Prevalence of and Factors Associated with Suboptimal Care before Initiation of Dialysis in the United States

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Abstract. Despite improvements in dialysis care, the mortality of patients with end-stage renal disease (ESRD) in the United States remains high. Factors that thus far have received scant attention, but could significantly affect morbidity and mortality in dialysis patients, are the timing and quality of care before the initiation of dialysis (pre-ESRD). Data from the new version of the Health Care Financing Administration (HCFA) 2728 Form were used to examine the prevalence of and factors associated with hypoalbuminemia, severe anemia, and erythropoietin (EPO) use among 155,076 incident chronic dialysis patients in the United States between April 1, 1995 and June 30, 1997. At initiation of dialysis, the median serum albumin and hematocrit were 3.3 g/dl and 28%, respectively. Sixty percent of patients had a serum albumin below the lower limit of normal and 51% had a hematocrit <28%. Overall, only 23% had received EPO pre-ESRD. Among patients with hematocrit <28%, only 20% were receiving EPO, compared to 27% among patients with hematocrit ≥28%. In a multivariate analysis that adjusted for diabetes, functional status, and demographic, socioeconomic, and geographic factors, the odds ratios for hypoalbuminemia, hematocrit <28%, and lack of EPO use were higher for African-Americans, patients with non-private insurance or no insurance, and patients who were started on hemodialysis. There were also significant differences in odds ratios for these outcomes between different geographic regions in the United States. The high prevalence of pre-ESRD hypoalbuminemia, hematocrit <28%, and lack of EPO use suggests that the quality of pre-ESRD care in the United States is suboptimal. Improvement in pre-ESRD care could potentially improve outcomes among ESRD patients.

Patients with end-stage renal disease (ESRD) experience significant morbidity and mortality and consume considerable health care resources. In 1995, the mean number of days per year that dialysis patients in the United States spent in the hospital was 11.4 for patients older than 65 yr and 9.6 for patients younger than 65 yr (1). In comparison, Medicare patients in general spent a mean of 7.1 hospital days per year (2). Moreover, despite recent improvements in mortality rates, the expected lifetimes for dialysis patients are between 16 and 37% of the age-, gender-, and race-matched U.S. population (1). Finally, the approximate cost of care for ESRD patients was $14.55 billion in 1996, and continues to grow each year (3).

The high morbidity and mortality of dialysis patients has stimulated research into potentially correctable factors that are associated with an increased risk of death. Several investigators have demonstrated that age, gender, race, nonrenal comorbidity, malnutrition, and dose of dialysis are strong predictors of death among dialysis patients (1,4–6). However, factors that thus far have received scant attention, but could significantly affect the morbidity and mortality of dialysis patients, are the timing and quality of care before the initiation of dialysis (pre-ESRD) (7,8). Optimal pre-ESRD care involves strategies to retard the progression of renal failure, judicious management of uremic complications, prevention or attenuation of comorbid conditions, adequate preparation for ESRD therapy, and timely initiation of dialysis.

Hypoalbuminemia and anemia are potential pre-ESRD factors that could influence outcomes on dialysis. Hypoalbuminemia has been shown to be a strong independent predictor of subsequent death on dialysis (9–14). Severe anemia of chronic renal failure is associated with left ventricular dilation, possibly left ventricular hypertrophy (LVH), and high output cardiac failure (15,16). Left ventricular geometry and LVH are important predictors of subsequent mortality and cardiac complications (17,18). Correction of anemia with erythropoietin (EPO) has been shown to significantly improve quality of life, exercise tolerance, work capacity, and LVH (19–23). Consequently, we selected pre-ESRD hypoalbuminemia, severe anemia, and lack of EPO use as indices of suboptimal quality of pre-ESRD care, and examined the prevalence of and factors associated with these indices among patients who began dialysis in the United States between April 1, 1995 and June 30, 1997.

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Materials and Methods

Data

The Medical Evidence (Medevid) Standard Analysis File of the U.S. Renal Data System (USRDS) contains all data from the new version of the ESRD Medical Evidence Form, which is also known as the Health Care Financing Administration (HCFA) 2728 Form. This form is completed by the dialysis or transplant center for all patients beginning or returning to ESRD treatment (dialysis or transplantation), regardless of whether they are covered by Medicare (about 92% of all new ESRD patients) or another type of insurance (1).

