


ORIGINAL ARTICLE

Low serum prealbumin concentration predicts long-term mortality in maintenance hemodialysis patients with hepatitis B and/or C virus infections

Dung Nguyen Huu,* Quyen Dao Bui Quy,[†] Tuan Nguyen Minh,[‡] Loc Nguyen Duc,[§] Cam Truong Dinh,[¶] Kien Nguyen Trung,^{||} Quyet Do,^{**} Tien Tran Viet^{††} and Thang Le Viet^{‡‡} 

*Center of Uro-Nephrology-Hemodialysis, Bach Mai Hospital, ^{||}Center of Hematology and Blood Transfusion, ^{**}Department of Nephrology – Hemodialysis, Military Hospital 103, ^{**}Director, Viet Nam Military Medical University, ^{††}Director, Military Hospital 103, Ha Noi, Departments of [†]Uro-Nephrology, [‡]Hemodialysis, Cho Ray Hospital, [§]Department of Hemodialysis, An Sinh Hospital and [¶]Vice Director, Military Hospital 175, Ho Chi Minh, Viet Nam

Key words

chronic kidney disease, hemodialysis, hepatitis virus infection, mortality, prognostic biomarker, serum prealbumin.

Accepted for publication 4 November 2021.

Correspondence

Assoc. Prof. Thang Le Viet, Department of Nephrology and Hemodialysis, Military Hospital 103, Vietnam Military Medical University, 261 Phung Hung, Ha Dong, Ha Noi, Vietnam. Email: lethangviet@yahoo.co.uk

Declaration of conflict of interest: The authors declare no conflict of interest, financial or otherwise. We had full access to all of the data in this study and we take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Financial support: None.

Abstract

Background and Aim: A low serum prealbumin concentration is common in maintenance hemodialysis patients with hepatitis B and C and may be associated with mortality. In this study, we assessed Department of Nephrology and Hemodialysis predictive value of a low serum prealbumin concentration on mortality in HD patients using reused low-flux dialyzers who were infected with hepatitis B and/or C virus.

Methods: We used serum prealbumin levels to predict the long-term mortality of 326 hemodialysis patients. The patients were divided into two groups: group 1 ($n = 140$, with hepatitis B and/or C virus infections), and group 2 ($n = 186$, without hepatitis virus infections).

Results: During a 5-year follow-up, there were 75 deaths due to all-cause mortality (23.0%). Mortality was significantly higher ($P < 0.001$) in patients with hepatitis B and/or C infection (44%) than in those without hepatitis infection (8%). Serum prealbumin was lower in the hepatitis infected group and mortality group than in non-infected group and survival group. Multivariate Cox regression analysis showed that long duration of HD and lower serum prealbumin and albumin were related to mortality in patients undergoing maintenance HD. Receiver operating characteristic curves showed that serum prealbumin had a good prognostic value in predicting mortality in both groups with hepatitis B and/or C virus infection and without hepatitis infection (AUC = 0.792 [95% confidence interval: 0.714–0.87], $P < 0.001$; cut-off value = 24.5 mg/dl, sensitivity = 62.3%, and specificity = 88.6%).

Conclusion: In HD patients, serum prealbumin was a good prognostic biomarker of mortality in both groups of patients with hepatitis B and/or C virus infections and without hepatitis infections.

Introduction

Maintenance hemodialysis (HD) is a common treatment for end-stage kidney disease in Vietnam. Patients can be treated with a dialyzer with a low ultrafiltration coefficient, and the filter can be reused six times according to the guidelines of the Vietnam Ministry of Health. Hepatitis virus infections are a challenging problem in patients on maintenance HD, due to issues related to dialyzer reuse and the technical steps involved.^{1–3} In Vietnam, the ratio of the hepatitis B virus (HBV) and/or hepatitis C virus (HCV) infections has reached 20–48%.

Malnutrition in patients on maintenance HD is a common problem in both developed and developing countries.^{4–6} Malnutrition combined with inflammation reduces the patient's quality of life as well as the survival rate.^{5,7,8} In HD patients infected

with HBV and/or HCV, the proportion of malnourished patients is high.^{5,6}

Prealbumin is a protein excreted by the liver. It is used to assess malnutrition in patients suffering from chronic diseases, including those on maintenance HD.^{9–11} Many previous studies have confirmed that serum prealbumin has prognostic value in predicting mortality in chronic patients, including those on maintenance HD.^{12–14} The value of serum prealbumin in the prognosis of mortality in patients undergoing maintenance HD and infected with HBV and/or HCV differs from that in uninfected patients.² So, we conducted this study to ascertain whether serum prealbumin is a predictor of all-cause mortality in maintenance HD patients with and without HBV and/or HCV infection.

