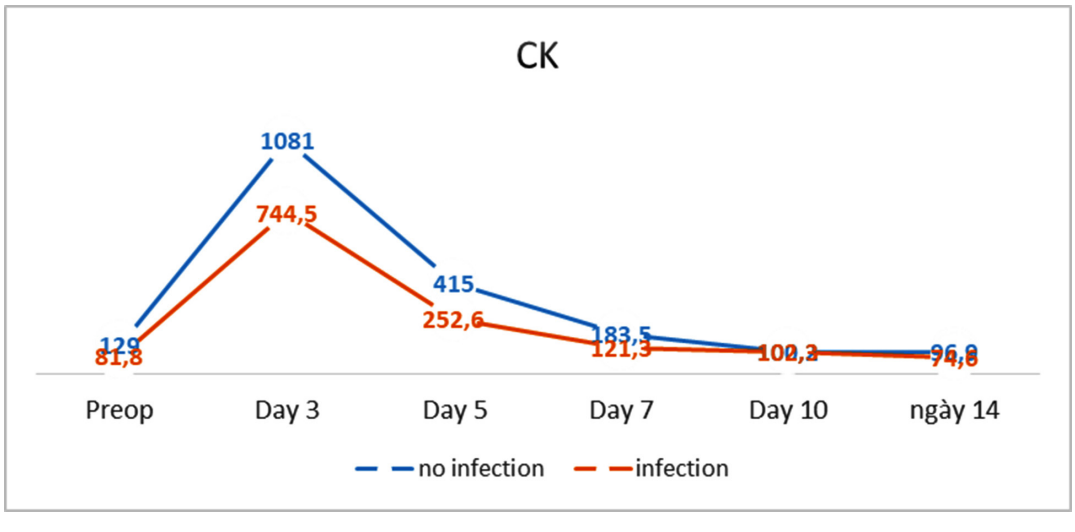

Fig. 2. Mean CK values between infected and non-infected patients, measured preoperatively and on days 3,5,7,10 and 14. Values are presented as mean±SD

The variables of age, number of surgical levels, and time of surgery were not related to infection status. Among 6 patients with infection, 5 patients had comorbidities, of which exogenous Cushing syndrome accounted for 3/6 (50%) (***Table 3***).

VAS scores 1 week after surgery significantly improved compared to preoperative values. Back pain VAS decreased from 5.88 ± 0.19 to 3.88 ± 0.61 (p < 0.001), while leg pain VAS decreased from 7.05 ± 0.16 to 1.5 ± 0.11 (p < 0.001).

Table 3. Analysis of infection status with other variables

Variables	No infection	Infection	*P*-value
Age	58.31±1.38	63±6.7	0.361
Number of surgical levels	2.04±0.1	2.83±0.5	0.056
Surgical time (min)	227.87±5.82	216.67±21.1	0.734
Comorbidity		Exogenous Cushing syndrome: 3 cases Diabetes mellitus and Hypertension: 2 cases No comorbidity: 1 case	

Discussion

CRP is produced by the liver in response to inflammation, infection, malignancy, and tissue damage with a relatively high sensitivity, rate of response, and range compared to other acute phase reactants [2]. However, the primary acute phase reaction of CRP is not specific to surgery or infection and can be caused by a number of conditions including necrosis, inflammatory disease, allergic complications of infection, and infectious disease and malignancies [8]. In the early postoperative period, numerous studies have described the normal kinetics of CRP as rapidly increasing, peaking on day 3, followed by a sharp decrease and then gradually decreasing with normalization on within 14–21 days. Deviations from the normal kinetics of CRP may indicate an infectious complication [11].

In the present study, similar to previous reports, CRP levels increased rapidly after surgery, peaked on day 3 and then gradually decreased. Patients with postoperative infection had a slow decrease in CRP levels and a tendency to increase again on the 7th postoperative day. Similarly, Kang *et al.* [12] found that infections had a rebound in CRP levels on day 5 or 7 postoperatively. Hotably, 72% of the non-infected patients did not demonstrate normalization of CRP by postoperative day 7, however their levels gradually decreased thereafter, whereas CRP levels in the infected group showed a secondary increase. In our cohort, CRP levels between the infected and non-infected groups was significantly different at day 10. Although, in the infected group, CRP level had a higher peak on day 3 (141.86±43 vs 97.35±8.5), but the difference was not statistically significant (p = 0.289).