The new version of the 2728 form contains information on patient demographics, insurance status, comorbid conditions, cause of ESRD, functional status, pre-ESRD use of EPO, employment status, ESRD treatment modality selected, and laboratory information. The laboratory values recorded should be obtained within 45 d before the initiation of dialysis, and include serum creatinine, and, for selected patients, blood urea nitrogen, urea clearance, and creatinine clearance. In addition, hemoglobin, hematocrit, serum albumin, and the lower limit of normal for serum albumin are recorded, as are the dates of the test.

The population for this analysis consisted of all patients starting ESRD therapy in the United States for whom a new 2728 form was received by HCFA, and who were included in the September 1997 update of the Medevid file of the USRDS. Since the new version of the 2728 form went in use in April 1995, only patients who started dialysis at or after that date were included. To limit this analysis to patients whose first ESRD treatment modality was dialysis, patients who received a transplant or returned to dialysis were excluded. Patients less than 18 yr of age and those with more than one 2728 form in the database were also excluded.

Analytical Methods

Age was categorized in 10-yr intervals for descriptive purposes and as 18 to 39, 40 to 64, and 65+ years for the statistical models. Race was categorized as Caucasian (reference group), African-American, or other. Insurance status was categorized as private (any employee group health or other private insurance; reference group), Medicare only, Medicaid only, Medicare and Medicaid only, other insurance, or no insurance. Employment status was defined as employment 6 mo before initiation of dialysis and was categorized as employed/student/homemaker (reference group), unemployed, or other (retired due to age/preference, retired due to disability or medical leave of absence). Patients were classified as having diabetes mellitus if diabetic nephropathy was recorded as the cause of ESRD. Gender, diabetes, inability to transfer, inability to ambulate, and dialysis modality were entered as dichotomous variables. Dialysis modality (hemodialysis [HD] or peritoneal dialysis [PD]) was defined as the anticipated long-term primary type of dialysis at the start of ESRD. The national average for ESRD networks for hypoalbuminemia, hematocrit <28%, and EPO use was chosen as the reference group for comparison of ESRD networks (18 regional organizations in the United States contracted by HCFA to provide oversight regarding quality of ESRD care and to maintain a patient-specific data registry).

Hypoalbuminemia was defined as serum albumin below the recorded lower limit of normal for the given laboratory for each patient, since serum albumin concentration can vary by as much as 0.4 to 0.5 g/dl depending on the test used to measure it (typically bromcresol green or bromcresol purple). However, the prevalence of hypoalbuminemia as defined by serum albumin below 3.5 g/dl was also examined to permit comparison with other studies that have used this definition. Severe anemia was defined as hematocrit below the mean for the study population (28%). This cutoff was also chosen because hematocrit levels below 28% were associated with a significantly increased risk of death in a recent study of dialysis patients (24).

Missing and out-of-range laboratory values were excluded, as were laboratory values dated after the dialysis start date. Acceptable ranges for serum albumin, the lower limit of normal for serum albumin, and hematocrit were 1.0 to 6.0 g/dl, 3.0 to 4.0 g/dl, and 10 to 45%, respectively. Selection of these ranges was based on the distribution of data and clinical judgment. Patients with laboratory values dated after the initiation of dialysis were analyzed separately.

Separate multivariate logistic regression analyses were performed to determine the factors associated with hypoalbuminemia (defined as serum albumin below the lower limit of normal), low hematocrit (<28%), and EPO use immediately before the start of dialysis. Patients with missing data for any of the covariates entered in the models were excluded. No attempt to impute missing data was made. The following independent variables were tested in all three models: demographics (age, gender, race), socioeconomic factors (insurance and employment status), geographic location (ESRD networks), functional status (ability to transfer and ambulate), diabetes, and initial dialysis modality (HD *versus* PD). For the severe anemia model, EPO use was also entered as a dichotomous independent variable. The EPO analysis was modeled with and without hematocrit as a variable. For the analyses of EPO and low hematocrit, only those patients who had data for both were included. Multivariate analyses stratified by age <65 and ≥65 yr were performed.

Statistical Analyses

Statistical analyses were performed using SAS version 6.12 (SAS Institute, Inc., Cary, NC).

