VALUE OF SERUM PLT/ALB AND CRP/ALB IN EVALUATING MUCOSAL HEALING AND THE RECURRENCE OF CROHN'S DISEASE

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ABSTRACT

Objective: *To explore the value of serological PLT/ALB and CRP/ALB in evaluating mucosal healing and the recurrence of Crohn's disease.*

Methods: *A total of 85 patients with Crohn's disease treated in our hospital from April 2017 to April 2019 were selected. According to the clinical and endoscopic healing criteria, the patients were divided into a mucosal healing group and a mucosal non-healing group. General data, serum ALB, PLT, CRP, PLT/ALB and CRP/ALB levels before and after treatment, as well as their correlations with SES-CD score and serum indexes, were compared to evaluate the value of mucosal healing. The patients were divided into recurrent and non-recurrent groups according to whether they relapsed. The levels of serum indexes and the value of serum indexes in predicting disease recurrence were compared between the two groups.*

Results: *After treatment, the level of ALB in the mucosal healing group was significantly higher than that in the mucosal non-healing group, while the levels of PLT, CRP, PLT/ALB and CRP/ALB decreased ($P < 0.05$). Serum ALB, PLT, CRP, PLT/ALB and CRP/ALB were correlated with SES-CD score. The AUC values of ALB, PLT, CRP, CRP/ALB and PLT/ALB were 0.712, 0.662, 0.774, 776 and 719, respectively. After treatment, ALB in the recurrent group was significantly lower than that in the non-recurrent group, while the levels of PLT, CRP, PLT/ALB and CRP/ALB increased ($P<0.05$). The AUC values of ALB, PLT, CRP, CRP/ALB and PLT/ALB for predicting disease recurrence were 0.641, 0.628, 0.643, 0.652 and 0.651, respectively.*

Conclusion: *the combined serum indexes (PLT/ALB and CRP/ALB) have high clinical value in evaluating mucosal healing and the recurrence of Crohn's disease.*

Keywords: *Serology PLT/ALB, CRP/ALB, crohn's disease, mucosal healing, disease recurrence, value.*

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Introduction

Crohn's disease (CD), also known as granulomatous enteritis, is a chronic non-specific inflammatory disease of the digestive tract that mostly occurs in the distal ileum and right colon. Its main clinical symptoms are abdominal pain, diarrhoea, intestinal obstruction, weight loss, etc., which can also be accompanied by fever, nutritional disorders and other extra-intestinal manifestations[(1)]. The aetiology and pathogenesis of CD remain unclear and may be related to infection, humoral immunity, cellular immunity and other factors[(2)]. At present, there is no special treatment for CD, which is mainly controlled by salicylate sulfasalazine, adrenocorticosteroids and other drugs to relieve clinical symptoms; however, patients are prone to recurrent attacks that are not easy to cure[(3)]. Studies have found that CD patients achieve mucosal healing after treatment and that the risk of disease recurrence is significantly reduced, which is an important indicator of clinical treatment effectiveness[(4)]. In recent years, the role of serological marker detection in the diagnosis and evaluation of CD has become an

area of research concern[5]. Most research is focused on studying the serological markers of inflammatory markers and antimicrobial antibodies, including inflammatory markers such as c-reactive protein (CRP), which is a type of protein synthesised by the liver that can combine with pneumococcal cell wall polysaccharides for CD detection since non-specific signs reflect systemic inflammation[6].

However, due to the low specificity of serological indicators and interference of multiple factors, it is impossible to predict CD by using a single indicator. In recent years, studies have found that the combined application of serum markers is more accurate and that the specificity of the PLT/ALB and CRP/ALB ratios is higher in evaluating the active stage of inflammation[7]. This study was conducted on patients with CD to explore the value of PLT/ALB and CRP/ALB in evaluating mucosal healing and the recurrence of CD[8].

Methods

General information

A total of 85 patients with CD admitted to our hospital from April 2017 to April 2019 were selected.

Inclusion criteria:

• Meet the clinical diagnostic criteria of CD;

• In our hospital, CD activity index (CDAI) score >150 before treatment and CDAI <150 after treatment (clinical remission stage);

• All patients had a colonoscopy and serological examination records before and after treatment.

