

Serum Albumin and Prealbumin Do Not Predict Recurrence in Patients with Breast Cancer

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Abstract. *Background:* We have previously reported that prealbumin and albumin may be sensitive indicators of the risk of recurrent disease in colorectal cancer; however, the relationship between preoperative prealbumin and cancer survival has not been fully-elucidated. The purpose of this study was to examine the relationship between preoperative nutritional conditions, including prealbumin and albumin concentrations, and the risk of recurrence in cases with breast cancer. *Patients and Methods:* One hundred and fifty-seven patients who underwent breast surgery were analyzed in this study. The detection limit of the prealbumin assay was 22 mg/dl; patients were divided in analytical groups of <22 mg/dl and ≥22 mg/dl. The detection limit of the albumin assay was 4.0 g/dl; patients were divided in analytical groups of <4.0 g/dl and ≥4.0 g/dl. The clinical features of these cases were reviewed according to prealbumin and albumin levels, and statistical analysis was performed. *Results:* Among 157 cases in this study, five (3.2%) had disease recurrence. Out of the eligible cases, 38 (24.2%) had decreased serum prealbumin and 19 (12.1%) had decreased serum albumin preoperatively. No statistically significant association of the preoperative prealbumin level was found with the clinicopathological variables. The only statistically significant association found for preoperative albumin level was age; age was higher in patients with low albumin levels. In short, we were unable to establish a connection between preoperative prealbumin or albumin and various clinical features, including recurrence, lymph node metastasis and tumor size. *Conclusion:* Prealbumin and albumin may be sensitive

indicators of disturbances in protein metabolism, and reflect inflammation activity and malnutrition. However, our results suggest that evaluation of serum prealbumin and albumin are not useful for predicting disease aggressiveness or recurrence in breast cancer.

Cancer frequently causes malnutrition. In recent years, the role of malnutrition as a predictor of survival in cancer has received considerable attention. There is increasing evidence to show that malnutrition is associated with poor survival in patients with various types of cancers (1-3). We have previously shown that prealbumin and albumin were sensitive indicators of the risk of recurrent disease in colorectal cancer (4). The measurement of serum albumin and prealbumin levels is easily performed, and the tests are widely used in clinical practice to predict nutritional status (5-8). Several nutritional features, including albumin, have been investigated for their possible value in predicting a poor outcome in various types of cancer (3, 9-14). The purpose of this study was to examine the relationship between preoperative nutritional condition, including prealbumin and albumin concentrations, and various clinicopathological features, as well as disease recurrence, in cases with breast cancer in order to identify possible predictors that might reflect the risk of recurrence.

Patients and Methods

One hundred and fifty-seven consecutive patients with breast cancer who underwent radical surgery at the Department of General Surgical Science, Graduate School of Medicine, Gunma University, from March 2007 to December 2013, were identified for inclusion in this study. Patients with recurrent tumors, neo-adjuvant chemotherapy, those who showed clinical signs of infection or other inflammatory conditions preoperatively, including pneumonia, and articular rheumatism, and those with incomplete clinical information were excluded from the study. Data were collected retrospectively. Informed consent was obtained from all patients. Blood samples were obtained preoperatively. The detection limit of the prealbumin assay was 22 mg/dl (15); patients were divided into analytical groups with <22 mg/dl and ≥22 mg/dl. The detection limit of the

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Key Words: Prealbumin, albumin level, breast cancer, nutrition, recurrence.

Table I. Clinicopathological characteristics and prealbumin concentration in patients with breast cancer.

Patients (n)	Prealbumin ≥22 mg/dl 119	Prealbumin <22 mg/dl 38	p-Value
Age (years, mean±SD)	58.6±11.2	58.4±15.2	0.521
Histological type (n)			0.650
Invasive ductal carcinoma	96	32	
Non-invasive ductal carcinoma	8	2	
Other	15	4	
Tumor size (mm, mean±SD)	21.4±17.5	22.3±14.2	0.393
Lymph node metastasis (n)	37 (31.1%)	15 (39.5%)	0.449
ER (n)	98 (82.4%)	32 (84.2%)	0.505
PgR (n)	90 (75.6%)	29 (76.3%)	0.560
HER2 (n)	23 (19.3%)	6 (15.8%)	0.412
Lymphatic invasion (n)	44 (37.0%)	16 (42.1%)	0.708
Vascular invasion (n)	12 (10.1%)	8 (21.1%)	0.975
Nuclear grade (n)			0.924
1/2	72	22	
3	47	16	
Albumin (g/dl, mean±SD)	4.3±0.3	4.1±0.3	0.999
CEA (ng/ml, mean±SD)	2.2±1.9	2.3±2.0	0.370
Recurrence (n)	4 (3.4%)	1 (2.6%)	0.650

ER: Estrogen receptor status; PgR: Progesterone receptor status ; HER2: human epidermal growth factor receptor 2 status; CEA: carcinoembryonic antigen.