Methods

Study design and setting. A total of 514 patients undergoing HD joined our study at the Hemodialysis Center, Bach Mai Hospital, Ha Noi, Vietnam. The data were collected in February 2011, and all patients were followed up to January 2016 to determine the ratio of mortality. We chose the patients in our hemodialysis center with the following criteria: age ≥ 18 years; duration of hemodialysis ≥ 3 months; willingness to participate in the study. All patients with acute infection, malignancy, using a high-flux dialyzer, or showing an active stage of HBV/HCV or HIV infection were excluded. The participating patients were treated with maintenance HD using bicarbonate and a low-flux membrane (Polyflux 14L). The parameter Kt/V was calculated by Daugirdas's formula. Where K is the dialyzer clearance of urea; t is the dialysis time; V is the volume of distribution of urea, approximately equal to patient's total body water.¹⁵ Each dialysis session lasted 3.5–4.5 h to achieve a total target of Kt/V (about 1.2 each session). We reused the dialyzer six times by a trained technician according to the guidelines of the Ministry of Health of Vietnam. After each dialysis session, the dialyzer was washed by hand using RO water for 30 min. Then, it was soaked and disinfected with a solution of peracetic acid (0.7%) and stored at a temperature of 2–8°C. Before reusing, we rinsed the dialyzer once more with RO water for 30 min and confirmed that there was no residual peracetic acid in the dialyzer (using a peracetic acid 2000 test strip).

Clinical diagnosis of primary renal diseases was performed. We diagnosed residual kidney function according to Daugirdas.¹⁵ Blood lipid disorder was diagnosed according to the 2013 KDIGO (The Kidney Disease Improving Global Outcomes) Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease¹⁶ (when the patient had one of the following levels: total cholesterol ≥ 200 mg/dl, low-density lipoprotein (LDL) cholesterol ≥ 130 mg/dl, high-density lipoprotein (HDL) cholesterol ≤ 40 mg/dl, and triglycerides ≥ 150 mg/dl). This study was approved by the Ethical Committee of Vietnam Military Medical University (No. 2134/QĐ/HVQY). Informed consent was obtained from all participants included in the study. No animals were used in this research. All research procedures involving humans were followed following the ethical standards of the committee responsible for human experimentation (institutional and national) and the Helsinki Declaration of 1975 (as revised in 2008).

In all regular HD patients, the HBsAg (hepatitis B surface antigen) was assessed by serological testing. The anti-HBV and anti-HCV antibodies were tested by enzyme-linked immunosorbent assay (ELISA). HBV-DNA and HCV-RNA were qualitatively estimated on positive samples for HBsAg and anti-HCV Ab, respectively, with a lower level of detection of 1.5 IU/ml. Based on the above results, 326 patients were divided into two groups: a group of HBV and/or HCV infection with 140 patients (G1), and a group of non-hepatitis virus infection with 186 patients (G2).

The number of patients with all-cause mortality was collected for 5 years.

Laboratory measurements. Blood was collected immediately before dialysis to measure routine hematologic and

biochemical indicators such as serum albumin, creatinine, blood urea nitrogen, high-sensitive C-reactive protein (hs-CRP), and hemoglobin. Serum prealbumin concentrations were measured using the electro-chemiluminescence immunoassay (ECLIA) method at the time of admission.

Statistical analyses. In the case of a normal distribution, continuous data were expressed as mean and standard deviation and compared using the Student *t*-test or one-way analysis of variance (ANOVA). All bias distributions were expressed as median (interquartile range) and compared using the Mann–Whitney *U* or Kruskal–Wallis test. Categorical data were expressed as the frequency (percentage) and compared using the Chi-square test or the Friedman test. Receiver operating characteristic (ROC) curves with the area under the curve (AUC) was calculated to predict mortality. Kaplan–Meier analysis and comparison of survival curves (log-rank test) were performed to evaluate that factors that influenced the survival time. Data were analyzed using the Statistical Package for Social Science (SPSS) software version 22.0 (Chicago, IL, USA). A *P*-value < 0.05 was considered significant.

Results

The results in Table 1 show that there were no differences in the mean age, body mass index (BMI), serum creatinine, albumin, hemoglobin concentration, and platelet count, as well as gender, etiology of chronic kidney diseases, the proportion of anemia, hypertension, and lipid disorder between G1 and G2.

However, the results of our study showed that G1 had a longer duration of HD, higher hs-CRP, urea concentration, and all-cause mortality, and a lower serum prealbumin concentration and the ratio of residual kidney function compared with G2 ($P < 0.01$).

As the results in Table 2 show, there was no difference in sex, BMI, causes of chronic renal failure, the ratio of residual kidney function, serum creatinine, serum albumin, hemoglobin concentration, platelet count, the proportion of anemia, and the ratio of lipid disorder between the different types of hepatitis virus infection.

However, there was a significant difference in age, duration of HD, BMI, and rate of hypertension between different types of hepatitis virus infection ($P < 0.05$). The proportion of all-cause mortality in the HCV infection group was the highest, followed by the combined HBV and HCV infection group and the hepatitis B virus infection group only ($P < 0.001$).

According to the results in Table 3, there was no difference in age, sex, BMI, causes of chronic renal failure, ratio of hypertension, serum creatinine, hemoglobin concentration, platelet count, and the proportion of anemia between the mortality and survival groups.

However, the duration of hemodialysis is longer, the ratio of residual kidney function is lower, serum urea and hs-CRP are higher, serum prealbumin and albumin are lower, rate of lipid disorder and ratio of hepatitis virus infection are higher in the mortality group compared to survival group ($P < 0.05$ and < 0.001).

