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Longitudinal Measures of Serum Albumin and Prealbumin Concentrations in Incident Dialysis Patients: the Comprehensive Dialysis Study

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Abstract

Objective—Serum albumin and prealbumin concentrations are strongly associated with the risk of death in patients on dialysis. Our study examined the association among demographic characteristics, body composition, co-morbidities, dialysis modality and access, inflammation and longitudinal measures of albumin and prealbumin in incident dialysis patients.

Design, Setting, Subjects and Outcome Measures—The Comprehensive Dialysis Study (CDS) is a prospective cohort study of incident dialysis patients; in this report we examined data from 266 Nutrition sub-study participants who donated serum. The independent variables of interest were baseline age, sex, race, Quetélet's (body mass) index, dialysis modality and access, diabetes, heart failure, atherosclerotic vascular disease, serum creatinine, and longitudinal measures of C-reactive protein. The outcomes of interest (dependent variables) were longitudinal measures of albumin and prealbumin concentrations, measured at study entry and every 3 months for one year.

Results—In multivariable mixed linear models, female sex, peritoneal dialysis, hemodialysis with a catheter, and higher C-reactive protein concentrations were associated with lower serum

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albumin concentrations, and serum albumin concentrations increased slightly over the year. In comparison, prealbumin concentrations did not significantly change over time; female sex, lower body mass index, diabetes, atherosclerotic vascular disease, and higher C-reactive protein concentrations were associated with lower prealbumin concentrations. Serum creatinine had a curvilinear relation with serum albumin and prealbumin.

Conclusions—Serum albumin increases early in the course of dialysis whereas prealbumin does not, and the predictors of serum concentrations differ at any given time. Further understanding of mechanisms underlying differences between albumin and prealbumin kinetics in persons on dialysis may lead to an improved approach to the management of protein energy wasting.

Keywords

Albumin; C-reactive protein; dialysis; end-stage renal disease; prealbumin

Introduction

Protein energy wasting (PEW) is characterized by loss of muscle, low protein or energy intake, low body weight or fat, unintentional weight loss, and abnormal biochemical measures.(1) Low serum albumin and prealbumin concentrations are important biochemical indicators of PEW, are commonly used in clinical practice to assess nutritional status, and are powerful predictors of mortality risk on dialysis.(2, 3) Both albumin and prealbumin are sensitive to protein calorie malnutrition and are negative acute phase proteins, exhibiting decreases in their serum concentration during episodes of inflammation.(4, 5) Longitudinal measures of albumin or prealbumin may provide more information about the risk of adverse outcomes on dialysis than single measures of these proteins.(6, 7) However, few studies have focused on factors associated with serum albumin and prealbumin concentrations over time in persons on dialysis. Previous studies of longitudinal measures of albumin have been limited by the inclusion of select participants,(4, 5) recruitment from a single center,(8) long time intervals between measures of albumin,(9) or lack of measures of inflammation.(10) Few studies have examined longitudinal measures of prealbumin. In the Comprehensive Dialysis Study (CDS), we sought to examine changes in albumin and prealbumin concentrations over one year in incident dialysis patients and whether age, race, sex, Quetélet's (body mass) index, diabetes, atherosclerotic vascular disease (ASVD), heart failure, dialysis modality and access at study entry, or longitudinal measures of C-reactive protein (CRP) were associated with longitudinal albumin and prealbumin concentrations.

Subjects and Methods

Study Participants

The CDS is a prospective cohort study of adults with end-stage renal disease (ESRD) who newly initiated maintenance hemodialysis or peritoneal dialysis in the U.S., participants were enrolled between September 2005 and June 2007. The CDS was designed to examine nutrition, functional status/physical activity, and quality of life in incident dialysis patients. The study design and cohort recruitment have been previously described in detail.(11) Briefly, a sample of 335 dialysis facilities throughout the U.S. was selected for participation in the CDS, with a subsample of 73 units selected for participation in the Nutrition sub-study. One component of the Nutrition sub-study was to provide serum samples at enrollment and quarterly for up to one year. A total of 1,678 incident dialysis patients from 297 facilities consented to participate in the surveys and/or laboratory component of the CDS. Of these, 1,279 participated only in the quality of life survey, 364 participated in the quality of life and nutrition surveys (231 of whom donated serum); and 35 donated serum

only. Nutrition sub-study participants who donated at least one serum sample constitute the cohort for this study.