Table II. Clinicopathological characteristics and albumin concentration in patients with breast cancer.

Patients (n)	Albumin ≥4.0 g/dl 138	Albumin <4.0 g/dl 19	p-Value
Age (years, mean±SD)	57.3±11.6	67.6±13.5	<0.001
Invasive ductal carcinoma	110	18	
Non-invasive ductal carcinoma	9	1	
Other	18	1	
Tumor size (mm, mean±SD)	22.0±17.5	18.9±9.1	0.774
Lymph node metastasis (n)	46 (33.3%)	6 (31.6%)	0.552
ER (n)	115 (83.3%)	5 (78.9%)	0.419
PgR (n)	106 (76.8%)	13 (68.4%)	0.294
HER2 (n)	23 (16.7%)	6 (31.6%)	0.964
Lymphatic invasion (n)	54 (39.1%)	6 (31.6%)	0.356
Vascular invasion (n)	19 (13.8%)	1 (5.3%)	0.265
Histological type (n)			0.542
Nuclear grade (n)			0.174
1/2	85	9	
3	53	10	
Prealbumin (mg/dl, mean±SD)	26.1±5.2	23.8±4.1	0.962
CEA (ng/ml, mean±SD)	2.3±2.0	2.2±1.2	0.584
Recurrence (n)	4 (2.9%)	1 (5.3%)	0.889

ER: Estrogen receptor status; PgR: progesterone receptor status ; HER2: human epidermal growth factor receptor 2 status; CEA: carcinoembryonic antigen.

albumin assay was 4.0 g/dl; patients were divided into analytical groups with <4.0 g/dl and ≥4.0 g/dl. In an adult, the normal range of serum albumin is defined as 4.0-5.0 g/dl and a level less than 3.5 g/dl is described as hypoalbuminemia. There were only two cases (1.3%) of hypoalbuminemia in the present study; therefore 4.0 g/dl was used as the detection limit of the albumin assay.

The clinical features of the 157 cases were reviewed according to the preoperative prealbumin and albumin levels, and statistical analysis was performed. Of the 157 cases, 38 (24.2%) had decreased serum prealbumin (Table I) and 19 (12.1%) had decreased serum albumin (Table II). Age, histological type, tumor size, lymph node metastasis, the expression of estrogen receptor (ER), the expression

of progesterone receptor (PgR), lymphovascular invasion at the primary tumor, nuclear grade, and serum tumor marker (carcinoembryonic antigen, CEA), as well as albumin and prealbumin were tested as possible predictors of disease recurrence. Serum albumin, prealbumin, and CEA were determined using an automatic biochemistry analyzer (Hitachi 7170; Hitachi Ltd., Tokyo, Japan). The overall median follow-up period was 5.3 months, and none of the patients died of surgical complications. For comparison, we retrospectively investigated the serum prealbumin and albumin levels in 14 patients with metastatic breast cancer and compared their levels with those of the present cases.

Univariate statistical analyses were conducted using the two-tailed Fisher exact test for few data, as well as unpaired, one-tailed *t*-tests. Differences were considered to be significant when $p < 0.05$.

Results

Clinicopathological characteristics and prealbumin and albumin concentrations. We analyzed the cases of 157 patients who underwent elective breast surgery. The mean age of the patients was 57.8 ± 12.7 years, with an age distribution of 28-85 years. Out of these cases, 38 (24.2%) had decreased serum prealbumin (Table I), and 19 (12.1%) had decreased serum albumin. The mean preoperative serum prealbumin and albumin were 25.7 ± 5.1 mg/dl and 4.2 ± 0.3 g/dl, respectively. Table I and II summarize not only the patients' characteristics, but also the results of the univariate analysis conducted to determine the relationship between preoperative serum prealbumin and albumin and clinical variables. No statistically significant association with preoperative prealbumin levels was found for the clinicopathological variables (Table I). A statistically significant association with preoperative albumin level was found only for age; age was higher in patients with low albumin levels (Table II). In short, we were unable to establish a connection between preoperative prealbumin or albumin and various clinical features, including recurrence, lymph node metastasis and tumor size. The average preoperative serum prealbumin and albumin levels in patients without disease recurrence, with disease recurrence and in patients with metastasis are shown in Figure 1. There were no significant differences between groups regarding these data.

