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Does Obesity-Related Hemodilution of Carcinoembryonic Antigen Exist in Non-Small Cell Lung Cancer Patients?

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Abstract

Background: Previous investigations reported inverse relationship between prostate-specific antigen concentration and body mass index (BMI). These results have been explained by a hemodilution effect among obese men. However, the hemodilution of serum carcinoembryonic antigen (CEA) concentration in obese patients with non-small cell lung cancer (NSCLC) has not been ever reported.

Methods: Consecutive 381 NSCLC patients were enrolled. A body surface area (BSA)-based and a hematocrit (HCT)-based equations were applied for plasma volume (PV) estimation. The relationship between BMI and PV, serum CEA concentration and CEA amount, representing the total amount of CEA protein within the circulation, were examined.

Results: Higher BMI was significantly associated with higher PV ($P < 0.001$). However, serum CEA concentration was not significantly associated with increasing BMI. Furthermore, there was no significant association between BMI and CEA amount. The 5-year survival rate of patients with a high serum CEA concentration was significantly lower than that of patients with a normal CEA. There was no difference in the prognostic significance of serum CEA concentration and CEA amount.

Conclusions: We failed to find the association between BMI and CEA, suggesting no or small hemodilution effect of CEA in NSCLC patients. Furthermore, the measurement of the CEA amount could not provide any additional information.

Keywords: Serum CEA; CEA amount; Body mass index; Hemodilution; Non-small cell lung cancer

Introduction

Carcinoembryonic antigen (CEA) is a glycoprotein involved in cell adhesion, is used as a tumor marker in a variety of tumors, and plays an important role in the prognosis of non-small cell lung cancer (NSCLC) patients [1-3].

Previous investigations reported that the serum concentration of serum prostate-specific antigen (PSA) level in obese patients with prostate cancer is lower compared with that in non-obese subjects [4-6]. These investigations showed that a lower serum PSA level was associated with increasing body mass index (BMI) [4-6]. The reason for this phenomenon has been considered as a hemodilution effect due to the larger vascular volume of obese patients [4-6]. On the other hand, others found no significant association between BMI and PSA [7, 8]. With regard to CEA, the relation between serum CEA concentration and obesity was also examined in colorectal cancer patients [9, 10]. However, the number of available studies investigating the association between BMI and serum CEA concentration is limited [9-12]. Despite the abundant literature on serum CEA concentration in NSCLC [1-3], there are no previous investigations on the hemodilution effect on serum CEA concentration in obese NSCLC patients. Therefore, in the present study, we investigated the association between BMI and serum CEA concentration in resected NSCLC patients.

Patients and Methods

This retrospective study had institutional review board approval, and the need to obtain patient consent was waived. Consecutive NSCLC patients who examined preoperative serum CEA concentration and underwent surgery from 2008 to 2013 in our hospital were enrolled into the present retrospective study. The collected records of 381 consecutive NSCLC patients were reviewed retrospectively.

The preoperative serum CEA concentration (ng/mL) was measured by enzyme immunoassay in a single laboratory at our hospital. The preoperative BMI was calculated as weight in kilograms divided by height in meters squared. According to the previous investigation [10], the following category was used: low BMI group (BMI < 18.5 kg/m^2), normal BMI group (BMI = 18.5 - 24.0 kg/m^2) and high BMI group (BMI > 24.0 kg/m^2). Two plasma volume (PV) equations were applied as follows: 1) body surface area (BSA)-based equation: the estimated body surface area (BSA) (m^2) was calculated as follows: $(\text{body weight})^{0.425} \times (\text{height})^{0.72} \times 0.2025$ [13]. The BSA-based PV (L) was calculated as BSA × 1.670 [14]. 2) Hematocrit (HCT)-based PV (L) was calculated as 0.07 × weight (kg) × (1 - HCT) [15]. The CEA amount (μg), representing the total amount of CEA within the circulation, was calculated as serum CEA

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Table 1. Clinical Characteristics of Patients Based on BMI

