Original Article

Hypoalbuminemia is a predictor of delayed postoperative bowel function and poor surgical outcomes in right-sided colon cancer patients

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Purpose: To determine the relationship between preoperative serum albumin and postoperative bowel function as well as surgical outcomes in right-sided colon cancer patients.
Methods: This retrospective study in a university hospital included 84 patients who underwent elective right hemicolectomy for adenocarcinoma of the right-sided colon between January 2004 and December 2005. The patients had a preoperative serum albumin assessment. Serum albumin less than 3.5 g/dL was regarded as hypoalbuminemia. Postoperative outcomes were classified into mortality, morbidity (infectious and noninfectious complications), time to first bowel movement, time to resume normal diet, and hospital stay.
Results: Forty males (48%) and forty-four females (52%) with a mean age of 64 (range, 27-89) years were included. Forty-eight patients (57%) had hypoalbuminemia. No 30-day postoperative mortality occurred. All 14 postoperative complications occurred in hypoalbuminemic cases. Therefore, 29% of the hypoalbuminemics had complications whereas none occurred in nonhypoalbuminemics (p=0.001). In univariate analysis, hypoalbuminemia and postoperative complications were the risk factors for delayed postoperative recovery of bowel function and prolonged length of hospital stay. In multivariate analysis, hypoalbuminemia was the significant risk factor for postoperative complications (p<0.001) and delayed time to first bowel movement (p=0.018) whereas postoperative complications were the significant risk factor for delayed time to resume normal diet (p<0.001) and prolonged hospital stay (p<0.001).
Conclusion: Hypoalbuminemia is a potential predictor of delayed recovery of bowel function postoperatively and significantly associated with postoperative complications in right-sided colon cancer patients undergone right hemicolectomy.

Key Words: hypoalbuminemia, colectomy, postoperative complications, ileus, nutrition

Introduction

Malnutrition is usually found in patients with gastrointestinal malignancy including colon cancer.[1] Serum albumin is one of the biochemical parameters commonly used in nutritional assessment.[2] Hypoalbuminemia (serum albumin less than 3.5 g/dL) often reflects malnourishment in the patients.[3] Malnourished patients have a higher risk of mortality, complications and prolonged hospital stay.[4,5] Colectomy is one of the leading procedures in surgical oncology. However, there is no report about the effect of hypoalbuminemia on postoperative bowel function after colectomy for colon cancer.

The aim of this study is to determine the relationship between preoperative serum albumin and postoperative bowel function as well as surgical outcomes in right-sided colon cancer patients who underwent right hemicolectomy.

Materials and methods

We carried out a retrospective study of patients with adenocarcinoma of right-sided colon who underwent right hemicolectomy between January 2004 and December 2005 at the Department of Surgery, Siriraj Hospital, Bangkok, Thailand. Patients with the American Society of Anesthesiologists status (ASA) class I to III underwent elective and curative procedures were included. The curative procedures are defined as no macroscopic residual tumor at the end of operation with preoperative and intraoperative tumor staging revealing no evidence of distant metastasis.

Patients would be excluded from the study for one of the following reasons: no preoperative mechanical bowel preparation, laparoscopic colectomy, palliative tumor resection, adjacent organ resection, previous intra-abdominal surgery, recurrent tumor, immunocompro mised

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host, cirrhosis or jaundice, antiplatelet drug or anticoagulant usage, and acute complicated conditions such as colonic obstruction or perforation.

The patients were interviewed for medical history and obtained a thorough physical examination. The preoperative tumor staging studies included barium enema, complete colonoscopy with biopsy, chest x-ray, liver ultrasonography or CT scan of upper abdomen, and serum chemistry. Each patient had preoperative serum albumin assessment. Serum albumin less than 3.5 g/dL was regarded as hypoalbuminemia.

Each patient underwent preoperative mechanical bowel preparation using 2 litres of polyethelene glycol a day prior to surgery. In the operating room, all patients received general anesthesia. Intravenous prophylaxis antibiotics were administrated. After abdominal exploration through a midline incision, we performed a standard oncological right hemicolectomy with high vessel ligation and wide excision. Either hand-sewn or stapled ileocolonic anastomosis was done. A nasogastric tube was inserted at the surgeon's discretion.

Routine postoperative care was provided to each patient. Time to first bowel movement (passing flatus) was recorded by nursing staff. The patients were allowed to have oral fluid if passing flatus. Resumption of normal diet was determined by the surgeon and, in turn, the patient's compliance. Patients were discharged from hospital if they had no fever, good appetite and were ambulant. All patients were scheduled for follow-up at 30 days postoperatively.