Discussion

Malnutrition in patients with cancer is a significant problem due to a variety of mechanisms involving the tumor and the host response to the tumor. Serum albumin and prealbumin are valuable markers for assessing patients' nutritional status (16). Recently, the serum albumin level was re-emphasized by extending its clinical use to determining the severity of disease, disease progression and prognosis (4, 17, 18). Prealbumin is considered to be as important as albumin in nutritional assessments. It is of interest that serum prealbumin has been reported to reflect changes in the

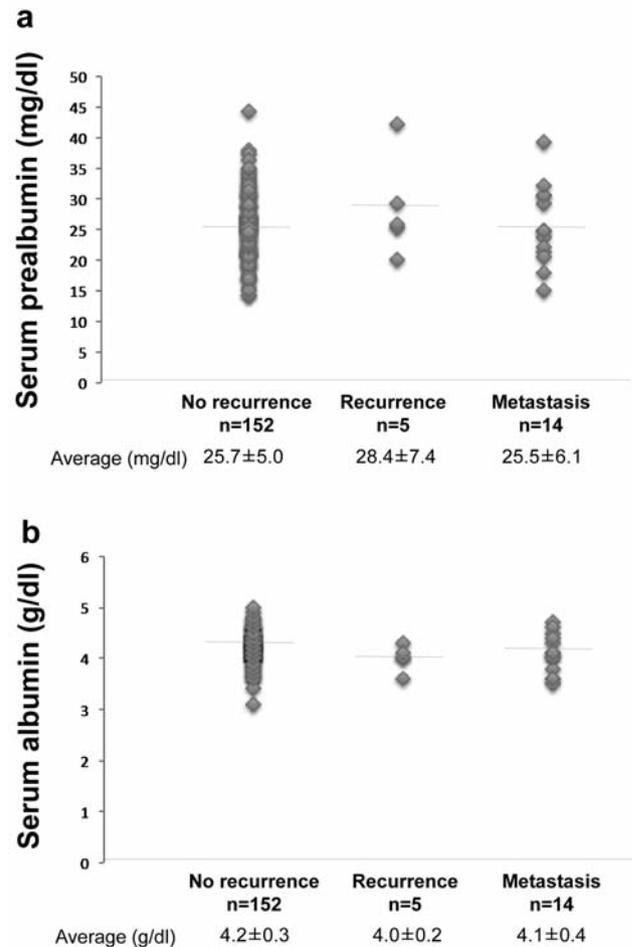


Figure 1. The average preoperative level of serum prealbumin (a) and albumin (b) in patients without disease recurrence, with disease recurrence ((a) $p=0.876$ and (b) $p=0.206$) and in patients with metastasis ((a) $p=0.435$ and (b) $p=0.092$).

patient's clinical status in certain cancer studies (19-22). We also reported that prealbumin and albumin were indicators of the risk of recurrent disease in colorectal cancer (4). However, in the present study we were unable to confirm an association between preoperative prealbumin and albumin and disease recurrence in patients with breast cancer.

Disease progression in cancer is dependent on the complex interaction between the tumor and the host inflammatory or immunological response (23). Carcinoma promotes the release of pro-inflammatory cytokines from tumor cells or an inflammatory response to the tumor infiltration or the immunovascular system (24-27). The serum albumin concentration is influenced by factors that result in low sensitivity and specificity to changes in nutritional status (28, 29). The interpretation of serum albumin is often difficult because non-nutritional factors,

such as hydration state and disease process, can obscure the effects of actual nutrient deprivation (3, 30). However, breast cancer progression is relatively slow; thus, prealbumin and albumin may not be ideal for assessing changes in the nutritional or other statuses over a long period of time. In fact, we found only slight or no hypoalbuminemia in patients with breast cancer, including patients with metastatic disease, in the current study.

This study has several limitations. Its major limitation is that it used retrospective methods of data collection. In addition, the number of cases was relatively small and the follow-up periods were relatively short. Additional research is needed to explore the putative association between albumin and prealbumin concentrations and the risk of recurrence.

Conclusion

Prealbumin and albumin may be sensitive indicators of disturbances in protein metabolism, and reflect inflammatory activity and malnutrition. However, we did not discover any association between serum albumin or prealbumin and disease recurrence or various clinicopathological characteristics in this study. These results suggest that evaluation of serum prealbumin and albumin are not useful for predicting disease aggressiveness or recurrence in breast cancer.

Conflicts of Interest

The Authors declare that they have no competing financial interests.

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