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Analysis of the clinical symptoms of patients complicated with acute intestinal obstruction after the surgery of colon cancer

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ABSTRACT

Objective: To study the content of serum inflammatory medium of the patients complicated with acute intestinal obstruction after the surgery of colon cancer.
Methods: A total of 150 patients with colon cancer received limited surgery treatment during the period of May 2012 to October 2015 were selected as the study objects. They were divided into postoperative ileus (POI) group and non-postoperative ileus (non-POI) group according to the presence or absence of intestinal obstruction. Then, the contents of serum procalcitonin (PCT), C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) were detected at the 1st, 3rd, 5th and 7th days after the surgery.
Results: The levels of serum PCT, CRP, TNF-α and IL-6 of two groups at the 1st day had no differences after the surgery. The level of serum PCT of POI group tended to increase and its levels of serum CRP, TNF-α and IL-6 tended to decrease at the 3rd, 5th and 7th days after the surgery, while the levels of serum PCT, CRP, TNF-α and IL-6 of non-POI group were decreased. The content of serum PCT of POI group and non-POI group at the 3rd day after the surgery had no differences ($P > 0.05$), and the level of serum PCT of POI group was higher than that of non-POI group at the 5th and 7th days after the surgery ($P < 0.05$). The levels of serum CRP, TNF-α and IL-6 of POI group and non-POI group had no differences at the 3rd, 5th and 7th days after the surgery ($P > 0.05$).
Conclusions: The raising of the content of serum PCT after the surgery can be used as the laboratory index to predict the incidence of acute intestinal obstruction after the surgery of colon cancer.

1. Introduction

Postoperative ileus (POI) mainly happens after major abdominal surgeries causing the clinical symptoms such as abdominal pain, abdominal distension, no flatus and defecation, *etc*. Colorectal cancer is a common malignant tumor in the digestive system, and the incidence and death rates of the disease were all tending to increase in recent years, and the main way in clinic to treat colorectal cancer is surgical resection[1–3]. Acute intestinal obstruction is a kind of serious complications that happens after the surgery of colon cancer, which will cause the prolonging of the hospitalized course and increase the rate of second surgery and rate of death. Early diagnosis of the intestinal obstruction that happens after the surgery of colon cancer is difficult, since it mainly depends on the clinical symptoms, physical signs and X-ray examination, which lacks of the effective laboratory indexes[4–6]. Intestinal obstruction that happens after the surgery of colon cancer is mainly inflammatory intestinal obstruction and early intervention can postpone the disease deterioration, alleviate the clinical symptoms and reduce the death rate[7,8].

Cytokines is the substance with multi-biological function *in vivo*, which is identified as the main factor that mediates the systemic inflammatory response syndrome. In the process of

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The study protocol was performed according to the Helsinki declaration and approved by the Affiliated Tumor Hospital of Zhengzhou University Ethics Committee. Informed written consent was obtained from the Affiliated Tumor Hospital of Zhengzhou University.

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activating the inflammatory reaction, various inflammatory cytokines are released and participate in blood circulation. Therefore, the detection of the changes of the related cytokines content in serum has indicative function on the inflammatory reaction after the surgery and can predict the incidence of different complications after the surgery[9,10]. Some researches has confirmed that the changes of the cytokines content in serum after the gastrointestinal surgery is related to the incidence of the intra-abdominal complications after the surgery. The procalcitonin (PCT), C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF-α) are the important mediators that mediate the acute inflammation of organism[11,12]. The contents of the serum inflammatory mediators of patients complicated with acute intestinal obstruction after the surgery of colon cancer were studied and analyzed in order to discuss whether they could be used as the laboratory indexes to predict the incidence of acute intestinal obstruction after the surgery of colon cancer.

2. Materials and methods

2.1. Clinical data of patients

A total of 150 patients with colon cancer received the limited surgery treatment during the period of May 2012 to October 2015 were selected as the study objects. All of them were diagnosed with colon cancer through the electron colonoscope examination and pathologic biopsy, and accorded with the indications of surgical resection. They were conducted with the open surgery of radical resection of colon cancer after general anesthesia without preventive colostomy. The exclusion criteria included patients received chemoradiotherapy before the surgery, patients with emergency surgery and patients using non-steroidal anti-inflammatory drugs and the immunosuppressor for a long time. The selected patients included 91 males and 59 females with the ages of 32–67 years and the average age of (51.9 ± 7.2) years.