Table 4 shows that long duration of hemodialysis and lower serum prealbumin and albumin are related to mortality in maintenance HD.

Table 1 Baseline demographic and laboratory characteristics of patients

	All patients (<i>n</i> = 326)	HBV and/or HCV infection (<i>n</i> = 140)	No hepatitis virus infection (<i>n</i> = 186)	<i>P</i> -value
Age (year)	47 (33–56)	49 (33–58)	44 (33.75–55)	0.169
Male (<i>n</i> , %)	186 (57.1)	77 (55)	109 (58.6)	0.515
Duration of hemodialysis (month)	47.5 (26–79)	74 (41.75–107.75)	35 (19–59)	<0.001*
BMI	19.17 ± 2.35	19.38 ± 2.25	19.02 ± 2.42	0.162
Hypertension (<i>n</i> , %)	244 (74.8)	104 (74.3)	140 (75.3)	0.84
Etiology (<i>n</i> , %)				
CGN	230 (70.6)	99 (70.7)	131 (0.4)	0.999
Chronic pyelonephritis	43 (13.2)	18 (12.9)	25 (13.4)	
Diabetic nephropathy	32 (9.8)	14 (10)	18 (9.7)	
Others	21 (6.4)	9 (6.4)	12 (6.5)	
Residual kidney function (<i>n</i> , %)	63 (19.9)	18 (12.9)	45 (24.2)	0.01*
Urea (mmol/L)	29.36 ± 6.92	30.67 ± 7.34	28.38 ± 6.43	0.003*
Creatinine (μmol/L)	824 (656.5–986)	841 (699–986.75)	801.5 (636.25–980)	0.275
Prealbumin (mg/dl)	33.12 ± 10.12	26.96 ± 7.21	37.77 ± 9.51	<0.001*
Albumin (g/L)	38.71 ± 3.56	38.37 ± 3.35	38.97 ± 3.7	0.137
hs-CRP (mg/L)	0.4 (0.1–0.7)	0.5 (0.2–0.8)	0.3 (0.1–0.6)	<0.001*
Hemoglobin (g/L)	103.19 ± 18.32	104.56 ± 18.23	102.16 ± 18.37	0.242
Anemia (<i>n</i> , %)	271 (83.1)	117 (83.6)	154 (82.8)	0.853
Platelet count (G/L)	232.95 ± 46.98	235.53 ± 48.11	231.01 ± 46.15	0.391
Lipid disorder (<i>n</i> , %)	213 (65.3)	99 (70.7)	114 (61.3)	0.077
Mortality due to all causes (<i>n</i> , %)	75 (23)	61 (43.6)	14 (7.5)	<0.001*

BMI, body mass index; CGN, chronic glomerulonephritis; HBV, hepatitis B virus; HCV, hepatitis C virus; hs-CRP, high sensitive C-reactive protein.

**P*-value <0.05.

Table 2 Comparison of laboratory parameters and clinical outcome in different types of hepatitis virus infection (*n* = 140)

	HBV+ (<i>n</i> = 28)	HCV+ (<i>n</i> = 98)	HBV+ and HCV+ (<i>n</i> = 14)	<i>P</i> -value
Age (year)	34 (26.25–52.25)	51 (38.5–58.25)	48 (33–58)	0.009*
Male (<i>n</i> , %)	18 (64.3)	50 (51)	9 (64.3)	0.352
Duration of hemodialysis (month)	40 (22.5–57.75)	83.5 (56.5–111.25)	51.5 (38–130.75)	<0.001*
BMI	18.59 ± 1.41	19.45 ± 2.27	20.52 ± 2.93	0.026*
Hypertension (<i>n</i> , %)	25 (89.3)	67 (68.4)	12 (85.7)	0.049*
Etiology (<i>n</i> , %)				
CGN	21 (75)	67 (68.4)	11 (78.6)	0.86
Chronic pyelonephritis	3 (10.7)	13 (13.3)	2 (14.3)	
Diabetic nephropathy	2 (7.1)	12 (12.2)	0 (0)	
Others	2 (7.1)	6 (6.1)	1 (7.1)	
Residual kidney function (<i>n</i> , %)	5 (17.9)	13 (13.3)	1 (7.1)	0.625
Urea (mmol/L)	27.83 ± 6.53	30.95 ± 7.47	34.38 ± 6.21	0.018*
Creatinine (μmol/L)	838.5 (712.25–955)	841 (693.75–986.25)	878.5 (406.5–1107.25)	0.92
Prealbumin (mg/dl)	28.82 ± 5.06	26.53 ± 7.74	25 ± 7.31	0.209
Albumin (g/L)	39.24 ± 3.42	38.26 ± 3.38	37.37 ± 2.8	0.199
hs-CRP (mg/L)	0.4 (0.2–0.675)	0.6 (0.2–1)	0.5 (0.3–1.1)	0.37
Hemoglobin (g/L)	105.93 ± 18.57	103.97 ± 18.09	105.93 ± 19.59	0.846
Anemia (<i>n</i> , %)	23 (82.1)	84 (85.7)	10 (71.4)	0.392
Platelet count (G/L)	241.42 ± 46.1	234.3 ± 49.19	232.35 ± 46.74	0.764
Lipid disorder (<i>n</i> , %)	22 (78.6)	68 (69.4)	9 (64.3)	0.55
Mortality due to all causes (<i>n</i> , %)	3 (10.7)	53 (54.1)	5 (35.7)	<0.001*

BMI, body mass index; CGN, chronic glomerulonephritis; HBV, hepatitis B virus; HCV, hepatitis C virus; hs-CRP, high sensitive C-reactive protein.

