

# Evaluation of hemodialysis patients' tumor marker



**ASSIGN  
BUSTER**

CEA tumor marker level associates comorbidity of hemodialysis patients

**Purposes:** Hemodialysis (HD) affects serum concentration of biomarkers. However, it remains unclear about the effect of HD on the levels of biomarkers, and efficacy of biomarkers in HD. The aim of this study is to evaluate the effects of HD on commonly used tumor markers.

**Methods:** A total of 28 unselected patients (22 men, 6 women) with end-stage renal disease (ESRD), treated with maintenance HD, were enrolled in this study. GOT and tumor markers CA-153, CA-125, and CEA are measured.

**Results:** The mean age was  $57.6 \pm 12.6$  years, HD duration was  $51.0 \pm 34.0$  months. Tumor marker CEA level is correlated to Charlson's score of HD patients, levels of CA153 and CA125 are not correlated to age, duration of dialysis and Charlson's score. GOT level is correlated to age, and Charlson's score. Mean value of CEA level ( $5.9 \pm 4.0$  ng/ml compared to normal value of 3 ng/ml for non-smoker and 5 ng/ml for smoker) is larger than normal value. Levels of CA153 ( $13.3 \pm 11.6$  U/ml), CA125 ( $35.2 \pm 38.9$  U/ml) and GOT value ( $20.4 \pm 8.9$  U/L) fall in normal range.

**Conclusions:** Concentration of CEA tumor marker is correlated with Charlson's score which strongly correlated with HD outcome. GOT value is correlated with age and Charlson's score which implies liver function drop in long term HD patients.

**Keywords:** biomarkers, End-Stage Renal Disease, evaluation, hemodialysis, CEA.

Introduction

<https://assignbuster.com/evaluation-of-hemodialysis-patients-tumor-marker/>

Hemodialysis (HD) is widely used for kidney failure patients who may represent a variety of underlying causes, including diabetes, hypertension, and glomerulonephritis. The dialysis membrane in artificial kidney tube filtrates out small molecules especially for small molecular weight proteins (i. e., <40 kDa) [1-3]. On the other hand, larger molecular weight proteins, e. g., tumor markers, are remaining in the blood, and had been evaluated in HD patients [4, 5]. The detection of tumor markers is important for cancer surveillance and follow-up, however, diagnostic validity of those markers are uncertain in HD patients. There are reports indicate that serum level of tumor markers will change after long term HD due to absorption of dialysis membrane, liver, kidney, or other organ's metabolism [6], but the variation trends are uncertain for each biomarker. Study of serum levels of five tumor markers, including the soluble cytokeratin 19 fragment (CYFRA), pro-gastrin-releasing peptide (ProGRP), serum levels of CYFRA and ProGRP together with conventional markers including carcinoembryonic antigen (CEA), squamous cell carcinoma antigen (SCC), neuron specific enolase (NSE), for lung cancer in patients with chronic renal failure indicate that mean concentration of CYFRA, CEA, SCC, and NSE except ProGRP were significantly increased with the severity of renal failure, and suggested a high false positive rates for tumor markers of lung cancer in patients with renal failure [5]. Recent studies of the diagnostic validity of prostate-specific antigen (PSA) among man receiving HD shows dialysis induced elevations in all forms of PSA immediately after hemodialysis [7]. However, Horinaga *et. al.* shows that cancer-free HD man demonstrated significantly lower PSA compared to controls [8]. Here we examine the serum level of commonly used molecular biomarkers, i. e., CA-153, CA125, CEA, and GOT of HD patients.

## Patient and materials

### *Study subjects*

Experiments performed in this study complied with the current laws and regulations in Taiwan, Republic of China. All procedures are followed by the ethnical guideline and approved by Kaohsiung Armed Forces Hospital committee, Taiwan. A total of 28 persons between the ages of 37 and 76 years with end-stage renal disease, receiving dialysis treatment three times per week, were enrolled in a prospective study in March 2008. Dialysis was carried out using a Nikkiso DBB-22B dialysis machine with 4 hours session. Dialyzer with APS 18MD (Asahi Kasei, Osaka, Japan, polysulfone membrane, surface area  $1.8 \text{ m}^2$ , *in vitro* clearances for urea, 198 ml/min for QB-200 ml/min). Blood flow rate was setting at 200 ml/min. Patients with vascular success insufficiency which can't reach required blood flow rate was excluded. Ultrafiltration rate ( $512 \pm 85 \text{ ml/h}$ ) was adjusted according to the patients' needs. The flow and temperature of the dialysate was 500 ml/min and  $37^\circ \text{C}$ , respectively. Vascular access was either via an arterio-venous fistula (sixteen treatments), graft (nine treatments), or a Perm catheter (three treatment). Serum CA-153, CA125, CEA, GOT levels were measured before and immediately after HD using low-flux membrane.