Results

Demographics and Clinical Characteristics

Forms on a total of 168,334 patients were available. Excluded were 7486 patients who had missing data for date of initiation of dialysis or who started dialysis before April 1, 1995, 3279 who received a transplant or returned to dialysis, 1548 who were <18 yr of age, and 945 with more than one 2728 form for the same patient. The final study population consisted of 155,076 patients who started dialysis between April 1, 1995 and June 30, 1997. The mean and median age were 61 and 64 yr, respectively; 47% were women, 61% were Caucasian, 43% had diabetic nephropathy as cause of ESRD, and in 87% HD was the initial modality. The characteristics of the excluded patients were very similar. The mean age of excluded patients was 61 yr, 46% were women, 59% were Caucasian, 43% had diabetes as the cause of ESRD, and for 87% HD was the initial dialysis modality.

Prevalence of and Factors Associated with Predialysis Hypoalbuminemia

Serum albumin was available in 110,843 (71%) patients. The mean and median predialysis serum albumin were 3.2 and 3.3 g/dl, respectively (Figure 1). In 13,087 patients, serum albumin was measured after the initiation of dialysis. The mean and median serum albumin concentration measured 1 to 21 (n = 11,128), 22 to 28 (n = 696), and ≥29 (n = 1263) d after the initiation of dialysis were 3.2 g/dl in each case.

The lower limit of normal for serum albumin was recorded

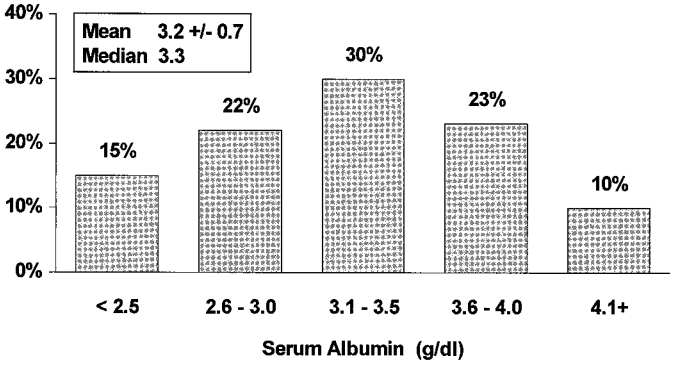

Figure 1. Serum albumin level at initiation of dialysis among 110,843 incident patients between April 1, 1995 and June 30, 1997 in the United States.

in 74,232 (48%) patients. Serum albumin was below the lower limit of normal in 60% of patients, and <3.5 g/dl in 62% of patients. The proportion of patients with serum albumin below the lower limit of normal was significantly higher among older patients, women, non-Caucasians, those covered by nonprivate insurance, uninsured, unemployed, those with diabetic nephropathy as the cause of ESRD, those unable to transfer and to ambulate, and those whose initial modality was HD (Table 1). The prevalence of hypoalbuminemia increased by 2% each year between 1995 and 1997.

In a multivariate analysis (Table 2), the covariates associated with higher odds of hypoalbuminemia were female gender (odds ratio [OR] = 1.20), African-American race (OR = 1.07), other non-Caucasian race (OR = 1.12), nonprivate insurance and no insurance (OR = 1.09 to 1.37), unemployed (OR = 1.20), diabetes (OR = 1.70), inability to transfer (OR = 1.62), inability to ambulate (OR = 1.72), and HD (OR = 1.70). Compared to the year 1995, the OR for hypoalbuminemia in 1996 and 1997 were 1.08 and 1.14, respectively. In the analysis stratified by age <65 and ≥65, the OR for hypoalbuminemia among diabetic patients younger than 65 yr was 2.12, whereas among diabetic patients older than 65 it was 1.37, compared to nondiabetic patients. Differences in OR for hypoalbuminemia of other variables were less striking between younger and older patients, and therefore the OR without stratification by age are reported. Finally, compared to the national average for ESRD networks, the OR for hypoalbuminemia were higher in six of 18 ESRD networks, with values ranging between 1.14 and 1.35 (Table 3).

Prevalence of and Factors Associated with Predialysis Hematocrit <28%

Hematocrit was available in 131,484 (85%) patients. Hematocrit values were normally distributed with a mean and median of 28% (Figure 2). In 13,124 patients, hematocrit was measured after the initiation of dialysis. The mean (median) hematocrit measured 1 to 21 (n = 11,175), 22 to 28 (n = 656), and ≥29 (n = 1293) d after the initiation of dialysis was 28 (28), 28 (29), and 29 (29) percent, respectively.