	Low BMI	Normal BMI	High BMI	Total	P value
Age					
≤ 65	19	68	37	124	0.070
> 65	40	149	68	257	
Gender					
Male	32	120	44	196	0.668
Female	27	97	61	185	
Smoking status					
Never	26	94	51	171	0.577
Current/former	33	123	54	210	
Histology					
Adenocarcinoma	42	161	91	294	0.016
Others	17	56	14	87	
pStage					
I	42	169	84	295	0.433
II-III	17	48	21	86	
pT status					
pT1	33	153	71	257	0.114
pT2-3	26	64	34	124	
pN status					
pN0	51	182	92	325	0.645
pN1-2	8	35	13	56	
CEA					
Normal	39	160	80	279	0.375
High	20	57	25	102	

CEA: carcinoembryonic antigen; BMI: body mass index.

concentration × estimated PV. Both CEA amount estimated by BSA and HCT were calculated. To determine the cut-off value of CEA amount, receiver operating characteristics (ROC) curve of CEA amount was analyzed, and cancer death was predicted by comparing the area under the curve. We decided the best cut-off value for BSA-based CEA amount was 12.09 (sensitivity: 78.65%; specificity: 50.0%; area under the ROC curve: 0.679) and HCT-based CEA amount was 10.52 (sensitivity: 77.58%; specificity: 52.0%; area under the ROC curve: 0.669).

Cumulative survival curves after surgery were calculated using the Kaplan-Meier method and differences were evaluated using the log-rank test. We used Wilcoxon rank-sum tests to assess associations between BMI and PV, serum CEA concentration and CEA amount, with P-values computed using the normal approximation. All statistical analyses were performed using JMP (SAS Institute Inc., Cary, NC, USA).

Results

The clinicopathological factors of patients based on BMI group were shown in Table 1. Among these NSCLC patients, 15.5% were categorized as low BMI, 57% as normal BMI, and 27.5% as high BMI. Age, gender, smoking status, pStage, pT status, pN status, and serum CEA concentration were not different between BMI groups. However, high BMI group had a statistically significant association with increasing adenocarcinoma histology (P = 0.016).

As shown in Table 2, the BSA-based PV was significantly increased with higher BMI (P < 0.001). Similarly, the HCT-based PV was also significantly associated with higher BMI (P < 0.001). However, there was no association between serum CEA concentration and BMI (P = 0.171). We could not find even the trend towards an association between increasing BMI and decreasing CEA.

The BSA-based CEA amount had no association with BMI (P = 0.842). The HCT-based CEA amount was not also significantly associated with increasing BMI (P = 0.598).

The survival of patients with preoperative high serum CEA concentration was significantly poorer than those with preoperative normal serum CEA (P < 0.001; Fig. 1a). Similarly, NSCLC patients with high CEA amount had a significantly worse survival than those with low CEA amount (P < 0.001; Fig. 1b, c). As shown in Figure 1, the result of BSA-based CEA

Table 2. Plasma Volume, Serum CEA Concentration and CEA Amount Based on BMI

	Low BMI	Normal BMI	High BMI	P value
BSA-based PV	2.3 ± 0.2	2.5 ± 0.2	2.7 ± 0.3	< 0.001
HCT-based PV	1.8 ± 0.3	2.3 ± 0.3	2.7 ± 0.4	< 0.001
Serum CEA concentration	28.1 ± 3.7	12.2 ± 0.8	15.5 ± 1.5	0.171
BSA-based CEA amount	25.5 ± 64.8	15.1 ± 31.6	15.4 ± 41.8	0.842
HCT-based CEA amount	20.1 ± 52.5	13.6 ± 29.2	15.1 ± 41.1	0.598

All values are expressed as mean ± standard deviation. BMI: body mass index; BSA: body surface area; HCT: hematocrit; PV: plasma volume; CEA: carcinoembryonic antigen.

amount was consistent with that of HCT-based CEA amount. Both CEA amount could not provide any useful information in addition to serum CEA concentration.