### *Blood/serum collection*

Serum samples were collected from HD patients during and after the course of HD treatment. 5 ml blood was collected in EDTA tube. The serum were then stored in  $4^\circ \text{C}$  and processed within 12 hours. The serum samples were

centrifuged at 2000 rpm for 10 min prior to splitting into aliquots and stored at -20 °C.

### *Laboratory methods*

The serum levels of CA-153, CA125, CEA and GOT were measured with Abbott AxSYM analyzer (Abbott Laboratories, Abbott Park, Ill). The reference ranges of the markers were: CA-153, 0-31.3 U/ml; CA-125, 0-35 U/ml; CEA, 0-3 ng/ml for non-smoker, and 0-5 ng/ml for smoker; GOT, 0-32 U/L.

### *Statistical analysis*

The data reported are means  $\pm$  standard deviations (SD). Pearson correlation coefficient ( $r$ ) was used for analyses of linear associations. Because the concentrations of serum tumor markers were not normally distributed, significance of differences was assessed by Wilcoxon Matched-Pairs Signed-Ranks Test. The level of statistical significance was always set at  $P < 0.05$ . Statistical analysis was performed using the statistical package SigmaStat 3.1 (Systat Software, Inc., San Jose, CA, USA).

## Results

### Baseline demographic and clinical data

We analyzed 28 patients, of which 22 were men and 6 were women. The baseline demographic and clinical data are summarized in Table 1. All patients are diagnosed as end-stage renal failure. The mean age was  $57.8 \pm 12.6$  years. Mean dialysis vintage was  $51.0 \pm 34.0$  months.

### Measurement of tumor marker concentration of hemodialysis patients

<https://assignbuster.com/evaluation-of-hemodialysis-patients-tumor-marker/>

The mean value of CA-153, CA125, and GOT fall in normal range ( $16.5 \pm 16.3$  before hemodialysis, and  $18.6 \pm 16.3$  after hemodialysis, compared with  $31.3$  U/ml normal value,  $35.2 \pm 38.9$  before dialysis, and  $34.3 \pm 41.2$  after hemodialysis, compared to  $< 35$  U/ml normal value, and  $22.1 \pm 10.6$  before hemodialysis,  $27.5 \pm 11.7$  after hemodialysis, compared to  $32$  U/L normal value), however, mean value of CEA are higher than normal ( $6.2 \pm 7.7$  before hemodialysis, and  $6.0 \pm 8.0$  after hemodialysis, compared to normal value of  $3$  ng/ml for non-smoker).

#### Correlates of serum markers

Correlations between serum markers levels and age, duration of dialysis and Charlson's score are tested. Of all variables, patient age and Charlson's score are correlated with levels of some serum markers. CEA level was correlated with Charlson's score ( $r = 0.42$ ,  $p = 0.03$ ) (Fig. 1). GOT level was correlated with age ( $r = 0.42$ ,  $p = 0.02$ ) (Fig. 2) and Charlson's score ( $r = 0.48$ ,  $p = 0.01$ ) (Fig. 3). Other variables, including CA-153, CA125 is not correlated with age ( $r = 0.07$ ,  $p = 0.7$ ;  $r = 0.2$ ,  $p = 0.3$ , respectively), and also not correlated with duration of HD, Charlson's score (Table 2).

#### Direct effect of hemodialysis on concentration of serum markers

Since the data of CA-153, CA125, CEA and GOT fail in normal distribution test, Wilcoxon signed rank test is chosen to compare groups before and after hemodialysis. Groups of CA-153, CA125, CEA, and GOT before hemodialysis are not significantly different to that after hemodialysis (Table 3).

## Discussion

CA-153, CA-125, CEA are commonly used tumor markers. CA-125 is a glycoprotein with high molecular weight ( $> 200$  kDa), and is a cancer antigen for monitor mesothelium especially for ovarian cancer. Recently, CA-125 is used to monitor mesothelial cell viability in PD patients [9, 10]. CEA is carcinoembryonic antigen with a molecular weight about 180-200 kDa, commonly used for monitoring gastric cancer [11], weakly correlate with carotid atherosclerosis [12], and with prognostic value of colorectal cancer in PD patients [13]. The mean value of CEA of 28 patients is higher than normal value, which is consistent with previous reports that patients with ESRD are usually with higher risk of cancer, and with higher levels of tumor markers [14]. In our cases, patient no. 2, 5, 9, 13 and 27 were expired within 1 year after diagnosis. Patient no. 2 is finally diagnosed as hepatoma, patient no. 5 is cirrhosis of liver and died in septicemia, patient no. 9 is died in leukemia, and patient no 13 is died in lung cancer. It shows that high levels of CEA correlated with Charlson's score which implies poor outcome, however it remain further confirmation. CA-153 is correlated to risk of liver disease. Though 8% patients were diagnosed liver diseases, but their GOT value fall in normal range, and CA-153 values of them were also normal.