Exclusion criteria:

• Complicated with other infectious diseases, ulcerative colitis, severe liver and kidney insufficiency and other digestive tract tumours, etc.;

• Complications such as intestinal obstruction and intestinal fistula occurred during the period before treatment;

• Had taken aspirin and other anti-inflammatory drugs before admission. Based on the results of the endoscopic examination, the intestinal mucosas of the patients were evaluated using the SES-CD scoring method.

Under this method, a score of 0-2 suggests mucosal healing that meets the clinical healing standard (CDAI<150 points); however, non-healing under endoscopy (SES-CD>2 points) is considered unbalanced healing. To meet the clinical and endoscopic healing standards (i.e., mucosal healing), there were 44 cases in the mucosal healing group (25 males and 19 females). According to the clinical classification, there were 11 cases of ileum type, 13 cases of colon type and 20 cases of ileum type. In the unhealed mucosa group, 41 cases were clinically healed (CDAI<150 points) but unhealed under endoscopy (SES-CD>2 points), including 27 males and 14 females (9 ileal, 14 colic and 18 ileal). There was no significant difference between the two groups (P>0.05).

Observation indicators

• 5ml of fasting venous blood was collected in the morning before and after treatment, centrifuged at 3000r/min for 10 min. The serum was then carefully separated. Serum albumin (ALB) and platelet (PLT) levels were detected by an automatic biochemical analyser, and serum CRP levels were detected by enzyme-linked immunosorbent assay (ELISA).

• Serum ALB, PLT, CRP, PLT/ALB and CRP/ALB levels were compared between the two groups before and after treatment.

• Serum ALB, PLT, CRP, PLT/ALB and CRP/ALB levels were compared between recurrent and non-recurrent patients.

Statistical methods

The SPSS 20.0 software package was used for the statistical analysis of the data. The measurement data were in accordance with a normal distribution, represented by ($\bar{x}\pm s$). An independent sample t-test was used for comparison between groups, and paired sample t-test was used for comparison before and after treatment. Statistical data were expressed by percentage, and the χ^2 test was used for comparison between groups. A non-parametric rank-sum test (Mann-Whitney U test) was used for non-normal distribution. A ROC curve was used to evaluate mucosal healing and disease recurrence. P<0.05 was considered statistically significant.

Results

Comparison of general data between the two groups

There was no significant difference in gender, age, CDAI score and disease site between the two groups (P>0.05), as shown in Table 1.

Comparison of serum ALB, PLT, CRP, PLT/ALB and CRP/ALB levels between the two groups before and after treatment

Before treatment, there were no significant differences in serum ALB, PLT, CRP, PLT/ALB and

CRP/ALB levels between the two groups (P>0.05). After treatment, the ALB level in the mucosal healing group was significantly higher than that in the mucosal unhealing group, while the PLT and CRP levels were significantly lower, and the PLT/ALB and CRP/ALB index levels were decreased. The differences were statistically significant (P<0.05) (see Table 2).

		n	Mucosal healing group (n=44)	Mucosal non-healing group (n=41)	χ^2/t	*P*
Gender (n)	Male	51	25	27	0.730	0.393
	Female	33	19	14		
Age (year)	<16	15	8	7	0.192	0.908
	17–40	49	26	23		
	>40	21	10	11		
CDAI score (points)			131.25±13.37	132.56±13.89	0.443	0.659
Site of disease (n)	Ileum	20	11	9	0.237	0.888
	Colon	27	13	14		
	Ileocolon	38	20	18		

Table 1: Comparison of general data between the two groups ($\bar{x}\pm s$).

Index	Mucosal healing group (n=44)		Mucosal non-healing group (n=41)		^bt	^bP
	Before treatment	After treatment	Before treatment	After treatment		
ALB (g/L)	34.27± 7.54	40.58± 5.63^{ab}	33.52± 6.71	35.24± 5.12^{a}	4.564	<0.001
PLT (G/L)	397.21± 147.52	291.35± 110.18^{ab}	395.48± 134.62	341.74± 99.12^{a}	2.211	0.030
CRP (mg/L)	40.01 (12.13-62.23)	1.42 (0.57-9.31)^{ab}	25.38 (13.88-40.11)	20.14 (5.71-38.87)^{a}	-4.125	0.000
PLT/ALB	12.45± 5.72	7.32± 3.67^{ab}	12.73± 5.86	9.87 ±3.41^{a}	3.312	0.001
CRP/ALB	1.12 (0.34-1.90)	0.02 (0.01-0.21)^{ab}	0.74 (0.36–1.37)	0.55 (0.13–1.08)^{a}	-4.135	0.001
t	0.483	0.056	-1.125	0.223	-0.954	
P	0.630	0.955	0.176	0.824	0.347	

Table 2: Comparison of serum ALB, PLT, CRP, PLT/ALB and CRP/ALB levels between the two groups before and after treatment ($\bar{x}\pm s$) [$M(Q_1–Q_3)$].
Note: Compared with before treatment, $^aP<0.05$; Compared with the untreated group, $^bP<0.05$.