Overall, 51% of patients had a hematocrit below 28%. The prevalence of hematocrit below 28% was higher among younger patients, women, non-Caucasians, those covered by non-private insurance (except for Veterans Affairs and other insurance), uninsured, unemployed, and those whose initial dialysis modality was HD (Table 1). Between 1995 and 1997, the prevalence of hematocrit <28% decreased by approximately 1% per year.

In a multivariate analysis (Table 2), the covariates associated with higher OR for hematocrit <28% were female gender (OR = 1.15), African-American race (OR = 1.40), other non-Caucasian race (OR = 1.33), nonprivate insurance (OR = 1.11 to 1.22), no insurance (OR = 1.34), and HD (OR = 1.48). Compared to the year 1995, the OR for 1996 and 1997 were 0.97 and 0.90, respectively. The results of the analyses stratified by age <65 and ≥65 were not significantly different. Finally, compared to the national average for ESRD networks, the odds for hematocrit below 28% were similar to the national average in nine ESRD networks and lower in the remaining nine ESRD networks (OR = 0.64 to 0.93) (Table 3).

Prevalence of and Factors Associated with Predialysis Use of EPO

Pre-ESRD EPO use information was available in 155,051 (99.9%) patients. Overall, only 23% of patients received EPO before initiation of dialysis. Among patients with hematocrit below 28%, only 20% had received EPO, compared to 27% among patients with hematocrit of 28% or greater. The prevalence of EPO use was higher among older patients, women, Caucasians, those covered by private insurance, employed, diabetic patients, those able to transfer and ambulate, and those on PD (Table 1). The proportion of patients receiving EPO increased by 3% between 1995 and 1997.

Multivariate analyses of the factors associated with pre-ESRD EPO use were performed with and without hematocrit as a covariate, as a relationship between hematocrit level and EPO use is likely to be present. There was a distinct inverse correlation between the proportion of patients who received EPO and the percentage of patients who had a hematocrit <28% among the ESRD networks (r = −0.65, P = 0.004) (Figure 3). With the exception of age, which became nonsignificant in the model including hematocrit as a covariate, the OR for the other predictor variables were very similar in both models. Consequently, the results of the multivariate model that adjusted for hematocrit are reported (Table 2). Female gender (OR = 1.28) and diabetes (OR = 1.18) were associated with higher odds for EPO use. African-American race (OR = 0.84), nonprivate insurance (OR = 0.66 to 0.89), no insurance (OR = 0.49), unemployment (OR = 0.89), inability to transfer (OR = 0.84), inability to ambulate (OR = 0.86), and HD (OR = 0.61) were associated with lower odds for EPO use. Compared to the year 1995, the OR for 1996 and 1997 were 1.12 and 1.17, respectively. The results of the analyses stratified by age <65 and ≥65 were not significantly different. Compared to the national average for ESRD networks, the OR for EPO use were lower in six of 18 ESRD networks, with values ranging between 0.64 and 0.90 (Table 3).

Table 1. Pre-ESRD hypoalbuminemia, hematocrit <28%, and EPO use among patients beginning dialysis in the United States[a]

Characteristic	Hypoalbuminemia[b] (n = 74,232)	Hematocrit <28% (n = 131,484)	EPO Use	
			Hematocrit <28% (n = 66,669)	Hematocrit ≥28% (n = 64,803)
Age group (yr)				
18 to 24	53%	68%	17%	25%
25 to 34	58%	62%	18%	24%
35 to 44	60%	56%	18%	25%
45 to 54	62%	54%	20%	26%
55 to 64	62%	52%	21%	27%
65 to 74	59%	47%	21%	28%
75 to 84	59%	45%	22%	27%
85+	62%	44%	21%	26%
Gender				
male	57%	49%	19%	24%
female	63%	53%	21%	30%
Race				
Caucasian	58%	46%	23%	28%
African-American	63%	59%	16%	23%
other	63%	55%	21%	27%
Insurance status				
private	55%	49%	24%	31%
Medicare only	62%	50%	19%	24%
Medicaid only	66%	59%	17%	22%
Medicare and Medicaid	67%	53%	20%	26%
Veterans Affairs and other insurance(s)	58%	46%	23%	29%
none	63%	62%	13%	16%
Employment status				
employed/student/homemaker	56%	53%	21%	29%
unemployed	65%	57%	17%	22%
other[c]	60%	47%	22%	27%
Cause of ESRD				
diabetic nephropathy	67%	50%	22%	29%
hypertension	52%	49%	18%	23%
glomerulonephritis	57%	54%	22%	30%
other	55%	51%	19%	25%
Ability to transfer				
yes	60%	51%	20%	27%
no	81%	50%	17%	20%
Ability to ambulate				
yes	59%	51%	21%	27%
no	76%	50%	18%	22%
Initial dialysis modality				
hemodialysis	62%	52%	19%	25%
peritoneal dialysis	48%	42%	29%	36%
Dialysis start (year)				
1995	58%	52%	19%	25%
1996	60%	51%	21%	27%
1997	62%	49%	22%	28%