Data were recorded included patient demographics, operative details (operative time, blood loss), pathological staging and postoperative outcomes. Postoperative outcomes, including mortality, morbidity (infectious and noninfectious complications), time to first bowel movement, time to resume normal diet, and hospital stay were analyzed.

All data were prepared and complied using the SPSS computer program (version 10.0 for Windows). Means and standard deviations were assessed. Kolmogorov-Samirnov test was used to test for the pattern of data distribution. Student's unpaired t-test was used to compare data between the two groups when they were normally distributed. The Mann-Whitney U test was used when the data were not normally distributed. Chi-square test and Fisher's exact test were used for quantitative data. Stepwise Regression Analysis was used for multivariate analysis in order to determine any confounding factors. A *p*-value of less than 0.05 was considered statistically significant.

Results

One hundred and twelve patients were enrolled. In accordance with exclusion criteria, eighty-four patients were left for the study. There were forty males (48%) and forty-four females (52%) with a mean age of 64 (range, 27-89) years. Forty-eight patients (57%) had hypoalbuminemia.

No demographic data or intraoperative findings, except age, were statistically different between the hypoalbuminemic and nonhypoalbuminemic groups as shown in Table 1.

No thirty-day postoperative mortality occurred in this study. Infectious complications were diagnosed in 11 patients; seven superficial surgical site infections, two pneumonias, one urinary tract infection and one anasto-

Table 1. Demographic data and intraoperative findings in nonhypoalbuminemic and hypoalbuminemic patients (mean ± SD)

	Nonhypoalbuminemic (n=36)	Hypoalbuminemic (n=48)	*p*-value
Age (years)	59.0 ± 15.8	67.1 ± 10.9 *	0.01
Male (%)	55.6	41.7	0.30
Body mass index	20.5 ± 2.8	21.2 ± 3.2	0.29
Operative time (min)	141.6 ± 62.2	153.6 ± 52.9	0.34
Blood loss (mL)	107.5 ± 96.5	127.6 ± 82.6	0.31
Pathological staging (%)			0.89
Stage 1	8.3	10.4	
Stage 2	30.6	31.3	
Stage 3	61.1	31.3	

* $p \leq 0.05$

Table 2. Univariate analysis of surgical outcomes (mean ± SD)

	Nonhypoalbuminemic (n=36)	Hypoalbuminemic (n=48)	*p*-value
Postoperative complications	0	14 **	0.001
Time to first bowel movement (hr)	55.3 ± 22.8	69.5 ± 29.0 *	0.018
Time to resume normal diet (days)	4.0 ± 1.1	4.9 ±1.9 *	0.011
Length of hospital stay (days)	6.8 ± 2.6	9.6 ± 4.7 **	0.001

* $p \leq 0.05$, ** $p \leq 0.01$

motic leakage. Three patients developed noninfectious complications during hospitalization; two acute renal failure and one peri-operative myocardial infarction. All of the 14 complications occurred in hypoalbuminemic patients. Therefore, 29% of the hypoalbuminemics had complications whereas none occurred in nonhypoalbuminemics (p=0.001). Regardless of pathological stage, time to first bowel movement, time to resume normal diet and postoperative hospitalization in hypoalbuminemic patients was significantly longer than nonhypoalbuminemic patients as shown in Table 2.

In univariate analysis, hypoalbuminemia and postoperative complications were the risk factors for delayed postoperative recovery of bowel function and prolonged length of hospital stay. In multivariate analysis, hypoalbuminemia was the significant risk factor for postoperative complications (p<0.001) and delayed time to first bowel movement (p=0.018) whereas postoperative complications were the significant risk factor for both delayed time to resume normal diet (p<0.001) and prolonged hospital stay (p<0.001).

Discussion

Malnutrition is a common problem in cancer patients that adversely affects surgical outcomes. The potential contributors to malnutrition in colon cancer patients are multiple including insufficient food and nutrient intakes, impairment of nutrient absorption, and increased catabolism. There are many tools to assess patient's nutritional status, ranging from clinical appraisal to anthropometric and various laboratory investigative measures or analyses. Serum albumin is a good and simple predictor of surgical risk and has a close correlation with the degree of malnutrition.[3] Albumin has a long metabolic half life of 20 days, so metabolic effects on its concentration reflect prolonged malnourishment as in cancer patients. Malnourished cancer patients have commonly increased whole protein turnover and subsequent body nitrogen loss.[6] Tumor induced inflammatory responses, such as increment of tumor necrosis factor and interleukin-6, also lead to impairment of hepatic protein synthesis.[7]