**P*-value <0.05.

As the results of the ROC curve model in Figures 1 and 2 show, serum prealbumin had a good prognostic value to predict mortality in both groups of hepatitis B and/or C virus infection and without hepatitis infection.

Based on the Kaplan–Meier analysis shown in Figures 3 and 4, patients with lower prealbumin concentrations (G1) had a significantly higher mortality rate compared with patients with higher serum prealbumin concentrations (G2) (*P* log-rank test < 0.001).

Table 3 Comparison of laboratory parameters and clinical outcome between mortality and survival group ($n = 326$)

	Mortality group ($n = 75$)	Survival group ($n = 251$)	<i>P</i> -value
Age (years)	49 (35–57)	45 (33–56)	0.351
Male ($n, \%$)	41 (54.7)	145 (57.8)	0.634
Duration of hemodialysis (month)	80 (64–116)	40 (23–67)	<0.001*
BMI	19.36 \pm 2.56	19.12 \pm 2.29	0.442
Hypertension ($n, \%$)	53 (70.7)	191 (76.1)	0.342
Etiology ($n, \%$)			
CGN	56 (74.7)	174 (9.3)	0.722
Chronic pyelonephritis	9 (12)	34 (13.5)	
Diabetic nephropathy	5 (6.7)	27 (10.8)	
Others	5 (6.7)	16 (6.4)	
Residual kidney function ($n, \%$)	7 (9.3)	56 (22.3)	0.013*
Urea (mmol/L)	31.68 \pm 7.94	28.67 \pm 6.44	0.001*
Creatinine (μ mol/L)	808 (643–933)	836 (675–986)	0.563
Prealbumin (mg/dl)	23.92 \pm 8.34	35.88 \pm 8.92	<0.001*
Albumin (g/L)	37.03 \pm 3.81	39.21 \pm 3.33	<0.001*
hs-CRP (mg/L)	0.6 (0.4–1.0)	0.3 (0.1–0.6)	<0.001*
Hemoglobin (g/L)	101.43 \pm 19.97	103.71 \pm 17.8	0.344
Anemia ($n, \%$)	63 (84)	208 (82.9)	0.818
Platelet count (G/L)	237.17 \pm 51.1	231.69 \pm 45.71	0.377
Lipid disorder ($n, \%$)	59 (78.7)	154 (61.4)	0.006*
Hepatitis virus infection ($n, \%$)	61 (81.3)	79 (31.5)	<0.001*

BMI, body mass index; CGN, chronic glomerulonephritis; hs-CRP, high sensitive C-reactive protein.

**P*-value <0.05.

Table 4 Multivariate Cox regression analysis to determine risk factor of mortality

Variable	Univariate Cox regression			Multivariate Cox regression		
	HR	95% CI	<i>P</i> -value	Adjusted HR	95% CI	<i>P</i> -value
Duration of hemodialysis (month)	1.021	1.016–1.026	<0.001*	1.014	1.009–1.019	<0.001*
Prealbumin (mg/dl)	0.892	0.87–0.915	<0.001*	0.91	0.886–0.935	<0.001*
Albumin (g/L)	0.841	0.789–0.897	<0.001*	0.84	0.779–0.906	<0.001*

CI, confidence interval; HR, hazard ratio.

**P*-value <0.05.

Discussion

In our study, the ratio of HBV and/or HCV infection was 42.9% (140/326 patients), in which the HBV infection rate was 8.6% (28/326 patients), that of HCV was 30% (98/326 patients), and the combined HBV and HCV infection rate was 4.3% (14/326 patients). The incidence of HCV infection varies between different dialysis centers and different countries, with the proportion ranging from 2.6% to 22.9%, while the incidence of HBV infection within dialysis units in developing countries varies between 2% and 20%.¹⁷ Kalantari *et al.*¹⁸ found that the prevalence of HBV-positivity and HCV-positivity in a study population of 499 chronic HD patients was 1.2% and 5.2%, respectively. In the study by Reddy *et al.*,¹⁹ 5.9% of patients were HCV positive and 1.4% were HBV positive. A combined HBV and HCV infection was observed in 3.7% of patients. Rached *et al.*²⁰ found that the prevalence of HBV and HCV infection rates in 3769 Lebanese HD patients was 1.6% and 4.7%, respectively. The incidence of HBV and/or HCV infection in our study was higher than in the other studies. This can be explained by the various other risk

factors for HBV and/or HCV infection in our HD patients, such as the long duration of hemodialysis, loss of residual kidney function, history of blood transfusion, and, especially, dialyzer reuse. Although dialyzer reuse strictly follows the regulations of the Ministry of Health of Vietnam, there are too many steps that increase HBV and/or HCV infection in our HD patients such as no separate wash areas for infected and uninfected patients, sharing some pieces of equipment between patients, and so on. The fact that the ratio of HCV infection was higher than HBV infection in our study can be explained as due to the lack of vaccine for HCV.