2.2. Grouping methods and diagnostic criteria of POI

The patients with colon cancer were divided into POI group and non-POI group according to the presence or absence of intestinal obstruction. The diagnostic criteria of POI reference to the criteria of adhesive ileus in the 7th version of Surgery: (1) medical history: history of abdominal surgery; (2) symptoms: abdominal pain, abdominal distension, nausea, vomiting and no flatus and defecation; (3) physical signs: obvious distension, pressing pain of abdomen, obviously touchable gastrointestinal shape and the peristaltic wave, no peritoneal irritation features and heared hyperactive bowel sounds; (4) imageological examination: multiple air-fluid levels observed through abdominal orthostatic X-ray examination and thickened intestine wall and agglomerate intestinal loop observed through abdominal CT plain scan.

2.3. Specimen collection and detection methods

About 10 mL peripheral venous blood of patients in the two groups at the 1st, 3rd, 5th days after the surgery was extracted, and centrifuged for 10 min with the centrifugal force of 12 000 r/min after placed under the room temperature for 10–15 min. Then, the upper serum was collected to detect the contents of PCT, CRP, TNF-α and interleukin-6 (IL-6) by using ELISA kits.

2.4. Statistical analysis

The SPSS 19.0 software was applied to input and analyze the data. The measurement data were expressed as mean ± SD, and the *t*-test was used for the analysis between the two groups. The enumeration data were expressed as frequency forms and analysed by *Chi*-square test. The Pearson's correlation analysis was adopted to detect the correlation between two variables. Differences were statistically significant when $P < 0.05$.

3. Results

3.1. Clinical materials of patients in the two groups

Genders, ages and body mass index of patients in the two groups had no significant differences ($P > 0.05$). The contents of serum carcinoembryonic antigen [(17.92 ± 2.85) *vs*. (19.14 ± 2.76) ng/mL], CA199 [(127.65 ± 19.37) *vs*. (130.18 ± 21.52) IU/mL], CA50 [(193.51 ± 26.29) *vs*. (191.03 ± 22.68) IU/mL], PCT [(72.61 ± 9.29) *vs*. (74.18 ± 10.33) pg/mL], CRP [(15.28 ± 2.15) *vs*. (14.59 ± 2.42) mg/L], TNF-α [(105.21 ± 15.86) *vs*. (107.36 ± 17.18) pg/mL] and IL-6 [(48.41 ± 7.49) *vs*. (50.12 ± 6.92) pg/mL] had no significant differences before the surgery ($P > 0.05$) (Table 1).

Table 1
Clinical materials of patients in the two groups.

Parameter	POI group (n = 14)	Non-POI group (n = 136)	P
Genders (Male/Female)	9/5	82/54	> 0.05
Ages (year)	52.90 ± 6.90	51.10 ± 7.80	> 0.05
Body mass index (kg/m^2)	21.30 ± 2.90	20.90 ± 3.10	> 0.05
Carcinoembryonic antigen (ng/mL)	17.92 ± 2.85	19.14 ± 2.76	> 0.05
CA199 (IU/mL)	127.65 ± 19.37	130.18 ± 21.52	> 0.05
CA50 (IU/mL)	193.51 ± 26.29	191.03 ± 22.68	> 0.05
PCT (pg/mL)	72.61 ± 9.29	74.18 ± 10.33	> 0.05
CRP (mg/L)	15.28 ± 2.15	14.59 ± 2.42	> 0.05
TNF-α (pg/mL)	105.21 ± 15.86	107.36 ± 17.18	> 0.05
IL-6 (pg/mL)	48.41 ± 7.49	50.12 ± 6.92	> 0.05

3.2. The postoperative contents of serum inflammatory cytokines

The levels of serum PCT of patients in the two groups at the 1st day after the surgery had no differences ($P > 0.05$), while the level of serum PCT of POI group tended to increase and the level of serum PCT of non-POI group tended to decrease at the 3rd, 5th and 7th days after the surgery. The contents of serum PCT of the two groups at the 3rd day after the surgery had no differences ($P > 0.05$), but the level of serum PCT of the POI group at the 5th and 7th days after the surgery was higher than that of the non-POI group ($P < 0.05$) (Table 2).