Data Collection and Measurements

We collected baseline data from the Medical Evidence Form (CMS 2728 Form) and a telephone interview administered by DataBanque Research Services (Pittsburgh, PA) when available. Of the analytic cohort, 35 participants did not participate in the telephone interview. We collected data on age, sex, race, Quetélet's (body mass) index (BMI), dialysis modality, dialysis access, history of diabetes, congestive heart failure (CHF), or ASVD, and serum creatinine at the time of outpatient dialysis initiation. For the purpose of this analysis, we classified race as white or other. We classified dialysis modality and access into one of the following categories: peritoneal dialysis, hemodialysis with an arteriovenous fistula (AVF) or arteriovenous graft (AVG), or hemodialysis with a dialysis catheter. We classified participants as having diabetes if diabetes was the primary cause of end-stage renal disease (ESRD) or if diabetes was listed among the co-morbidities. Participants were considered to have ASVD if atherosclerotic heart disease, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, or amputation was listed among the co-morbidities.

There were few missing data elements. The mean sex-stratified BMI was imputed for one participant with missing BMI. For one participant with missing hemodialysis access, we classified the dialysis access as “catheter” given the recent initiation of dialysis and prevalence of catheters in the CDS population.

Blood was drawn at study entry and every 3 months for the first year of study at the participating dialysis unit. We measured albumin, pre-albumin, and CRP concentrations in duplicate on each serum sample using a Beckman Array 360 nephelometer. Coefficients of variation (CoV) for each assay were as follows: albumin inter assay CoV 8.3%, intra assay Cov 0.2%; prealbumin inter assay CoV 4.3%, intra assay CoV 1.1%; and CRP inter assay CoV 9.2%, intra assay CoV 3.6%. If the two measures on any given sample differed within the duplicates by more than 1%, we repeated testing. We used the mean concentration of the duplicate serum albumin, pre-albumin, and CRP concentrations in the statistical analyses.

Statistical Analyses

The explanatory variables of interest were demographics, co-morbidities, dialysis modality and access, BMI, serum creatinine, and longitudinal measures of CRP. The dependent variables of interest were longitudinal changes in serum albumin and pre-albumin (measured at 0, 3, 6, 9 and 12 months). Albumin and prealbumin were examined as separate outcomes.

Baseline characteristics were described using means for continuous variables and proportions for categorical variables. The mean, median, and interquartile range of serum albumin and prealbumin concentrations over time were examined using boxplots. The associations among demographics, BMI, dialysis modality and access, co-morbidities, serum creatinine and longitudinal measures of CRP with albumin and prealbumin were examined using linear mixed models with robust standard errors. These models incorporate sampling weights per the survey design, and accommodate within-center correlation. Centered versions of the continuous covariates (age, BMI, and serum creatinine) were created by subtracting the mean value of age, mean value of BMI for males, and mean value of serum creatinine from the corresponding covariate values. The centered covariate variables were used in the statistical analyses.

Lowess curves and models including quadratic terms were examined to assess whether modeling the association between serum albumin and prealbumin and each of the centered continuous covariates (age, BMI, and serum creatinine) and the time variable as linear was

appropriate. If the association did not appear to be linear or the quadratic term was significant, then the centered quadratic term for that covariate was retained in the model. To examine whether changes in albumin (or prealbumin) over time differed based on age, sex, race, diabetes, dialysis modality and access type, or time under observation we tested time × covariate interaction terms in the models. To examine the possible bias due to participant discontinuation, we created two categories of time under observation: ≤ 6 months or > 6 months. We then checked the interaction of changes in albumin (or prealbumin) over time with the time under observation variable. We also conducted sensitivity analyses using maximum likelihood fits since they are resistant to bias due to selective dropout of participants, even when that dropout is associated with previously measured outcomes.

Because albumin and prealbumin have different ranges of values, we compared differences in the observed effect size by using standardized outcomes (subtracting the mean and dividing by the standard deviation), allowing for the effect size of a given covariate to be compared between albumin and prealbumin regardless of the scale of the outcome. All statistical analyses were performed using SAS 9.2 (Cary, NC) and StataSE 11 (College Station, TX).

