นิพนธ์ต้นฉบับ

การใช้ตัวชี้วัดทางภาวะโภชนาก่อนผ่าตัดเพื่อติดตามการฟื้นตัวหลังผ่าตัด ในผู้ป่วยมะเร็งกระเพาะปัสสาวะที่เข้ารับการผ่าตัดกระเพาะปัสสาวะออกทั้งหมด

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างระดับ prealbumin ในเลือดก่อนผ่าตัดกับภาวะฟื้นตัว และภาวะแทรกซ้อนที่เกิดขึ้นหลังผ่าตัด ในผู้ป่วยมะเร็งกระเพาะปัสสาวะที่รับการรักษาโดยการผ่าตัดกระเพาะปัสสาวะออกทั้งหมด และทำทางเดินปัสสาวะเทียม ในโรงพยาบาลศิริราช

ผู้ป่วยและวิธีการศึกษา: ใช้การศึกษาแบบ cohort study โดยมีกลุ่มผู้ป่วยมะเร็งกระเพาะปัสสาวะที่เข้ารับการผ่าตัดกระเพาะปัสสาวะออกทั้งหมดและทำทางเดินปัสสาวะเทียมในโรงพยาบาลศิริราช ระหว่างเดือนกันยายน 2555 ถึงเดือนกรกฎาคม 2557 จำนวนทั้งสิ้น 45 รายเป็นกลุ่มการศึกษา ข้อมูลที่ศึกษานำมากจากเวชระเบียนผู้ป่วยใน โดยมีการบันทึกตัวแปรทางภาวะโภชนาการก่อนรับการผ่าตัดได้แก่ ระดับ prealbumin และ albumin ในเลือด ค่าดัชนีมวลกาย เป็นต้น ซึ่งค่า prealbumin ในเลือดที่น้อยกว่า 18 mg/dL ถือว่าเป็นกลุ่มที่มีระดับ prealbumin ในเลือดต่ำ เพื่อนำไปหาความสัมพันธ์กับภาวะฟื้นตัว และภาวะแทรกซ้อนในระหว่างนอนโรงพยาบาลของผู้ป่วยหลังผ่าตัด

ผลการศึกษา: ผู้ป่วยที่ผ่านเกณฑ์เพื่อศึกษา 40 ราย เป็นเพศชาย 34 ราย และเพศหญิง 6 ราย มีอายุเฉลี่ย 64.89 ปี ผู้ป่วยที่มีค่าระดับ prealbumin ในเลือดก่อนผ่าตัดที่นำไปศึกษาได้จำนวน 36 ราย เป็นกลุ่มที่มีระดับ prealbumin ต่ำ จำนวน 12 ราย ในการวิเคราะห์ univariate analysis พบว่า กลุ่มที่มีระดับ prealbumin ในเลือดต่ำก่อนผ่าตัด มีแนวโน้มใช้เวลาในการฟื้นตัวหลังผ่าตัด (เวลาที่สามารถเริ่มรับประทานอาหาร, เริ่มขับถ่ายอุจจาระได้) นานกว่ากลุ่มที่มีระดับ prealbumin ปกติ แต่ไม่มีนัยสำคัญทางสถิติ โดยภาวะแทรกซ้อนในระหว่างนอนโรงพยาบาลของผู้ป่วยที่ระดับ prealbumin ต่ำนั้นมีมากกว่ากลุ่มที่มีระดับ prealbumin ในเลือดปกติอย่างมีนัยสำคัญทางสถิติ (IRR = 2.25, p = 0.004, 95%CI 1.25-4.07)

สรุป: ระดับ prealbumin ในเลือดก่อนผ่าตัดส่งผลต่อผลการผ่าตัด โดยที่ระดับ prealbumin ในเลือดที่ต่ำสัมพันธ์การภาวะแทรกซ้อนที่มากขึ้นในผู้ป่วยมะเร็งกระเพาะปัสสาวะที่รับการรักษาโดยการผ่าตัดกระเพาะปัสสาวะออกทั้งหมดและทำทางเดินปัสสาวะเทียมในโรงพยาบาลศิริราช

คำสำคัญ: มะเร็งกระเพาะปัสสาวะ การผ่าตัดกระเพาะปัสสาวะออกทั้งหมด albumin ในเลือด

Original article

Nutritional Markers that Predict Postoperative Outcomes in Patients who undergo Major Urological Operations.

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Abstract

Objective: To determine the impact of serum prealbumin and postoperative outcomes in patients who underwent radical cystectomy for bladder cancer and urinary diversion using intestinal segments.