The levels of serum CRP, TNF-α and IL-6 of patients in the two groups had no differences at the 1st day after surgery

Table 2
The postoperative content of PCT (pg/mL).

Time	POI group (n = 14)	Non-POI group (n = 136)	P
1st day after surgery	131.51 ± 17.83	128.39 ± 16.67	> 0.05
3rd day after surgery	142.32 ± 16.95	118.49 ± 20.35	> 0.05
5th day after surgery	226.21 ± 31.37^{*ab}	46.64 ± 7.44^{ab}	< 0.05
7th day after surgery	317.54 ± 42.65^{*abc}	20.31 ± 4.28^{abc}	< 0.05

*: Compared within non-POI group at the same time point, $P < 0.05$;
^{a}: Compared within one group at the 1st day after surgery, $P < 0.05$;
^{b}: Compared within one group at the 3rd day after surgery, $P < 0.05$;
^{c}: Compared within one group at the 5th day after surgery, $P < 0.05$.

($P > 0.05$). The levels of serum CRP, TNF-α and IL-6 of POI group and non-POI group tended to decrease at the 3rd, 5th and 7th days after surgery, but the levels of these items of the two groups at the 3rd, 5th and 7th days after surgery had no differences ($P > 0.05$) (Tables 3–5).

Table 3
The content of serum CRP after surgery (mg/L).

Time	POI group (n = 14)	Non-POI group (n = 136)	P
1st day after surgery	23.48 ± 4.58	24.19 ± 3.95	> 0.05
3rd day after surgery	30.14 ± 4.28^{a}	28.51 ± 4.81^{a}	> 0.05
5th day after surgery	19.15 ± 2.74^{ab}	17.29 ± 2.96^{ab}	> 0.05
7th day after surgery	14.49 ± 1.96^{abc}	10.29 ± 1.69^{abc}	> 0.05

^{a}: Compared within one group at the 1st day after surgery, $P < 0.05$;
^{b}: Compared within one group at the 3rd day after surgery, $P < 0.05$;
^{c}: Compared within one group at the 5th day after surgery, $P < 0.05$.

Table 4
The content of serum TNF-α after surgery (μg/mL).

Time	POI group (n = 14)	Non-POI group (n = 136)	P
1st day after surgery	182.23 ± 20.15	170.18 ± 24.12	> 0.05
3rd day after surgery	177.76 ± 19.18	158.64 ± 20.36	> 0.05
5th day after surgery	133.28 ± 18.59 ^{ab}	119.34 ± 20.33 ^{ab}	> 0.05
7th day after surgery	93.50 ± 10.29 ^{abc}	84.11 ± 9.39 ^{abc}	> 0.05

^{a}: Compared within one group at the 1st day after surgery, $P < 0.05$;
^{b}: Compared within one group at the 3rd day after surgery, $P < 0.05$;
^{c}: Compared within one group at the 5th day after surgery, $P < 0.05$.

Table 5
The content of serum IL-6 after surgery (μg/mL).

Time	POI group (n = 14)	Non-POI group (n = 136)	P
1st day after surgery	78.21 ± 9.33	80.14 ± 10.17	> 0.05
3rd day after surgery	73.24 ± 10.28	75.21 ± 9.28	> 0.05
5th day after surgery	50.22 ± 9.51^{ab}	46.78 ± 6.58^{ab}	> 0.05
7th day after surgery	32.29 ± 5.28^{abc}	28.39 ± 4.48^{abc}	> 0.05

^{a}: Compared within one group at the 1st day after surgery, $P < 0.05$;
^{b}: Compared within one group at the 3rd day after surgery, $P < 0.05$;
^{c}: Compared within one group at the 5th day after surgery, $P < 0.05$.