The study was approved by the Committees on Human research at the University of California, Davis and San Francisco, and the Clinical Research Subcommittee of the Research and Development Committee at the San Francisco Veterans Affairs Medical Center.

Results

A total of 266 CDS Nutrition sub-study participants with laboratory measures were included in our study; these participants were from a total of 56 participating dialysis facilities. The mean age of participants was 62 years, 55% were male, 71% were white, 68% were on hemodialysis with a catheter as the vascular access, and 8% were on peritoneal dialysis (Table 1). The cohort was characterized by a high prevalence of diabetes, heart failure, and ASVD. The median time from dialysis initiation to the first blood draw was 6 months (10^{th} percentile 4.5 months, 90^{th} percentile 9.5 months). The number of participants decreased with follow-up, with a total of 200, 179, 172, and 164 participants donating blood samples at months 3, 6, 9, and 12, respectively. During follow-up, a total of 79 participants discontinued the study; of these, 22 died and 13 were transplanted. Other causes of study discontinuation included recovery of kidney function, participant moving to a non study-site, or withdraw of the study site or patient from the study. In addition, blood samples were not collected for all participants at each quarter for a number of reasons, including: participant refusal, nonadherence, hospitalization, vacation, study site not responding, study site placed on hold, staff missing the blood draw, or errors in the transfer of blood samples.

In general, serum albumin increased whereas prealbumin remained relatively stable over time (Figures 1a and 1b). Individually, older age, ASVD, heart failure, peritoneal dialysis, hemodialysis with a catheter, and higher CRP concentrations were significantly associated with lower serum albumin concentrations (Table 2). In adjusted models, longer vintage, as measured in 3 month intervals, was associated with higher concentrations of serum albumin whereas female sex, peritoneal dialysis, hemodialysis with a catheter, and higher CRP levels were associated with lower serum albumin concentrations (Table2). We observed a nonlinear association between serum creatinine and serum albumin concentrations; for the majority of participants, a higher serum creatinine was associated with a higher serum albumin whereas among participants with the highest serum creatinine values, a higher serum creatinine was associated with a lower albumin concentration (Table 2). The change in albumin was not different based on age, sex, race, diabetes, or dialysis modality and

access type (p-values for time by covariate interactions were 0.76, 0.31, 0.30, 0.75, and 0.64 respectively). The change in albumin over time did not differ based on duration of follow-up (p-value for the interaction was 0.15).

Individually, diabetes, ASVD, heart failure, higher CRP concentration were associated with lower serum prealbumin concentrations; serum creatinine and prealbumin had a nonlinear association (Table 3), similar to the relation described between serum creatinine and albumin. Table 3 shows results of the mixed model for prealbumin with simultaneous adjustment for all covariates. The associations between age, sex, race, diabetes, dialysis modality and access and serum prealbumin did not change over time (p-values for time by covariate interactions were 0.48, 0.82, 0.43, 0.94, and 0.75 respectively). The change in prealbumin did not differ based on time under observation (p-value for the interaction was 0.37)

While peritoneal dialysis was associated with statistically significantly lower serum albumin concentrations, peritoneal dialysis was not associated with prealbumin concentrations. In contrast, lower BMI, ASVD, and diabetes were associated with lower serum prealbumin concentrations but not with serum albumin concentrations. Given these observed differences between certain covariates and their associations with albumin and prealbumin, we were interested in determining whether there were meaningful differences in effect size. When we examined standardized outcomes, the BMI coefficients were 0.006 (p-value=0.27) and 0.028 (p-value =0.0002) for albumin and prealbumin, respectively. Thus the association between BMI and prealbumin was more than 4-fold greater than the association between BMI and albumin. The coefficient for peritoneal dialysis (as compared with hemodialysis with an AVF/AVG) was −0.65 (p-value=0.008) and 0.22 (p-value=0.42) for albumin and prealbumin, respectively. The coefficients for diabetes were −0.12 (p-value=0.18) and −0.24 (p-value=0.03) and the coefficients for ASVD were −0.04 (p-value=0.74) and −0.36 (p-value=0.0001) for albumin and prealbumin, respectively, indicating stronger associations with prealbumin than with albumin for these covariates.