Material and Methods: A cohort study of 45 patients who underwent radical cystectomy with urinary diversion at Siriraj Hospital between September 2012 and July 2014. Nutritional variables included prealbumin, albumin, and body mass index (BMI). Patients with preoperative prealbumin less than 18 mg/dL were considered to be in the hypoprealbuminemia group. Postoperative recovery parameters and complications were obtained in order to investigate outcomes.

Result: Forty of 45 patients (89%) were eligible for this study. Thirty-four males (85%) and 6 females (15%) were included with at mean age of 64.8 ($\pm$9) years old. Thirty-six patients had a preoperative prealbumin level. Twelve patients (33%) had hypoprealbuminemia. In univariateanalysis, postoperative complications were higher in patients who had hypoprealbuminemia than in the other groups (IRR = 2.25, p = 0.003, 95%CI 1.25-4.07). Although the postoperative recovery period was longer in patients with hypoprealbuminemia, this finding is not statistically significant.

Conclusion: Serum prealbumin has an impact on postoperative outcomes. Low levels of prealbumin correlate with overall complications.

Keywords: bladder cancer, radical cystectomy, serum albumin

Introduction

Bladder cancer is one of most common genitourinary cancers and the fourth most common cancer in males. There are approximately 74,690 new cases of urinary bladder cancer annually in the USA[1]. In Thailand, the incidence rate of bladder cancer is 4.6 and 1.1 per 100,000 of population in males and females, respectively[2]. Radical cystectomy with urinary diversion is a standard treatment for patients with muscle invasive bladder cancer[3]. However, this extensive surgical procedure causes high rates of postoperative complications[4]. Nutritional deficiency is a well known risk factor for postoperative complications. Historically, albumin levels have been used to determine of nutritional status. At present, prealbumin is a marker for protein malnutrition; it has a shorter half-life (2 day) than albumin and can represent acute illness[5].

The aim of this study is to determine the impact of serum prealbumin and postoperative outcomes in patients who underwent radical cystectomy with urinary diversion using intestinal segments for bladder cancer.

Materials and Methods

We performed a prospective cohort study of 45 patients with bladder cancer who underwent radical cystectomy with urinary diversion between September 2012 and July 2014 at the Division of Urology, Siriraj Hospital, Bangkok, Thailand. The following patients were excluded from this study: (1) those with severe cirrhosis, Child Pugh B or C; (2) those who receieved preoperative corticosteroid therapy, and (3) those with cutaneous ureterostomy urinary diversion-type.

Patient demographic data and postoperative outcomes were reviewed from medical records. Each patient had a preoperative serum prealbumin, albumin and other nutritional variables assessment. Serum prealbumin less than 18 mg/dL was regarded as hypoprealbuminemia, while albumin less than 3.5 g/dL was defined as the hypoalbumin group. Data were recorded, including patient characteristics, operative details (operative time, blood loss), and pathological staging. Postoperative outcomes, including recovery parameters such as time to start feeding, time to pass stool, time to resume normal diet, postoperative stay and intrahospital postoperative complications, were analyzed. The definitions of postoperative complications are shown in Table 1.

The data were analyzed with SPSS ver.22 and STATA Ver.11. We used student's unpaired T-test and the Mann Witney U test to compare the continuous data between the two groups; the chi-square test and Fisher exact test were used to determine any correlation between the variables and postoperative outcomes. P-value less than 0.05 was considered to be statistically significant.

Results

Forty-five patients were enrolled. In accordance with the exclusion criteria, forty patients remained in the study. There were thirty-four males (85%) and six females (15%) with a mean age of 64.8$\pm$9 years. Thirty-six patients had a preoperative prealbumin level, and twelve patients (33%) had hypoprealbuminemia. The overall patient demographic data are shown in Table 2. No demographic data or intraoperative details were statistically different between the hypoprealbumin and normoprealbumin groups as shown in Table 3. In univariate analysis, the postoperative recovery period including time to start feeding, time to

pass stool and postoperative stay were higher in patients with hypoprealbuminemia than those in another group, but no statistical significance was determined as shown in Table 4. No postoperative intrahospital mortality occurred in this study. Total number of complications recoded was fifty-eight events, and the most frequent complications were non-infectious. Eleven infectious complications were diagnosed: five urinary tract infections, three bacteremia or sepsis, two wound complications and one pulmonary infection as shown in Table 5. Incidents of electrolyte abnormality that required intervention in the hypoprealbumin group were higher than in the normoprealbumin group as shown in table 6. The incidence rate of postoperative complications in hypoprealbuminemic patients was higher than in the normal groups, with statistical significance (IRR = 2.25, 95%CI = 1.25-4.07, P = 0.004), whereas in the hypoalbuminemic group, no difference in the incidence rate of complications could be demonstrated (IRR = 1.56, 95%CI = 0.85-2.79, P = 0.113) as shown in Table 7.