In our study, we chose only patients who underwent right hemicolectomy for adenocarcinoma to analyze the association of pre-operative serum albumin and postoperative bowel function because the extent of oncological resection is quite uniform and the ileoceacal valve was removed. In univariate analysis, we found that hypoalbuminemia was significantly associated with delayed recovery of postoperative bowel function

We hypothesize that the delayed recovery of bowel function in hypoalbuminemic patients may be for at least three reasons. The first one is reduced synthesis of gut hormones, such as motilin and cholecystokinin in hypoalbuminemic patients.[8] The second is impairment of enterocyte and colonocyte regeneration in severely malnourished patients.[9, 10] The third is that hypoalbuminemia may result in anastomotic swelling and edema of the intestinal wall.[11] However, attempts to shorten the duration of ileus by the early postoperative infusion of albumin to restore normal serum albumin concentrations in postaortic surgery patients do not show any beneficial effect.[12]

In multivariate analysis, only delayed time to first bowel movement was associated with preoperative hypoalbuminemia whereas delayed time to resume normal diet and prolonged length of hospital stay were associated with postoperative complications. This may be explained by the mechanism that postoperative complications, especially infection, lead to impaired bowel function via mediators of systemic inflammatory response as the second stressful condition. In addition, the complications directly result in prolonged hospital stay.

Malnutrition also impairs cell mediated immunity and resistance to infection.[13] In hypoalbuminemia, alteration in cytokine metabolism especially impairs interleukin-1 activity and defects in the complement system have also been detected. Therefore, in the hypoalbuminemic group, surgical site infections and remote infections such as pneumonia were commonly found.

Malnutrition has an adverse effect on colonic healing which may present with anastomotic leakage. Low serum albumin concentration is associated with decreased collagen content of anastomoses and lower colonic bursting pressures.[14, 15] Testini *et al* demonstrated that hypoalbuminemia is one of the risk factors for anastomotic dehiscence in colorectal surgery and healing remains a process depending more on the patient than on any aspect of the surgical technique.[16]

In hypoalbuminemic patients, acute renal failure commonly occurred in postoperative period especially associated with massive blood loss. Serum albumin is responsible for 75–80% of the plasma colloid osmotic pressure (COP). Albumin is thus the major determinant of the plasma COP component of Starling's equation for fluid flux across the capillary wall.[7] Inadequate fluid replacement and low plasma COP lead to insufficient intravascular volume and poor splanchnic blood supply. Many investigations, however, do not support the correction of albumin as useful, either on the basis of plasma COP changes or on outcome.[17, 18]

Conclusion

Hypoalbuminemia is a potential predictor of delayed recovery of bowel function postoperatively and significantly associated with postoperative complications in right-sided colon cancer patients undergone right hemicolectomy. Its causes are almost certainly multiple in the clinical setting studied and it is attention to these which may improve prognosis. In the meantime, correction of established hypoalbuminemia by albumin infusion cannot be shown to improve outcomes.

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低血清白蛋白是右側結腸癌病人術後大腸功能延遲及不良手術結果之預測因子

目的：探討右側結腸癌病人術前血清白蛋白與術後大腸功能及手術結果之相關。
方法：這個回溯性研究是在大學醫院進行，共有 84 名病人在 2004 年 1 月至 2005 年 12 月完成右側結腸腺癌的選擇性右側大腸切除。病人經過術前血清白蛋白評估，低於 3.5g/dL 視為低白蛋白血症。術後結果分為死亡、疾病(感染與非感染併發症)、第一次排便時間、第一次恢復正常飲食時間及住院天數。
結果：有 40 名男性(48%)及 44 名女性(52%)參與研究，平均年齡為 64 歲(範圍 27-89 歲)。48 名病人(57%)有低白蛋白血症。沒有 30 天術後死亡的情形發生。14 名有術後併發症者均為低白蛋白血症的病例。因此，有 29%的低白蛋白血症者有併發症，反之非低白蛋白血症者則未發生(p<0.001)。單變項分析發現，低白蛋白血症與術後併發症為延遲術後大腸功能恢復及延長住院天數的危險因子。多變項分析中，低白蛋白為術後併發症(p<0.001)及延後第一次排便時間(p=0.018)的顯著危險因子，而術後併發症為延後恢復正常飲食時間(p<0.001)及延長住院天數(p<0.001)的危險因子。
結論：低白蛋白血症是右側結腸病人完成右側大腸切除後，延後術後大腸功能恢復的潛在預測因子，並與術後併發症有顯著相關。

關鍵字：低白蛋白血症、結腸切除術、術後併發症、腸阻塞、營養。