Discussion

In our study of longitudinal serum albumin and prealbumin concentrations, we found that serum albumin concentrations increased whereas prealbumin concentrations did not change over time on average. Sex, dialysis modality, dialysis access type, serum creatinine and inflammation were associated with the serum albumin concentrations over time. While some of the correlates of prealbumin were the same as those observed for albumin, prealbumin concentrations were also associated with BMI, diabetes, and ASVD and were not associated with modality. Although serum albumin and prealbumin are directly correlated, each explains less than 25% of the concentration of the other(3) and these proteins have unique biological determinants and functions.

Serum albumin concentrations in patients on dialysis are determined by the rate of synthesis, fractional catabolic rate, volume of distribution, urinary and other extracorporeal losses, including loss across the peritoneal membrane or across the dialyzer with hemodialysis.(12) Albumin synthesis increases in response to protein calorie intake and decreases in response to inflammation whereas the albumin fractional catabolic rate increases in the presence of inflammation but is suppressed in the presence of protein energy malnutrition, thereby protecting the plasma albumin pool.(12, 13) Numerous factors, including decreases in plasma volume, improvement in nutrition, and a decrease in urinary protein excretion as residual kidney function declines, may be responsible for the increase in serum albumin observed during the early course of dialysis.

Importantly, using longitudinal measures of CRP concentrations and albumin, we were able to examine the association of inflammation with serum albumin during one year of follow-up. Similar to prior studies with measures of inflammation,(4, 5) we found that higher CRP concentrations were inversely associated with serum albumin concentrations. Each doubling of CRP was associated with a decrease in albumin of 0.11 g/dL during the one year of study.

Hemodialysis with a catheter and peritoneal dialysis were each associated with significantly lower serum albumin concentrations when compared to hemodialysis with an AVF or AVG. The observed association between hemodialysis with a catheter and lower serum albumin concentration is likely multifactorial and due to higher rates of infection,(14) increased inflammation,(15) and an increased prevalence and severity of co-morbidities in persons on hemodialysis with catheters. Although we adjusted for demographics, inflammation as measured by CRP, and co-morbidities, residual confounding may account for some of the observed association between hemodialysis with a catheter and albumin concentrations. Peritoneal dialysis was also associated with notably lower serum albumin when compared to hemodialysis with an AVF/AVG, presumably as a consequence of transperitoneal losses of albumin.(16) Total albumin synthesis is between 12 to14 grams per day, and transperitoneal losses of albumin average 4 to 5 grams per day,(16) representing more than 30% of the rate of albumin synthesis. Thus transperitoneal losses are substantial relative to the fractional synthetic rate, and the compensatory mechanisms of decreasing the albumin catabolic rate and increasing albumin synthesis may not be sufficient to balance transperitoneal losses.

Peritoneal dialysis was not associated with lower serum prealbumin concentrations whereas it was associated, as expected, with lower serum albumin concentrations. Prior studies have observed that peritoneal dialysis patients on average have higher prealbumin concentrations as compared with hemodialysis patients.(17) Although the underlying mechanisms of higher prealbumin concentrations in persons on peritoneal dialysis than persons on hemodialysis are not well understood, potential explanations include: 1) prealbumin being less sensitive to external loss than albumin secondary to the higher fractional synthesis rate of prealbumin(18) and/or 2) alterations in prealbumin metabolism due to loss of a regulatory molecule through peritoneal dialysis, similar to changes in cholesterol metabolism.(17)

The association between serum creatinine and albumin is complex, as serum creatinine reflects numerous biological factors including residual kidney function and muscle mass. Extremely high values of serum creatinine at the time of dialysis initiation may represent lack of access to care, acute or rapid deterioration in kidney function, or noncompliance, which could in turn explain the inverse association with albumin at the very highest levels of serum creatinine. For the majority of CDS participants, however, higher serum creatinine concentrations were associated with higher serum albumin concentrations, potentially reflecting the correlations among serum creatinine and muscle mass, nutrition, residual kidney function and urinary protein losses.

Interestingly, women had 0.11 g/dl lower serum albumin concentrations on average compared with men. Although other studies have also found female sex associated with lower serum albumin concentrations,(10) biological mechanisms to explain this association are not well understood.