Of the 6 infected patients, there were three cases of urinary tract infection with positive urine test for white blood cells and nitrites. One patient developed a superficial infection after suture removal on day 10, characterized by purulent discharge; Staphylococcus epidermidis was isolated on culture, and the patient was successfully treated with oral antibiotics. There were 2 patients diagnosed with deep infection, presenting with fever, back pain, increased white blood cell count, elevated CRP levels. MRI demonstrated soft tissue inflammatory changes in the surgical area, without evidence of abscess formation and negative blood cultures. These patients with deep infection received intravenous antibiotics. All patients recovered with conservative treatment.

CK, an enzyme that catalyzes biochemical reactions in the body, the concentration of CK in the blood will help reflect the activity status and health of the muscle mass. CK also recorded a rapid increase after surgery and peaked on day 3, then gradually decreased [9]. In current study, CK peaked (1047.33±90.2) on day 3, then gradually decreased and 81% of patients returned to normal levels on day 10 postoperatively. The difference in CK levels between the infected and non-infected groups was not statistically significant.

Analysis of other factors including age, surgical time, number of surgical levels were not related to infection status. Although in the infection group there were more surgical levels and older age, but the difference was not statistically significant (p>0.05). Notably, five of six patients in the infection group had comorbidities, including three cases of exogenous Cushing syndrome (accounting for 50%).

Regarding clinical outcomes, MIS-TLIF demonstrated favorable short-term results. Pain scores assessed using the VAS showed significant improvement one week after surgery compared with preoperative surgery. Back pain VAS decreased from 5.88±2 0.19 to 3.88±0.61; p<0.001, while leg pain VAS decreased from 7.05±0.16 to 1.5±0.11; p<0.001.

Overall, this study demonstrates that serial CRP measurements provides clinically useful information for the early identification of postoperative infection following MIS-TLIF. Consistent with previous reports [13,14]. CRP peaked on postoperative day 3 in all patients. However, infected patients showed delayed normalization and secondary elevation, particularly after postoperative day 7, distinguishing them from non-infected patients.

Although CK also increased after surgery, reflecting muscle injury, it did not differ significantly between infected and non-infected groups. This finding supports the interpretation that CK is primarily a marker of surgical trauma rather than infection [15].

Importantly, a substantial proportion of non-infected patients had persistently elevated CRP levels in the early postoperative period, emphasizing that single CRP measurements should not be overinterpreted. Instead, CRP trends over time — especially after postoperative day 7–10 — appear to be more informative. Given the

small number of infection cases, the findings should be interpreted as demonstrating an association rather than definitive predictive value.

Limitations

Limitations of this study include its retrospective design, the relatively small number of infection cases, and the absence of multivariable analysis to adjust for potential confounding factors. In addition, steroid exposure, which may influence CRP responses, was only partially accounted for through comorbidity data and could not be evaluated in detail. Recent studies and systematic reviews have likewise emphasized the importance of CRP kinetics over single absolute cutoff values for the early detection of postoperative infection after spine surgery, while also indicating the limited diagnostic role of muscle injury markers such as CK [16, 17]. These contemporary findings are consistent with our results and support the use of serial CRP monitoring in conjunction with clinical assessment rather than reliance on isolated laboratory measurements. Future prospective studies with larger sample sizes and standardized protocols are warranted to validate these observations and to establish clinically meaningful thresholds for postoperative CRP interpretation.

Conclusions

Serial monitoring of CRP is a simple and reliable supportive tool for the early detection of postoperative infection after MIS-TLIF, particularly when CRP levels fail to decline or demonstrate a secondary increase after postoperative day 7–10. CK does not appear to provide additional diagnostic value for infection. CRP trends should be interpreted in conjunction with clinical findings to guide early diagnosis and management. These findings indicate an association rather than definitive predictive value and should be interpreted in light of the study's retrospective design and limited number of infections.

Disclosure

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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