There are many reports indicated that long term hemodialysis may affect levels of biomarkers. We showed that biomarkers alter non-significantly after one HD procedure. It is interesting that recent report indicated acute effects of HD treatment on up- or down regulation of apoptotic genes in blood leucocytes [15] Tumor markers were produced by neoplastic cells, and can also be secreted by normal tissue. Many chronic diseases, e. g.,

inflammation, chronic bronchitis, cirrhosis of liver and renal diseases, affect the metabolism and elimination of tumor markers, may contribute the long term elevation of tumor markers. Our data show that short term effect of HD on patients is not significant. And all 4 serum markers are not correlated with duration of HD. It seems that the response of patients to HD doesn't directly affect levels of these serum markers. However, CEA and GOT are shown to be candidates markers for monitoring HD outcome as they are positively correlated with Charlson's score.

Table I Baseline demographic and clinical data

N = 28

|                                      |                  |
|--------------------------------------|------------------|
| Sex (M : F)                          | 22:: 6           |
| Age (years)                          | 57. 8 ± 12.<br>6 |
| Duration of dialysis (months)        | 51. 0 ± 34.<br>0 |
| Body height (cm)                     | 164. 0 ± 7.<br>5 |
| Body weight (kg)                     | 66. 2 ± 13.<br>2 |
| Body mass index (kg/m <sup>2</sup> ) | 23. 7 ± 4.       |



5

Renal diagnosis, no. cases (%)

Glomerulonephritis 43

Diabetic nephropathy 29

Polycystic kidney 14

Hypertensive nephrosclerosis 4

Gouty nephropathy

Major comorbidity, no. cases (%) 39

Diabetes mellitus 36

Ischaemic heart disease 4

Cerebrovascular disease 14

Peripheral vascular disease 4

Moderate or severe liver disease 11

Any tumor, leukemia, lymphoma 7

Modified Charlson's comorbidity  
score\* 6.3 ± 3.3

## Dialysis adequacy

Total Kt/V  $1.3 \pm 0.4$

Residual GFR (mL/min per 1.73  
m<sup>2</sup>)  $6.8 \pm 3.5$

NPCR (g/kg per day)  $1.3 \pm 0.4$

Cr (mg/dl)  $9.1 \pm 2.8$

GFR, glomerular filtration rate; NPCR, normalized protein catabolic rate,

\*Modified Charlson's comorbidity score is calculated according to Beddhu S, 2000.

Table II. Correlation of serum markers and age, duration of HD, and Charlson's score.

|         | Age of patients | Duration of HD | Charlson's score |
|---------|-----------------|----------------|------------------|
| CA153   | 0.0688          | -0.162         | 0.313            |
| p value | 0.728           | 0.409          | 0.105            |
| CA125   | 0.202           | -0.139         | 0.202            |

|         |        |         |        |
|---------|--------|---------|--------|
| p value | 0.302  | 0.48    | 0.302  |
| CEA     | 0.264  | -0.132  | 0.475  |
| p value | 0.175  | 0.505   | 0.0106 |
| GOT     | 0.436  | -0.0682 | 0.422  |
| p value | 0.0205 | 0.73    | 0.0254 |

Table III. Comparison of serum tumor markers before and after hemodialysis

| BioMarkers | Hemodialysis | Mean $\pm$ SD (n-13)   | P-value |
|------------|--------------|------------------------|---------|
| CA-153     | Before       | 16.5 $\pm$ 16.3 (U/ml) | 0.75    |
|            | After        | 18.6 $\pm$ 16.3 (U/ml) |         |
| CA125      | Before       | 43.0 $\pm$ 48.6 (U/ml) | 0.99    |
|            | After        | 47.3 $\pm$ 51.7 (U/ml) |         |

|     |        |                     |      |
|-----|--------|---------------------|------|
| CEA | Before | 5.9±4.0<br>(ng/ml)  | 0.42 |
|     | After  | 6.6±4.6<br>(ng/ml)  |      |
| GOT | Before | 24.0±11.0<br>(U/ml) | 0.76 |
|     | After  | 27.5±11.7<br>(U/ml) |      |

### Legends to Figures

Figure 1. Scatter plots, regression line, and 95% confidence intervals reflecting correlations between serum levels of CEA and Charlson's score of 28 HD patients.

Figure 2. Scatter plots, regression line, and 95% confidence intervals reflecting correlations between serum levels of GOT and Charlson's score of 28 HD patients.

Figure 3. Scatter plots, regression line, and 95% confidence intervals reflecting correlations between serum levels of GOT and age of 28 HD patients.