Our study is one of few to examine correlates of longitudinal measures of prealbumin, and we identified important associations that differed from those with albumin. Interestingly, higher BMI was associated with higher prealbumin but not albumin concentrations. In the general population, prealbumin concentrations are higher in obese individuals and correlate with total adiposity as well as visceral fat mass.(19) Hepatocytes and adipocytes secrete serum retinol-binding protein 4 (RBP4), a carrier protein that interacts with and binds

prealbumin in the circulation.(19) In ob/ob mice, RBP4 has enhanced binding capacity for prealbumin and prealbumin mRNA is increased in the liver.(20) Therefore, the association between visceral adiposity and prealbumin concentrations may be due to decreased clearance as a consequence of increased RBP4 binding and/or increased synthesis of prealbumin in obese individuals.

Our study has several strengths. First, the CDS Nutrition sub-study cohort was recruited from dialysis centers across the US and included patients receiving care at nearly 60 different dialysis facilities, improving the generalizability of findings compared to studies from a single center or single dialysis provider. Second, our cohort included incident patients on hemodialysis and peritoneal dialysis, therefore allowing for a more general understanding of changes in albumin and prealbumin concentrations in the period following initiation of dialysis. Third, we examined measurements of albumin and prealbumin over the course of a year as opposed to limiting our analyses to a single measure, allowing for a better understanding of factors associated with longitudinal measures of these proteins. As such, we were able to determine whether key demographic and clinical characteristics were associated with *persistent* differences in the concentration of key laboratory proxies for nutrition. Fourth, we incorporated time-varying CRP in our models, so that we could account for the complex interplay between acute and chronic inflammation and these protein concentrations. Fifth, all laboratory test results were determined in a single laboratory using batched samples and identical methods. Finally, our cohort consisted of patients new to dialysis; therefore the associations among co-morbidities and serum prealbumin or albumin concentrations may be somewhat more accurate as patients tend to accumulate comorbid conditions with increasing dialysis vintage.

Our study had several limitations. First, dialysis modality and vascular access were only evaluated at the time of study entry. Unobserved changes in dialysis modality and vascular access over time limit the interpretation of findings with respect to these variables. Second, we did not have measures of residual kidney function or urinary protein and therefore we cannot make conclusions regarding the effect of residual kidney function or proteinuria (or the expected decline in proteinuria with the decline in residual kidney function) on serum albumin and prealbumin concentrations, factors that may be particularly relevant in the early course of dialysis. Third, we did not examine dialysis factors such as adequacy or dialyzer type. However, a previous study by Leavey *et al.* found no association among dialysis factors and trends in albumin concentrations over time.(10) Fourth, we do not have measures of total body water and therefore cannot determine how changes in total body water over time influence longitudinal changes in albumin and prealbumin. Fifth, we did not examine dietary factors and the influence of protein intake on longitudinal changes in albumin and prealbumin. Last, our study population may be healthier than the general dialysis population as reflected by the relatively low mortality (8%) and high transplant rate (5%) over the one year of study. In summary, serum albumin concentrations tend to increase whereas prealbumin concentrations remain relatively stable in incident dialysis patients during one year of follow-up. Serum albumin and prealbumin concentrations are associated with sex, inflammation, and serum creatinine, and prealbumin is further associated with body composition, ASVD and diabetes. Serum albumin, but not prealbumin concentrations, are associated with dialysis modality and access type.

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Practical Application

The findings from our study highlight that albumin and prealbumin do not change in parallel during the early course of dialysis and that the clinical correlates of each protein differ. Although albumin and prealbumin each decrease in response to inflammation and to significant protein malnutrition, albumin and prealbumin respond differently to correction of malnutrition and external loss. Further examination of mechanisms underlying differences between albumin and prealbumin kinetics may lead to an improved approach to the monitoring and management of PEW in persons with end-stage renal disease on maintenance dialysis.