[a] 155,076 patients who began dialysis between April 1, 1995 and June 30, 1997. ESRD, end-stage renal disease; EPO, erythropoietin.
[b] Hypoalbuminemia was defined as serum albumin below the lower limit of normal recorded in the HCFA 2728 Form in each patient.
[c] Includes retired due to age/preference, retired due to disability, and medical leave of absence.

Table 2. Factors associated with pre-ESRD hypoalbuminemia, hematocrit <28%, and EPO use among patients beginning dialysis in the United States[a]

Characteristic	Hypoalbuminemia[b] (n = 67,841)	Hematocrit <28% (n = 117,835)	EPO Use (n = 117,835)
Age (ref. = 18 to 39 yr)			
40 to 64	1.00 (0.95 to 1.06)	0.78 (0.75 to 0.82)	1.00 (0.96 to 1.06)
65+	0.91 (0.86 to 0.97)	0.64 (0.62 to 0.67)	1.00 (0.94 to 1.05)
Female (ref. = male)	1.20 (1.16 to 1.24)	1.15 (1.12 to 1.18)	1.28 (1.24 to 1.32)
Race (ref. = Caucasian)			
African-American	1.07 (1.03 to 1.11)	1.40 (1.36 to 1.44)	0.84 (0.81 to 0.87)
other race	1.12 (1.06 to 1.20)	1.33 (1.27 to 1.39)	0.94 (0.90 to 1.00)
Insurance status (ref. = private)			
Medicare only	1.19 (1.13 to 1.26)	1.12 (1.08 to 1.17)	0.76 (0.72 to 0.79)
Medicaid only	1.27 (1.19 to 1.35)	1.22 (1.16 to 1.27)	0.66 (0.63 to 0.70)
Medicare and Medicaid	1.27 (1.20 to 1.35)	1.11 (1.06 to 1.16)	0.80 (0.76 to 0.84)
Veterans Affairs and other insurance(s)	1.09 (1.04 to 1.14)	1.02 (0.99 to 1.06)	0.89 (0.86 to 0.93)
none	1.37 (1.28 to 1.47)	1.34 (1.27 to 1.41)	0.49 (0.45 to 0.52)
Employment status (ref. = employed)			
unemployed	1.20 (1.14 to 1.27)	1.00 (0.96 to 1.04)	0.89 (0.85 to 0.94)
other[c]	1.12 (1.08 to 1.17)	0.92 (0.89 to 0.95)	1.04 (1.00 to 1.08)
Diabetes (ref. = nondiabetic)	1.70 (1.64 to 1.75)	0.98 (0.96 to 1.00)	1.18 (1.15 to 1.22)
Inability to transfer (ref. = ability to transfer)	1.62 (1.38 to 1.91)	1.04 (0.93 to 1.15)	0.84 (0.74 to 0.96)
Inability to ambulate (ref. = ability to ambulate)	1.72 (1.57 to 1.88)	0.99 (0.93 to 1.05)	0.86 (0.79 to 0.92)
Hemodialysis (ref. = peritoneal dialysis)	1.70 (1.62 to 1.78)	1.48 (1.43 to 1.53)	0.61 (0.59 to 0.64)
Dialysis start (ref. = 1995)			
1996	1.08 (1.04 to 1.11)	0.97 (0.95 to 1.00)	1.12 (1.09 to 1.16)
1997	1.14 (1.09 to 1.19)	0.90 (0.87 to 0.93)	1.17 (1.12 to 1.21)

[a] 155,076 patients who began dialysis between April 1, 1995 and June 30, 1997. ref., reference. Other abbreviations as in Table 1.
[b] Hypoalbuminemia was defined as serum albumin below the lower limit of normal recorded in the HCFA 2728 Form in each patient.
[c] It includes retired due to age/preference, retired due to disability, and medical leave of absence.