Discussion

We demonstrated that high BMI patients had higher PV, in agreement with the results of previous investigations [4-6]. It was also previously demonstrated that the serum PSA concentration in obese individuals was lower compared with normal-weight individuals [4-6]. The hemodilution may therefore be a most considerable reason for the lower serum PSA concentrations among obese men with prostate cancer [4-6]. Compared with theses previous investigations, we failed to find no association between serum CEA concentration and BMI in NSCLC patients. In agreement with our results, some investigations also found no significant association between BMI and PSA [7, 8]. The reason for this discrepancy is unknown. Some possible reasons for this might be as follows. First, the present study represents a retrospective surgical cohort from a single institution. The characteristics of resected NSCLC patients may not reflect the all staged NSCLC patients and/or general population. Second, the present study is the first investigation for NSCLC. There are no previous investigations that showed the relationship between BMI and serum CEA concentration in NSCLC. Third, in the present study, the number of extremely obese Japanese patients is small. The patients with BMI > 27.5 and > 30 were only 5.0% (19/381) and 1.3% (5/381) of our study population, respectively. Yoshiike et al [16] reported that the standardized prevalence of obesity (BMI ≥ 30.0) in Japanese adults was quite low compared with the data in western populations. Therefore, because of small number of obese patients, there is a possibility that we might fail to find a hemodilution of CEA in Japanese NSCLC patients.

We found a statistical significant association between high BMI and higher PV, but not found the association between high BMI and serum CEA concentration. Therefore, it is easy to understand that increasing BMI is associated with increasing CEA amount. However, our result showed that there was no association between BMI and CEA amount in NSCLC patients. Therefore, the power of the obesity-related CEA hemodilution in NSCLC patients might be weak, and the hemodilution effect in the obese NSCLC patients might be clinically negligible.

Previous investigations showed the prognostic significance of serum CEA concentration in NSCLC [1-3]. If the power of the hemodilution effect in the obese NSCLC patients is strong, the prognostic significance of CEA amount might be more useful than that of serum CEA concentration. However, we could not find any differences between the survival curve based on serum CEA concentration and that based on CEA amount. Taken together, there might be no need to adjust the preoperative serum CEA concentration in relation to the BMI when used to predict the prognostic assessment in NSCLC patients.

The main limitations of our study are that all patients were surgery patients and the number of patients was small. Therefore, a large cohort study will be required to confirm our results.

Conclusions

In conclusions, we failed to find the association between BMI

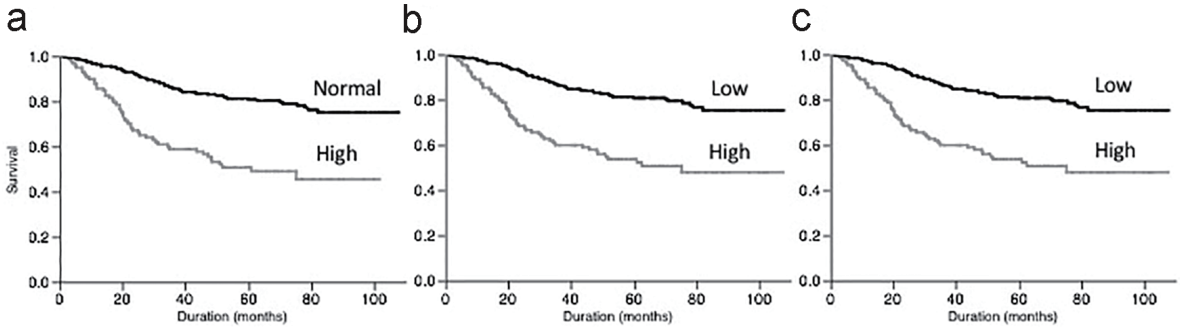

Figure 1. Survival of patients according to serum CEA concentration (a), BSA-based CEA amount (b) and HCT-based CEA amount (c).

and CEA, suggesting the hemodilution effect in the obese NSCLC patients might be clinically negligible. Furthermore, the measurement of the CEA amount could not provide any additional information. Therefore, we believe that there is no need to adjust the preoperative serum CEA concentration in relation to the BMI in NSCLC patients.

Conflicts of Interest

The authors have declared that no conflicts of interest exist.

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