Correlation analysis between serum ALB, PLT, CRP, PLT/ALB, CRP/ALB and SES-CD score

Serum ALB, PLT, CRP, PLT/ALB and CRP/ALB were significantly correlated with SES-CD score (see Table 3).

Mucosal healing evaluated by ALB, PLT, CRP, PLT/ALB and CRP/ALB indexes after treatment

A ROC curve was used to evaluate the AUC of mucosal healing evaluated by ALB. The results were 0.662 for PLT, 0.774 for CRP, 0.719 for CRP/ALB and 0.719 for PLT/ALB (see Table 4).

Index	Before treatment		After treatment	
	r	*P*	*r*	*P*
ALB	-0.452	0.001	-0.403	0.003
PLT	0.415	0.004	0.254	0.023
CRP	0.431	0.000	0.341	0.006
PLT/ALB	0.468	0.000	0.287	0.035
CRP/ALB	0.479	0.001	0.376	0.001

Table 3: Correlation analysis between serum ALB, PLT, CRP, PLT/ALB, CRP/ALB levels and SES-CD score ($\bar{x}\pm s$).

Detection index	Sensitivity (%)	Specificity (%)	Right index (%)	AUC
ALB>36.35	85.47	56.24	40.37	0.712
PLT<281	82.15	58.74	32.48	0.662
CRP<3.75	78.54	67.28	50.23	0.774
CRP/ALB<0.147	77.31	71.36	51.39	0.776
PLT/ALB<7.864	69.28	75.89	44.87	0.719

Table 4: Mucosal healing evaluated by ALB, PLT, CRP, PLT/ALB and CRP/ALB indexes after treatment.
Note: Accuracy index (%) = sensitivity + specificity - 100%.

Comparison of ALB, PLT, CRP, PLT/ALB and CRP/ALB levels between recurrent and non-recurrent groups

After follow-up, there were 19 cases of recurrence in the mucosal healing group (recurrence rate: 43.18%) and 26 cases of recurrence in the mucosal non-healing group (recurrence rate: 63.41%), with statistically significant differences (P<0.05). After treatment, ALB in the recurrence group was significantly lower than that in the non-recurrence group, while PLT, CRP, PLT/ALB and CRP/ALB levels were higher, with statistically significant differences between groups (P<0.05) (see Table 5).

Index	Non-recurrence group (n=40)	Recurrence group (n=45)	t	P
ALB (g/L)	38.41±5.63	35.12±5.17	2.800	0.006
CRP (mg/L)	2.74 (0.61-11.47)	12.17 (2.03-31.75)	-2.035	0.029
PLT (G/L)	291.25±84.11	345.24±115.27	2.479	0.015
PLT/ALB	7.65±3.14	9.58±4.18	2.417	0.018
CRP/ALB	0.09 (0.02-0.30)	0.38 (0.08-1.17)	-2.136	0.025

Table 5: Comparison of ALB, PLT, CRP, PLT/ALB and CRP/ALB levels between the recurrence group and non-recurrence groups ($\bar{x}\pm s$).

Evaluating disease recurrence after treatment using serum ALB, PLT, CRP, PLT/ALB and CRP/ ALB indexes

The AUC of ALB was 0.641, while PLT was 0.628, CRP was 0.643, CRP/ALB was 0.652 and PLT/ALB was 0.651 (see Table 6).

Detection index	Sensitivity (%)	Specificity (%)	Right index (%)	AUC
ALB>36.35	59.32	68.42	26.45	0.641
PLT<313	59.47	72.11	29.32	0.628
CRP<3.75	49.21	79.21	30.28	0.643
CRP/ALB>0.33	52.13	81.25	34.26	0.652
PLT/ALB>9.92	47.85	86.48	32.47	0.651

Table 6: ALB, PLT, CRP, PLT/ALB and CRP/ALB indexes evaluated for disease recurrence after treatment.