According to some studies, most patients infected with HBV and/or HCV have no symptoms. Therefore, if the follow-up time is too short, it may not be possible to fully assess the consequences of chronic hepatitis B/C infection.^{21,22} Chronic infections such as chronic viral hepatitis can impair health-related quality of life by affecting memory, neurocognitive function, concentration, attention, and sexual function.^{23,24} Hepatitis virus infection is related to mortality in regular HD patients. Kalantar-Zadeh *et al.*²⁵ found that HCV infection was more strongly

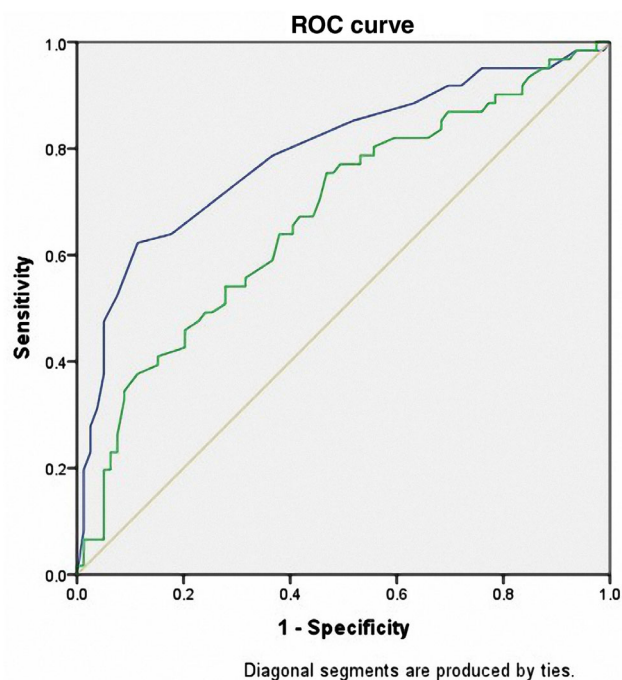


Figure 1 Receiver operating characteristics (ROCs) curves for prediction of hospital mortality (prealbumin, albumin) in hemodialysis patients with hepatitis B virus (HBV) and/or hepatitis C virus (HCV) infection. Serum prealbumin: area under the curve (AUC) = 0.792 (95% confidence interval [CI]: 0.714–0.87), $P < 0.001$; cut-off value = 24.5 mg/dl, sensitivity = 62.3%, specificity = 88.6%. Serum albumin: AUC = 0.676 (95% CI: 0.586–0.766), $P < 0.001$; cut-off value = 38.95 g/L, sensitivity = 75.4%, specificity = 53.2%. Serum prealbumin concentration had a better predictive value of 5-year all-cause mortality than serum albumin in maintenance hemodialysis patients with HBV and/or HCV infection. Source of the curve: (—) prealbumin, (—) albumin, and (—) reference line.

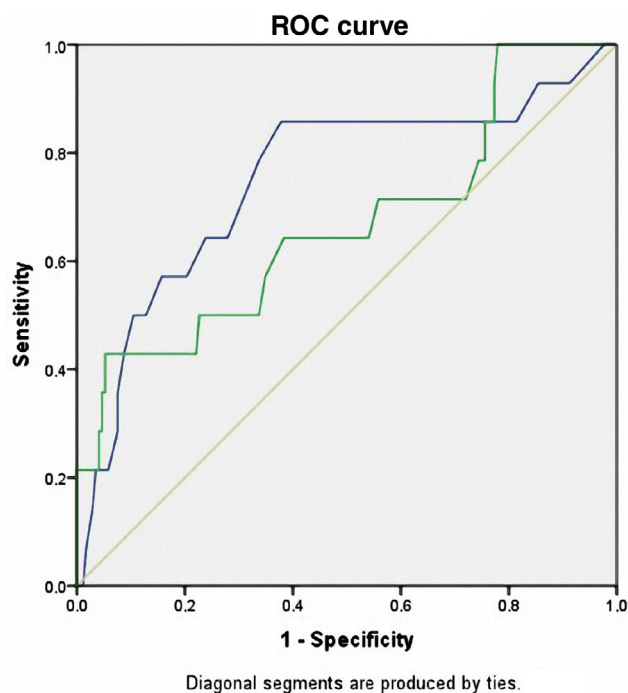


Figure 2 Receiver operating characteristics (ROCs) curves for prediction of hospital mortality (prealbumin, albumin) in hemodialysis patients without hepatitis virus infection. Serum prealbumin: area under the curve (AUC) = 0.75 (95% confidence interval [CI]: 0.597–0.902), $P = 0.002$; cut-off value = 38.5 mg/dl, sensitivity = 85.7%, specificity = 62.2%. Serum albumin: AUC = 0.667 (95% CI: 0.5–0.835), $P = 0.038$; cut-off value = 34.25 g/L, sensitivity = 42.9%, specificity = 94.8%. Serum prealbumin concentration had also a better predictive value of 5-year all-cause mortality than serum albumin in maintenance hemodialysis patients without hepatitis virus infection. Source of the curve: (—) prealbumin, (—) albumin, and (—) reference line.

associated with all-cause mortality than HCV-negative status in a study of 13 000 HD patients in the United States. A study by Fabrizi *et al.*²⁶ found that HD can negatively affect the likelihood of HCV infection. The results indicated that the estimated relative risk of liver-related death in HD patients with anti-HCV-positive was 1.57 times higher (95% confidence interval [CI]: 1.33–1.86; $P < 0.001$) than in anti-HCV negative patients.