Discussion

The results of this study demonstrate a high prevalence of hypoalbuminemia and severe anemia, and infrequent use of EPO among patients starting dialysis in the United States. This high prevalence of factors that have been shown to be predictors of poor outcomes among dialysis patients strongly suggest that pre-ESRD care in the United States is suboptimal, and may be one of the factors contributing to the high morbidity, mortality, and resource utilization among dialysis patients in the United States.

Hypoalbuminemia, defined as a serum albumin below the lower limit of normal, was present in 60% of patients beginning dialysis between the years 1995 and 1997. Hypoalbuminemia at the time of initiation of dialysis is a strong predictor of subsequent mortality on dialysis. In the USRDS Case Mix Severity Study of 3399 patients who began dialysis in 1986–1987, compared to patients with a serum albumin level of 3.5 to 4.0 g/dl, the adjusted relative risk of death among patients with serum albumin levels of 3.0 to 3.5, 2.5 to 3.0, and <2.5 g/dl were 1.20, 1.66, and 2.16, respectively, for HD patients and 1.09, 1.79, and 1.92, respectively, for PD patients (9,10). Furthermore, hypoalbuminemia has been associated with increased rates of hospitalization in both ESRD and other patient populations, particularly in acutely ill and elderly patients (25,26). In the Canadian Hemodialysis Morbidity Study, Churchill and colleagues observed that a low serum albumin was associated with an increased risk of hospitalization for infectious disease, pulmonary edema, and access thrombosis (27). Consequently, the high prevalence of hypoalbuminemia among patients starting dialysis in the United States is a major cause for concern.

The explanation for the high prevalence of hypoalbuminemia among patients beginning dialysis in the United States is multifactorial. First, as renal function declines, spontaneous dietary protein restriction occurs. Indeed, an evaluation of 1687 patients in the baseline phase of the Modification of Diet in Renal Disease (MDRD) Study, before any intervention, revealed a direct correlation between GFR measured by iothalamate and nutritional status (28). Mean protein intake (g/kg per d) estimated from urine urea nitrogen declined steadily from 1.07 at GFR of 70 ml/min per 1.73 m^2, to 1.02, 0.93, and 0.80 at GFR of 45, 25, and 9 ml/min per 1.73 m^2, respectively. Second, declining renal function is associated with multiple derangements in protein metabolism leading to loss of lean body mass and increased essential amino acid and nitrogen requirements (29). Third, despite the fact that patients with chronic renal failure are at high risk for malnutrition, only half of all dialysis patients recollect having been seen by a dietitian before the start of dialysis (1). Fourth, other factors

Table 3. Adjusted odds ratios for pre-ESRD hypoalbuminemia, hematocrit <28%, and EPO use in different geographic regions of the United States[a]

ESRD Network[b]	Hypoalbuminemia[c] (n = 67,841)	Hematocrit <28% (n = 117,835)	EPO Use (n = 117,835)
1	0.99 (0.87 to 1.13)	0.84 (0.78 to 0.91)	1.40 (1.28 to 1.54)
2	0.88 (0.79 to 0.98)	0.99 (0.93 to 1.06)	1.22 (1.13 to 1.33)
3	1.20 (1.08 to 1.34)	0.95 (0.88 to 1.01)	1.00 (1.00 to 1.00)
4	1.22 (1.09 to 1.36)	0.90 (0.85 to 0.96)	0.95 (0.87 to 1.03)
5	1.08 (0.96 to 1.21)	0.93 (0.87 to 0.99)	1.04 (0.96 to 1.13)
6	0.95 (0.86 to 1.05)	0.96 (0.91 to 1.02)	0.75 (0.69 to 0.81)
7	0.95 (0.85 to 1.06)	0.86 (0.80 to 0.91)	1.17 (1.08 to 1.27)
8	1.02 (0.90 to 1.15)	1.06 (0.99 to 1.14)	0.92 (0.84 to 1.00)
9	1.14 (1.03 to 1.27)	1.00 (1.00 to 1.00)	0.90 (0.83 to 0.97)
10	1.26 (1.13 to 1.41)	0.95 (0.89 to 1.02)	0.64 (0.58 to 0.70)
11	1.00 (0.90 to 1.12)	0.97 (0.92 to 1.03)	0.89 (0.82 to 0.96)
12	1.14 (1.01 to 1.28)	0.95 (0.88 to 1.02)	1.22 (1.12 to 1.34)
13	1.35 (1.20 to 1.52)	0.90 (0.84 to 0.97)	0.79 (0.72 to 0.86)
14	1.00 (0.90 to 1.11)	1.03 (0.97 to 1.10)	1.19 (1.10 to 1.29)
15	0.98 (0.87 to 1.10)	0.83 (0.77 to 0.89)	0.77 (0.70 to 0.84)
16	0.98 (0.86 to 1.11)	0.64 (0.59 to 0.69)	1.27 (1.16 to 1.40)
17	1.00 (1.00 to 1.00)	0.84 (0.78 to 0.90)	1.51 (1.39 to 1.65)
18	1.03 (0.93 to 1.14)	0.83 (0.78 to 0.88)	1.18 (1.09 to 1.27)