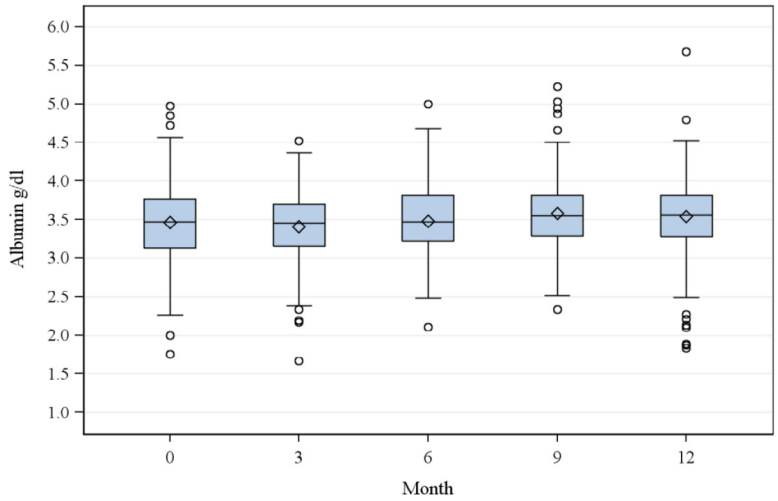

Figure 1a. Albumin Concentrations in the Comprehensive Dialysis Study

Boxplots showing the concentrations of serum albumin at study entry and months 3, 6, 9 and 12. The box represents the interquartile range (IQR) with the lower line representing the lower quartile (25^{th} percentile) and the upper line representing the upper quartile (75^{th} percentile), the median is represented by the horizontal line within the box. The whiskers are drawn to the maximum data value that is less than 1.5 times the IQR. The diamond represents the mean.

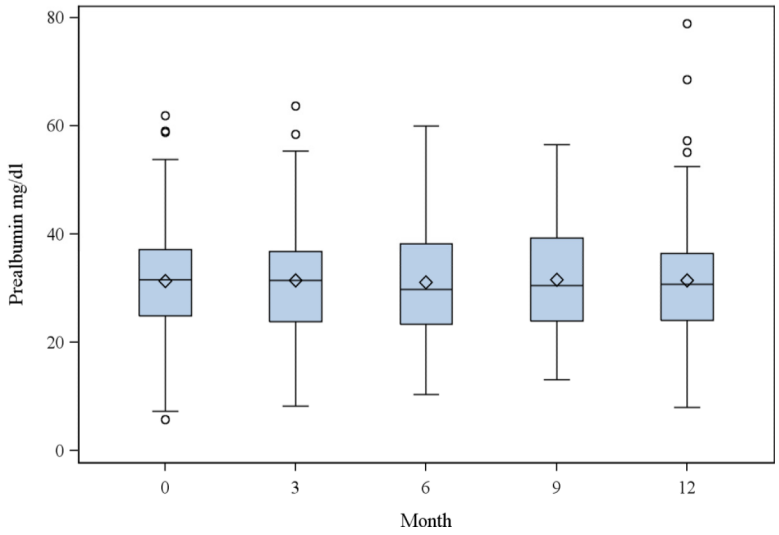

Figure 1b. Prealbumin Concentrations in the Comprehensive Dialysis Study

Boxplots showing the concentrations of serum prealbumin at study entry and months 3, 6, 9, and 12. The box represents the interquartile range (IQR) with the lower line representing the lower quartile (25^{th} percentile) and the upper line representing the upper quartile (75^{th} percentile), the median is represented by the horizontal line within the box. The whiskers are drawn to the maximum data value that is less than 1.5 times the IQR. The diamond represents the mean.

Table 1

Baseline Characteristics of Included Comprehensive Dialysis Study Nutrition Participants

	N= 266
Age, years	62 ± 14
Male	147 (55)
Race	
White	189 (71)
Black	68 (26)
Other	9 (3)
Body mass index	29.8 ± 7.8
Diabetes	152 (57)
ASVD	96 (36)
Heart Failure	85 (32)
Dialysis Modality and Access	
Hemodialysis, AVF or AVG	63 (24)
Hemodialysis, Catheter	180 (68)
Peritoneal Dialysis	22 (8)
Baseline Albumin, g/dL	3.5 ± 0.5
Baseline Prealbumin, mg/dL	31.4 ± 9.2
Baseline C-Reactive protein, mg/L	7.45 [3.95, 12.75]
Baseline Serum Creatinine, mg/dL	6.20 [4.70, 8.20]