When comparing the clinical and paraclinical characteristics of the mortality and survival groups, we found that there were many features related to mortality, including long duration of hemodialysis, low ratio of residual renal function, high rate of dyslipidemia, and, especially, the high rate of hepatitis virus infection. In addition, high serum urea and hs-CRP levels as well as low serum prealbumin and albumin are factors associated with mortality (Table 3). However, when multivariate analysis included only dialysis time, prealbumin and albumin levels were independent factors associated with mortality in our patients. Thus, inflammation and malnutrition are factors associated with mortality in HD patients using reused low-flux dialyzers.

The changes in serum prealbumin and albumin concentration in acute and chronic liver diseases were investigated. Albumin had been used as a useful indicator of liver function for a long time, but serum prealbumin has been noted for its clinical significance only in regular HD patients. In our study, we found that the level of serum prealbumin in G1 was significantly lower than in G2, with $P < 0.001$ (Table 1), but there was no difference in serum prealbumin concentration between different types of hepatitis virus infection (Table 2). We also did not find any difference in the levels of serum albumin between G1 and G2 or between the different types of hepatitis virus infection (Tables 1,2). Protein-energy wasting (PEW) is characterized by muscle loss, low protein or energy intake, low or high body weight, unintentional weight loss, and low serum albumin and prealbumin concentrations. Therefore, albumin and prealbumin concentration are often used in clinical practice to assess nutritional status and prognosis risk of death on dialysis.^{10,27,28} Recently, Chertow *et al.*²⁹ confirmed that low prealbumin concentration was associated with mortality and hospitalization due to infection. Lee *et al.*³⁰ also used serum prealbumin to predict

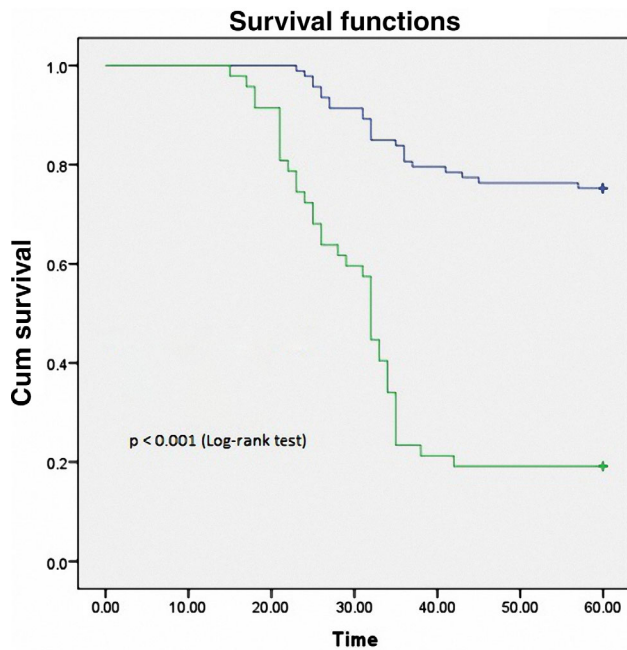


Figure 3 Kaplan–Meier analysis for all-cause mortality of 140 hemodialysis patients with hepatitis B virus and/or hepatitis C virus infection, classified according to prealbumin level in two groups. Patients with lower prealbumin concentrations (green line: serum prealbumin level < 24.5 mg/dl) had a significantly higher mortality rate compared to those with higher serum prealbumin concentrations (blue line: serum prealbumin \geq 24.5 mg/dl) (log-rank test, $P < 0.001$). Prealbumin >24.5 mg/dl: (—) 0.00, (—) 1.00, (—) 0.00-censored, and (—) 1.00-censored.

mortality in peritoneal dialysis (PD) patients and confirmed that low serum prealbumin concentration was an independent and sensitive predictor for mortality in incident PD patients, showing a good correlation with nutritional and inflammatory markers. Our results showed that both prealbumin and albumin are predictors for all-cause mortality in both groups of patients with HBV and/or HCV infection and without hepatitis virus infection (Figs 1,2). However, the predictive value of serum prealbumin was stronger than that of a serum albumin with $P < 0.001$. Based on the Kaplan–Meier analysis results (Figs 3,4), we found that serum prealbumin level of <38.5 mg/dl led to a significantly higher death rate compared with serum prealbumin concentrations of \geq 38.5 mg/dl in HD patients without hepatitis virus infection, while in the HD patients with HBV and/or HCV infection, a serum prealbumin level of <24.5 mg/dl led to a significantly higher death rate compared with serum prealbumin concentrations of \geq 24.5 mg/dl. The result confirmed that low serum prealbumin had a good predictive value for 5-year all-cause mortality, not only in the group of HD patients with HBV and/or HCV infection but also in the group without hepatitis virus infection.