4. Discussion

CRP, TNF-α and IL-6 are the common indexes which are used in clinic to evaluate the degree of inflammatory reaction, and the contents of these inflammatory mediators in serum are consistent with the inflammatory reaction. CRP is the acute-phase protein compounded and secreted by liver. When the organism is hurt, infected or shows inflammatory reactions, the compounding contents of CRP will increase rapidly, and the content of serum CRP will raise 10 times or more within several hours[13,14]. The content of serum CRP of patients with colon cancer were analyzed and confirmed that the contents of serum CRP of patients in POI group and non-POI group at the 3rd day after surgery were all higher than those at the 1st day after surgery, while it gradually decreased at the 5th and 7th days after surgery. This showed that the trauma of the organism caused by the surgery will aggravate the inflammatory reaction and the compound and the secretion of CRP, and the content of serum CRP was elevated at first and then decreased in the process of recovery after the surgery. The contents of serum CRP of the two groups were further compared and no statistical differences was found, which indicated that the changes of the content of CRP were mainly related to the trauma caused by the surgery, and the intestinal obstruction will not cause the changes of the content of CRP. Therefore, the content of serum CRP cannot predict the intestinal obstruction after the surgery of colon cancer.

TNF-α and IL-6 are the inflammatory cytokines with multi-biological functions *in vivo*, which participate in the activation and amplification of the inflammatory reaction. The origin of TNF-α and IL-6 is the activated mononuclear macrophage and its serum content is changed on the early stage of inflammatory reaction[15,16]. TNF-α can not only mediate the inflammatory reaction directly to injure the tissues, but also can cause the cascade amplification of the inflammatory reaction[17]. IL-6 participates in the adjustment of the inflammatory reaction and immune reaction, which can not only gather inflammatory cell and amplify the inflammatory reaction, but can facilitate the proliferation and the activation of B cells and increase the compound and the secretion of the antibody[18]. The contents of serum TNF-α and IL-6 of patients with colon cancer were analyzed and confirmed that the contents of serum TNF-α and IL-6 of the two groups decreased gradually after the surgery, and the contents of them in the two groups had no statistical differences. This indicated that the intestinal obstruction after the surgery of colon cancer would not cause the changes of the contents of TNF-α and IL-6. Similar to the content of CRP, the detection of the contents of serum TNF-α and IL-6 cannot predict the intestinal obstruction after the surgery of colon cancer.

PCT is the precursor substance of calcitonin, which is compounded and secreted by C cells in the medullary thyroid. The content of serum PCT under the physiological condition of healthy people is quite low, which is usually lower than 0.05 ng/mL. The hepatic cells and the cells of other parenchymal organs become the main origins of serum PCT, when the organism is injured and infected[19]. Because the parenchymal organs compound a plenty of PCT and the expression of hydrolytic enzymes that needed to the subsequent transformation hasn't increased, the content of PCT would increase obviously. The important mechanism of the intestinal obstruction after the surgery is the infiltration of the inflammatory cells in the basic

bowel wall, which presents as aseptic inflammation, and PCT plays an important role in this process[19,20]. The content of serum PCT of patients with colon cancer was analyzed and confirmed that the level of serum PCT of POI group at 3rd, 5th and 7th days after the surgery was gradually increased and that of the non-POI group was gradually decreased, which indicated that the intestinal obstruction after the surgery of colon cancer was closely related to the changes of the content of PCT. The differences of the serum PCT of the two groups were further analyzed and came out that the contents of serum PCT of patients in the two groups at the 3rd day after the surgery had no differences, but the contents of POI group at the 5th and 7th days after the surgery were higher than those of the non-POI group, which indicated that the intestinal obstruction after the surgery of colon cancer can be predicted through monitoring the content of serum PCT after the surgery.

In conclusion, the raise of the serum PCT content can be used as the laboratory index to predict the acute intestinal obstruction after the surgery of colon cancer.

Conflict of interest statement

The author reports no conflict of interest.

References

[1] Oh HK, Ihn MH, Son IT, Park JT, Lee J, Kim DW, et al. Factors associated with failure of enhanced recovery programs after laparoscopic colon cancer surgery: a single-center retrospective study. *Surg Endosc* 2016; **30**(3): 1086-93.

[2] Borreman P, Vangertruyden G, Houben B. Severe acute postoperative gastric dilatation. *Acta Chir Belg* 2015; **115**(3): 232-3.

[3] Moghadamyeghaneh Z, Hwang GS, Hanna MH, Phelan M, Carmichael JC, Mills S, et al. Risk factors for prolonged ileus following colon surgery. *Surg Endosc* 2016; **30**(2): 603-9.

[4] Robb WB, Mariette C. Strategies in the prevention of the formation of postoperative adhesions in digestive surgery: a systematic review of the literature. *Dis Colon Rectum* 2014; **57**(10): 1228-40.