Discussion

Nutritional deficiency is a common problem in cancer patients that adversely affects surgical outcomes[6]. Malnutrition also impairs cell mediated immunity and resistance to infection[7]. Nutritional status can be measured by preoperative weight loss, BMI, and nutritional biological markers[8]. Serum albumin is a good and simple predictor of surgical risk and has a correlation with the degree of malnutrition.

Lohsiriwat[8], et al. studied hypoalbuminemia in colon cancer patients who underwent right hemicolectomy, and proposed that hypoalbuminemia is a potential predictor of delayed recovery of bowel function postoperatively and significantly associated with postoperative complications.

Limitation of the albumin is relatively large body pool and a half life of 20 days that do not fully reflect short term malnutrition. Prealbumin may be used as a marker with a higher sensitivity for screening patients with a high risk of malnutrition due to a short half-life (2 days),

Table 1. Definitions of postoperative complications

	Complications	Definition
Infectious Complication	Urinary tract infection	Confirm by urine culture, urinalysis
	Bacteremia, sepsis	Confirm by blood culture
	Wound complication	Seroma, hematoma, dehiscence, wound infection requiring wound repair
	Pulmonary infection	Pneumonia, bronchiolitis, etc
Non-infectious Complication	Intestinal obstruction	No gas passage or other symptom suspected intestinal obstruction, the findings of suspected mechanical obstruction
	Ileus	Vomitting during meals after surgery or difficulty with diet progression, the findings of suspected paralytic obstruction
	Bleeding	Requiring blood transfusion or intervention
	Pulmonary complication	Atelectasis, pleural effusion, respiratory failure
	Renal complication	Acute renal failure
	Neurovascular	Cerebrovascular accident, deep vein thrombosis, Neurapraxia
	Electrolyte abnormality	Requiring intervention

Table 2. Overall baseline characteristics

Variable	
Age, yr, mean (±S.D)	64.8 (±9.0)
Gender, no(%)	
Male	34 (85)
Female	6 (15)
BMI, mean (±S.D.)	22.5 (±4.9)
Type of surgery, no(%)	
Open	30 (75)
Laparoscopic	10 (25)
Type of diversion, no(%)	
Ileal conduit	33 (82.5)
Neobladder 7 (17.5)	
Prealbumin, mg/dL (±S.D.)	21.4 (±7.1)
Albumin, g/dL (±S.D.)	3.7 (±0.4)
Blood loss, ml, median (range)	1,075 (100-5500)
Time to start feeding, day, mean (±S.D.)	3.9 (±1.7)
Time to resume normal diet, day, median(range)	6 (3-33)
Post operativestay, day, mean (±S.D.)	15.6 (±6.5)

Table 3. Demographic data and operative finding in hypoprealbuminemia and normoprealbuminemia

	Hypoprealbumin n = 12	Normoprealbumin n = 24	P-value
Age, yr, mean (±S.D.)	64.2 (±11)	65.5 (±8.2)	0.94
Gender, no (%)			0.55
Male	10 (83.3)	21 (87.5)	
Female	2 (16.7)	3 (12.5)	
BMI, mean (±S.D.)	21.4 (±5.7)	22.4 (±3.9)	0.39
Type of surgery, no (%)			0.67
Open	9 (75)	18 (75)	
Laparoscopic	3 (25)	6 (25)	
Type of diversion, no (%)			0.43
Ileal conduit	9 (75)	20 (83.3)	
Neobladder	3 (25)	4 (16.7)	
Operativetime, min, mean (±S.D.)	379 (±157)	374 (±124)	0.89
Blood loss, ml, median (range)	975 (100-2,350)	1025 (300-5,500)	0.60

which is not affected by hydrational status and lower body pool than albumin. This study showed six patients (50%) in the hypoprealbumin group, but they had normal serum albumin levels. The normal range of prealbumin level was 15-46 mg/dL, but varied due to different centers. Bae[9], et al. used prealbumin less than 18 mg/dL as a marker for predicting complications, especially infectious complications after surgery, in patients who underwent gastric surgery due to benign or malignant gastric disease. In our study, we chose to study postoperative bowel recovery function in only patients who underwent radical cystectomy with urinary diversion using intestinal segments.