The study still has some limitations. It did not determine the status of chronic liver disease, cirrhosis, and the stratification of liver function. Second, the study did not measure the number of hepatitis B and C viruses in negative HBsAg and anti-HCV

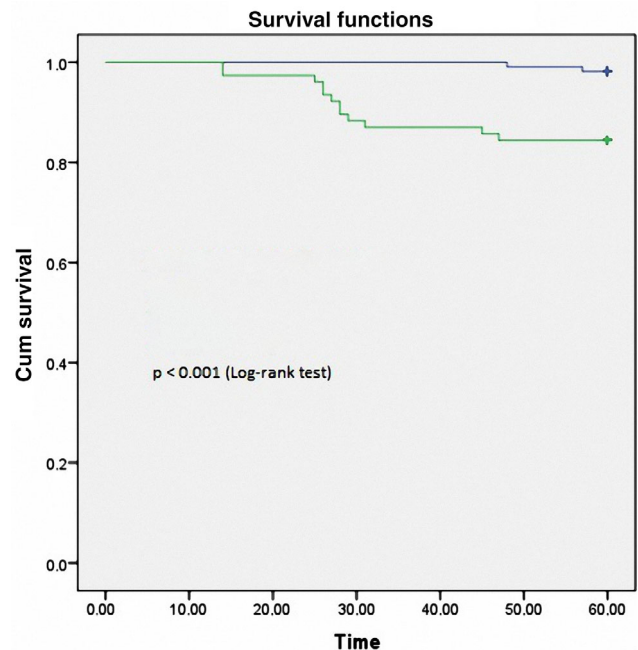


Figure 4 Kaplan–Meier analysis for all-cause mortality of 186 hemodialysis patients without hepatitis virus infection, classified according to prealbumin level in two groups. Patients with lower prealbumin concentrations (green line: serum prealbumin level < 38.5 mg/dl) had a significantly higher mortality rate compared with those with higher serum prealbumin concentrations (blue line: serum prealbumin \geq 38.5 mg/dl) (log-rank test, $P < 0.001$). Prealbumin >38.5 mg/dl: (—) 0.00, (—) 1.00, (—) 0.00-censored, and (—) 1.00-censored.

samples and also not determine the genotypes of hepatitis viruses. Third, we did not control fully other inflammation sources or nutrient intake. Therefore, we cannot have a more in-depth discussion of the impact of hepatitis virus infection on the overall condition and mortality rate in HD patients treated with reused low-flux dialyzers.

Conclusion

In conclusion, low serum prealbumin concentration was a good predictor of 5-year all-cause mortality in both groups of HD patients with HBV and/or HCV infection and without hepatitis virus infection.

References

- Al Zabadi H, Rahal H, Fuqaha R. Hepatitis B and C prevalence among hemodialysis patients in the West Bank hospitals, Palestine. *BMC Infect. Dis.* 2016; **16**: 41. <https://doi.org/10.1186/s12879-016-1359-8>.
- Malhotra R, Soin D, Grover P *et al.* Hepatitis B virus and hepatitis C virus co-infection in hemodialysis patients: a retrospective study from a tertiary care hospital of North India. *J. Nat. Sci. Biol. Med.* 2016; **7**(1): 72–4.
- Malyszko J, Zawierucha J, Marcinkowski W *et al.* The prevalence of hepatitis C and B among patients on hemodialysis and on renal