[5] Xu C, Chi P. [Relevant factor analysis on postoperative ileus following radical resection for colorectal cancer]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2014; **17**(4): 361-4. Chinese.

[6] Hussain AS, Warrier R, Papaconstantinou HT. Small bowel intussusception causing a postoperative bowel obstruction following laparoscopic low anterior resection in an adult. *Proc (Bayl Univ Med Cent)* 2014; **27**(2): 128-30.

[7] Procacciante F, De Luca M, Abilaliaj V, Chiaretti M, Diamantini G. Post-operative ileus in hemicolectomy for cancer: open versus laparoscopic approach. *Ann Ital Chir* 2013; **84**(5): 557-62.

[8] Miłek T, Ciostek P. Implantation of a new enteral stent in obstructive colorectal cancer using interventional radiology in patients over 70 years of age. *Wideochir Inne Tech Maloinwazyjne* 2015; **10**(2): 155-60.

[9] Morais TC, Arruda BR, de Sousa Magalhães H, Trevisan MT, de Araújo Viana D, Rao VS, et al. Mangiferin ameliorates the intestinal inflammatory response and the impaired gastrointestinal motility in mouse model of postoperative ileus. *Naunyn Schmiedeb Arch Pharmacol* 2015; **388**(5): 531-8.

[10] Wu Z, Boersema GS, Dereci A, Menon AG, Jeekel J, Lange JF. Clinical endpoint, early detection, and differential diagnosis of postoperative ileus: a systematic review of the literature. *Eur Surg Res* 2015; **54**(3–4): 127-38.

[11] Su'a BU, Hill AG. Perioperative use of chewing gum affects the inflammatory response and reduces postoperative ileus following major colorectal surgery. *Evid Based Med* 2015; **20**(5): 185-6.

[12] Costes LM, van der Vliet J, Farro G, Matteoli G, van Bree SH, Olivier BJ, et al. The spleen responds to intestinal manipulation but does not participate in the inflammatory response in a mouse model of postoperative ileus. *PLoS One* 2014; **9**(7): e102211.

[13] Gavela T, Cabeza B, Serrano A, Casado-Flores J. C-reactive protein and procalcitonin are predictors of the severity of acute appendicitis in children. *Pediatr Emerg Care* 2012; **28**(5): 416-9.

[14] Fujii T, Sutoh T, Kigure W, Morita H, Katoh T, Yajima R, et al. C-reactive protein level as a possible predictor for early postoperative ileus following elective surgery for colorectal cancer. *Hepatogastroenterology* 2015; **62**(138): 283-5.

[15] Lin YM, Li F, Shi XZ. Mechanical stress is a pro-inflammatory stimulus in the gut: *in vitro, in vivo* and *ex vivo* evidence. *PLoS One* 2014; **9**(9): e106242.

[16] Quirino IE, Carneiro MB, Cardoso VN, das Graças Carvalho Dos Santos R, Vieira LQ, Fiuza JA, et al. Arginine supplementation induces arginase activity and inhibits TNF-α synthesis in mice spleen macrophages after intestinal obstruction. *JPEN J Parenter Enter Nutr* 2016; **40**(3): 417-22.

[17] Condino G, Calabrese E, Zorzi F, Onali S, Lolli E, De Biasio F, et al. Anti-TNF-alpha treatments and obstructive symptoms in Crohn's disease: a prospective study. *Dig Liver Dis* 2013; **45**(3): 258-62.

[18] Buchholz BM, Chanthaphavong RS, Billiar TR, Bauer AJ. Role of interleukin-6 in hemopoietic and non-hemopoietic synergy mediating TLR4-triggered late murine ileus and endotoxic shock. *Neurogastroenterol Motil* 2012; **24**(7): 658-69.

[19] Zhu P, Liang Z, Fu J, Chen W, Wang Z, Jiang H, et al. Procalcitonin in abdominal exudate to predict prolonged postoperative ileus following colorectal carcinoma surgery. *Int J Biol Markers* 2013; **28**(2): 187-91.

[20] Meyer ZC, Schreinemakers JM, Mulder PG, Schrauwen L, de Waal RA, Ermens AA, et al. Procalcitonin in the recognition of complications in critically ill surgical patients. *J Surg Res* 2014; **187**(2): 553-8.