Table 4. Univariate analysis of post-operative outcomes

	Hypoprealbumin n = 12	Normoprealbumin n = 24	P-value
Time to start feeding, day, mean (±S.D.)	5 (±2.6)	3.6 (±0.8)	0.15
Time to pass stool, day, mean (±S.D.)	6.2 (±1.9)	5.5 (±1.4)	0.35
Time to resume normal diet, day, median (range)	6 (4-33)	6 (3-14)	0.37
Post operativestay, day, mean (±S.D.)	17 (±9.9)	15.4 (±4.7)	0.86
Post operative blood transfusion, n (%)	4 (33.3)	5 (20.8)	0.34
	Hypoalbumin n = 11	**Normoalbumin n = 28**	**P-value**
Time to start feeding, day, mean (+S.D.)	4.5 (+2)	3.8 (+1.8)	0.53
Time to pass stool, day, mean (+S.D.)	5.7 (+1.3)	5.6 (+1.8)	0.70
Time to resume normal diet, day, median (range)	6 (4-10)	5.5 (3-33)	0.30
Post operativestay, day, mean (+S.D.)	15 (+6.5)	15.6 (+6.6)	0.61
Post operative blood transfusion, n (%)	1 (9)	9 (32.1)	0.23

Table 5. Overall post-operative complications

Complication	Number (%)
Non infection	
Electrolyte abnormality	26 (45.6)
Bleeding (required blood transfusion)	7 (12.3)
Ileus	5 (8.8)
Neurapraxia	5 (8.8)
DVT	2 (3.5)
UGIB	1 (1.8)
Infection	
UTI	5 (8.8)
Sepsis	3 (5.3)
Pulmonary infection	1 (1.8)
Wound complication	2 (3.5)
Total	57 (100)

Table 6. Univariate analysis of operative complications

	Hypoprealbumin (n=12)	Normoprealbumin (n=24)	P-value
Non infection (No.)			
Electrolyte abnormality	11	12	0.03
Bleeding (required blood transfusion)	3	3	0.38
Ileus	3	2	0.31
Neurapraxia	3	2	0.31
Deep vein thrombosis	2	0	0.11
Upper GI Bleeding	1	0	0.33
Infection (No.)			
UTI	2	2	0.59
Sepsis	2	1	0.25
Pulmonary infection	1	0	0.33
Wound complication	1	1	0.56
	Hypoalbumin (n=11)	**Normoalbumin (n=28)**	**P-value**
Non infection (No.)			
Electrolyte abnormality	10	15	0.60
Bleeding (required blood transfusion)	0	6	0.16
Ileus	2	2	0.56
Neurapraxia	1	4	1.00
Deep vein thrombosis	1	1	0.49
Upper GI Bleeding	1	0	0.28
Infection (No.)			
UTI	2	3	0.61
Sepsis	2	1	0.19
Pulmonary infection	1	0	0.28
Wound complication	0	2	1.00

Table 7. Incidence of overall postoperative complications

	Overall complication (No.)	Time (day)	Incident rate 100 person	IRR (95%CI)	P-value
Hypoprealbumin	29	207	14	2.25 (1.35-4.07)	0.004
Normoprealbumin	23	370	6.2	1	
Hypoalbumin	20	165	12.1	1.56 (0.85-2.79)	0.113
Normoalbumin	34	437	7.7	1	

We hypothesized that malnutrition status affects recovery of bowel function by reduceing the synthesis of gut hormones, impairing enterocyte regeneration, and causing anastomosis swelling or edema. Hypoprealbumin delayed the time to start feeding (5 days) compared with the normal prealbumin (3.6 days) group and the hypoalbumin group (4.8 day), but the differences do not reach statistical significance.

Geilsler[10] investigated 114 patients with ovarian cancer who underwent surgical cytoreduction, and proposed that postoperative complications increased with lower prealbumin levels. In this study, the incidence rate of complications in hypoprealbuminemic was higher than in the normal prealbumin group. Statistical significance is indicated by the serum prealbumin response that correlates with patient outcomes.

Conclusion

This study showed that preoperative serum prealbumin had an impact on postoperative outcomes. Prealbumin is a good potential predictor of postoperative complications in patients who have undergone radical cystectomy with urinary diversion using intestinal segments. A low level of prealbumin correlates with overall complications.

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