- transplantation waiting list in Poland has significantly decreased during the last 10 years. *Int. Urol. Nephrol.* 2018; **50**(8): 1555–6.
- 4 Maraj M, Kuśnierz-Cabala B, Dumnicka P *et al.* Malnutrition, inflammation, atherosclerosis syndrome (MIA) and diet recommendations among end-stage renal disease patients treated with maintenance hemodialysis. *Nutrients.* 2018; **10**(1): 69. <https://doi.org/10.3390/nu10010069>.
 - 5 Kang SS, Chang JW, Park Y. Nutritional status predicts 10-year mortality in patients with end-stage renal disease on hemodialysis. *Nutrients.* 2017; **9**(4): 399. <https://doi.org/10.3390/nu9040399>.
 - 6 Harvinder GS, Swee WCS, Karupaiah T *et al.* Dialysis malnutrition and malnutrition inflammation scores: screening tools for prediction of dialysis-related protein-energy wasting in Malaysia. *Asia Pac. J. Clin. Nutr.* 2016; **25**(1): 26–33.
 - 7 Qureshi AR, Alvestrand A, Divino-Filho JC *et al.* Inflammation, malnutrition, and cardiac disease as predictors of mortality in hemodialysis patients. *J. Am. Soc. Nephrol.* 2002; **13**: S28–36.
 - 8 Rambod M, Bross R, Zitterkoph J *et al.* Association of malnutrition-inflammation score with quality of life and mortality in hemodialysis patients: a 5-year prospective cohort study. *Am. J. Kidney Dis.* 2009; **53**(2): 298–309.
 - 9 Beck FK, Rosenthal TC. Prealbumin: a marker for nutritional evaluation. *Am. Fam. Physician.* 2002; **65**(8): 1575–9.
 - 10 Chertow GM, Ackert K, Lew NL *et al.* Prealbumin is as important as albumin in the nutritional assessment of hemodialysis patients. *Kidney Int.* 2000; **58**(6): 2512–7.
 - 11 Cano NJM, Roth H, Aparicio M *et al.* Malnutrition in hemodialysis diabetic patients: evaluation and prognostic influence. *Kidney Int.* 2002; **62**(2): 593–601.
 - 12 Pupim LB, Caglar K, Hakim RM *et al.* Uremic malnutrition is a predictor of death independent of inflammatory status. *Kidney Int.* 2004; **66**(5): 2054–60.
 - 13 Rambod M, Kovesdy CP, Bross R *et al.* Association of serum prealbumin and its changes over time with clinical outcomes and survival in patients receiving hemodialysis. *Am. J. Clin. Nutr.* 2008; **88**(6): 1485–94.
 - 14 Msaad R, Essadik R, Mohtadi K *et al.* Predictors of mortality in hemodialysis patients. *Pan Afr. Med. J.* 2019; **33**: 61. <https://doi.org/10.11604/pamj.2019.33.61.18083>.
 - 15 Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V : an analysis of error. *J. Am. Soc. Nephrol.* 1993; **4**: 1205–13.
 - 16 Sarnak MJ, Bloom R, Muntner P *et al.* KDOQI US commentary on the 2013 KDIGO Clinical Practice Guideline for lipid management in CKD. *Am. J. Kidney Dis.* 2015; **65**(3): 354–66.
 - 17 Joukar F, Besharati S, Mirpour H *et al.* Hepatitis C and hepatitis B seroprevalence and associated risk factors in hemodialysis patients in Guilan province, north of Iran: HCV and HBV seroprevalence in hemodialysis patients. *Hepat. Mon.* 2011; **11**(3): 178–81.
 - 18 Kalantari H, Ebadi S, Yaran M *et al.* Prevalence and risk factors of hepatitis B and C viruses among hemodialysis patients in Isfahan, Iran. *Adv. Biomed. Res.* 2014; **3**: 73.
 - 19 Reddy GA, Dakshinamurthy KV, Neelaprasad P *et al.* Prevalence of HBV and HCV dual infection in patients on haemodialysis. *Indian J. Med. Microbiol.* 2005; **23**(1): 41–3.
 - 20 Rached AA, El Khoury L, El Imad T *et al.* Incidence and prevalence of hepatitis B and hepatitis C viruses in hemodialysis patients in Lebanon. *World J. Nephrol.* 2016; **5**(1): 101–7.
 - 21 Zahedi MJ, Darvish Moghaddam S, Alavian SM *et al.* Seroprevalence of hepatitis viruses B, C, D and HIV infection among hemodialysis patients in Kerman Province, South-East Iran. *Hepat. Mon.* 2012; **12**(5): 339–43. <https://doi.org/10.5812/hepatmon.5969>.
 - 22 Fabrizi F, Messa P, Basile C *et al.* Hepatic disorders in chronic kidney disease. *Nat. Rev. Nephrol.* 2010; **6**(7): 395–403. <https://doi.org/10.1038/nrneph.2010.37>.
 - 23 Afsar B, Ozdemir NF, Sezer S *et al.* Quality of life is not related with liver disease severity but with anemia, malnutrition, and depression in HCV-infected hemodialysis patients. *Hemodial. Int.* 2009; **13**(1): 62–71. <https://doi.org/10.1111/j.1542-4758.2009.00329.x>.
 - 24 Foster GR. Quality of life considerations for patients with chronic hepatitis C. *J. Viral Hepat.* 2009; **16**(9): 605–11. <https://doi.org/10.1111/j.1365-2893.2009.01154.x>.
 - 25 Kalantar-Zadeh K, Kilpatrick RD, McAllister CJ *et al.* Hepatitis C virus and death risk in hemodialysis patients. *J. Am. Soc. Nephrol.* 2007; **18**: 1584–93.
 - 26 Fabrizi F, Martin P, Dixit V *et al.* Meta-analysis: effect of hepatitis C virus infection on mortality in dialysis. *Aliment. Pharmacol. Ther.* 2004; **20**: 1271–7.
 - 27 Fouque D, Kalantar-Zadeh K, Kopple J *et al.* A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int.* 2008; **73**(4): 391–8.
 - 28 Avram MM, Mittman N, Bonomini L *et al.* Markers for survival in dialysis: a seven-year prospective study. *Am. J. Kidney Dis.* 1995; **26**(1): 209–19.
 - 29 Chertow GM, Goldstein-Fuchs DJ, Lazarus JM *et al.* Prealbumin, mortality, and cause-specific hospitalization in hemodialysis patients. *Kidney Int.* 2005; **68**(6): 2794–800.
 - 30 Lee KH, Cho JH, Kwon O *et al.* Low prealbumin levels are independently associated with higher mortality in patients on peritoneal dialysis. *Kidney Res. Clin. Pract.* 2016; **35**(3): 169–75.