Discussion

CD is a chronic inflammatory granulomatous disease of the digestive tract with unknown aetiology, which can affect all segments of the digestive tract from mouth to anus. Most of the lesions are intestinal ulcers, which can affect the whole layer of the digestive tract, resulting in a thickening of the intestinal wall, narrowing of the intestinal lumen and intestinal penetration[9]. In recent years, the incidence of CD has gradually increased, which may be related to social industrialisation. Some studies have found that smoking history is positively correlated with the incidence of CD, and multiple factors such as genetics and infection may lead to CD[10]. In clinical practice, there is no radical cure for CD. Drug treatment is mostly used to control the active stage of the disease and alleviate the disease to prevent complications[11]. Recent studies have found that the intestinal mucosa of patients with clinical remission (CR) after treatment continued to show inflammatory activity. Therefore, the intestinal mucosa of patients with CR after treatment may not heal, leading to disease recurrence[12]. A follow-up examination is required for patients who have been clinically relieved after treatment. However, a colonoscopy will increase patients' pain and lead to their inability to have regular re-examination, which is not conducive to disease monitoring[13]. The detection of serum markers is widely used in clinical practice, which can effectively assess the prognosis of the disease. While previous studies have confirmed that serum markers are correlated with the active stage of CD, there are few studies on the value of evaluating mucosal healing and CD recurrence[14]. Studies have found that CRP has been clinically used to evaluate the activity of intestinal inflammation, while its ALB is synthesised in the liver to reflect intestinal inflammation and nutrient level, which can be used as an indicator to evaluate the active stage of CD and reflect the inflammatory state of the body[15]. ALB, CRP and PLT indicators can all be used as indicators to evaluate the active stage and recurrence of CD; however, the specificity of using serum indicators alone to evaluate CD is low. Therefore, scholars have proposed the optimisation of CRP/ALB indicators to evaluate CD activity and the optimisation of PLT/ALB indicators to evaluate the prognosis of CD[16].

The results of this study showed that serum ALB, PLT, CRP, PLT/ALB and CRP/ALB indicators were significantly correlated with SES-CD score, indicating that serological indicators could be used to determine the CD activity and mucosal healing ability of patients. ALB alone showed 85.47% sensitivity, 56.24% specificity and 40.37% correctness index. CRP alone showed 78.54% sensitivity, 67.28% specificity and 50.23% correctness index. Moreover, an optimised CRP/ALB index showed 77.31% sensitivity and 77.36% specificity. The accuracy index was 51.39%, the sensitivity of the PLT/ALB index was 69.28%, the specificity was 75.89% and the accuracy index was 44.87%, which indicates that the optimisation index had a higher specificity and accuracy index than a single serological index.

The course of CD is prolonged and recurrent, and patients in CR are at risk of disease recurrence. Since patients with intestinal mucosa still have inflammatory activity, there is a risk of recurrence[17]. Current studies on CD mainly focus on disease recurrence. Some studies have confirmed that the inflammatory indicators of patients in CR with non-healing mucosa under endoscopy are significantly higher than those with mucosal healing. Therefore, patients in CR will stop taking drugs, thereby leading to disease recurrence[18]. Clinically, endoscopic examination is mainly used to diagnose the disease and evaluate the activity. SES-CD is used to score the intestinal tract of patients, which can predict the disease. However, due to the influence of multiple factors, the assessment is not accurate and the use of serological indicators can effectively predict the recurrence of the disease[19]. The results of this study showed that ALB, CRP and PLT alone had a low specificity in predicting disease recurrence, while the optimised CRP/ALB index-with an AUC of 0.652, sensitivity of 52.13% and specificity of

81.25%-could better evaluate the disease recurrence of patients, followed by PLT/ALB index (sensitivity: 47.85%). Its specificity was 86.48%, indicating that the serum optimisation index could increase the test efficiency.

In conclusion, the combined serum indicators PLT/ALB and CRP/ALB are more effective in evaluating mucosal healing, predicting the recurrence of the disease and helping to reduce the recurrence rate of the disease. However, due to the limited sample size and short analysis time, it is necessary to accumulate samples to further explore the value of serological PLT/ALB and CRP/ALB in evaluating mucosal healing and CD recurrence.

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