Data presented as mean ± sd, number (%) or median [interquartile range]; AVF or AVG: arteriovenous fistula or arteriovenous graft

Table 2

Univariate and Multivariable Mixed Effects Models for Albumin

	Univariate		Multivariable	
	Estimate (SE)	**p-value**	**Estimate (SE)**	**p-value**
Time, 3 month intervals	*Varies		0.02 (0.01)	0.01
Age, per 10 years	−0.07 (0.02)	0.01	−0.04 (0.02)	0.07
Sex, Female	−0.11 (0.06)	0.08	−0.11 (0.04)	0.01
Race, White	−0.01 (0.08)	0.87	0.06 (0.08)	0.49
Body Mass Index	−0.005 (0.003)	0.10	0.003 (0.003)	0.27
Diabetes	−0.11 (0.06)	0.06	−0.06 (0.04)	0.18
ASVD	−0.10 (0.05)	0.04	−0.02 (0.05)	0.74
Congestive Heart Failure	−0.16 (0.07)	0.02	−0.07 (0.06)	0.22
Dialysis Modality, Access**				
Peritoneal Dialysis	−0.22 (0.11)	0.05	−0.31 (0.12)	0.01
Hemodialysis, Catheter	−0.14 (0.06)	0.03	−0.16 (0.04)	<0.0001
CRP, per 2-fold increase	−0.11 (0.01)	<0.0001	−0.11 (0.01)	<0.0001
Serum Creatinine†	0.05 (0.01)	<0.0001	0.03 (0.01)	0.001
Serum Creatinine^2	−0.004 (0.0005)	<0.0001	−0.002 (0.001)	<0.0001

Multivariable model adjusted for all variables shown.

*Each univariate model also adjusts for time, but its coefficient varies somewhat across the models.

**Referent category: Hemodialysis with arteriovenous fistula or arteriovenous graft

†Serum creatinine modeled as a quadratic term due to curvilinear relationship. At a serum creatinine of 7 mg/dL, an increase in serum creatinine of 1 mg/dL was associated with an increase of albumin of 0.03 g/dL; a serum creatinine above 14.5 mg/dL was associated inversely with serum albumin.; CRP: C-reactive protein; SE: standard error

Table 3

Univariate and Multivariable Mixed Effects Models for Prealbumin

	Univariate		Multivariable	
	Estimate (SE)	**p-value**	**Estimate (SE)**	**p-value**
Time, 3 month intervals	Varies*		0.10 (0.19)	0.61
Age, per 10 years	−0.77 (0.48)	0.11	0.40 (0.45)	0.38
Sex, Female	− 1.59 (1.15)	0.17	−2.61 (0.61)	<0.0001
Race, White	−1.00 (1.03)	0.33	0.14 (1.06)	0.89
Body Mass Index	0.08 (0.07)	0.27	0.28 (0.07)	0.0002
Diabetes	−2.87 (1.31)	0.03	−2.41 (1.10)	0.03
ASVD	−4.70 (0.96)	<0.0001	−3.64 (0.94)	0.0001
Congestive Heart Failure	−3.39 (1.22)	0.01	−0.63 (1.15)	0.58
Dialysis Modality, Access**				
Peritoneal Dialysis	3.64 (2.82)	0.20	2.24 (2.80)	0.42
Hemodialysis, Catheter	−1.21 (1.62)	0.45	−1.67 (0.86)	0.052
CRP, per 2-fold increase	−2.22 (0.29)	<0.0001	−2.27 (0.22)	<0.0001
Serum Creatinine†	1.02 (0.18)	<0.0001	0.62 (0.16)	0.0001
Serum Creatinine^2	−0.07 (0.01)	<0.0001	−0.05 (0.01)	<0.0001

Multivariable model adjusted for all variables shown.

*Each univariate model also adjusts for time, but its coefficient varies somewhat across the models.

**Referent category: Hemodialysis with arteriovenous fistula or arteriovenous graft

†Serum creatinine modeled as a quadratic term due to curvilinear relationship. At a serum creatinine of 7, each 1 mg/dL increase in serum creatinine was associated with an increase in prealbumin of 0.62 mg/dL. Serum creatinines above 13.2 mg/dL were associated inversely with serum prealbumin concentrations; CRP: C-reactive protein; SE: standard error