[a] Adjusted for age, gender, race, insurance, employment status, diabetes, inability to transfer, inability to ambulate, initial dialysis modality, and year. The ESRD network closest to the national average for prevalence of hypoalbuminemia, hematocrit <28%, and EPO use was used as the reference group for the respective multivariate models.

[b] ESRD Network 1: CT, MA, ME, NH, RI, VT; ESRD Network 2: NY; ESRD Network 3: NJ, PR, VI; ESRD Network 4: DE, PA; ESRD Network 5: DC, MD, VA, WV; ESRD Network 6: GA, NC, SC; ESRD Network 7: FL; ESRD Network 8: AL, MS, TN; ESRD Network 9: IN, KY, OH; ESRD Network 10: IL; ESRD Network 11: MI, MN, ND, SD, WI; ESRD Network 12: IA, KS, MO, NE; ESRD Network 13: AR, LA, OK; ESRD Network 14: TX; ESRD Network 15: AZ, CO, NM, NV, UT, WY; ESRD Network 16: AK, ID, MT, OR, WA; ESRD Network 17: AS, CA (northern), HI, GU; ESRD Network 18: CA (southern).

[c] Hypoalbuminemia was defined as serum albumin below the lower limit of normal recorded in the HCFA 2728 Form in each patient.

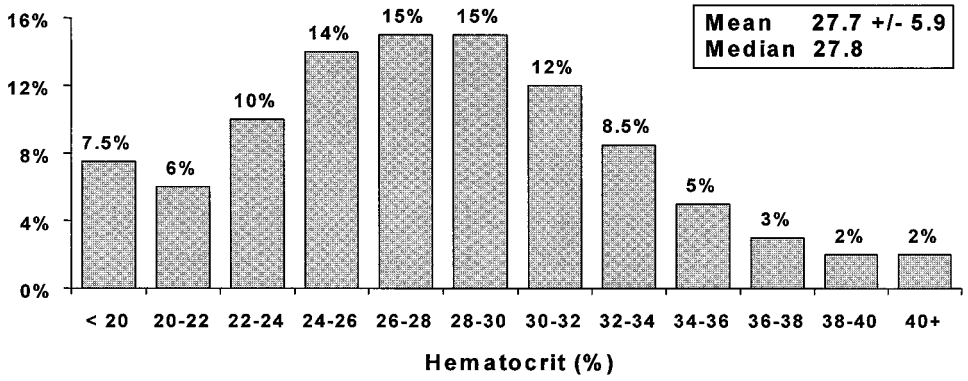

Figure 2. Hematocrit level at initiation of dialysis among 131,484 incident patients between April 1, 1995 and June 30, 1997 in the United States.

such as liver disease, nephrotic syndrome due to diabetic nephropathy or other causes, and volume overload may be important contributors to low serum albumin. Finally, the high OR for hypoalbuminemia among women, non-Caucasian patients, diabetic patients, patients without private insurance, and patients who were unemployed, unable to transfer or unable to ambulate suggests that a wide variety of physical and socioeconomic factors may contribute to hypoalbuminemia during the pre-ESRD period.

The prevalence of hypoalbuminemia in this study is higher than has been reported previously. Among patients who began dialysis in 1986–1987, the USRDS Case Mix Severity Study reported a 50% prevalence of hypoalbuminemia within 2 to 6 wk of the start of dialysis (10). Likewise, among 439 patients who began HD in the first quarter of 1994 in the state of Michigan, the prevalence of hypoalbuminemia at 1 mo after the initiation of dialysis was 54% (30). The higher prevalence of hypoalbuminemia in our study could be attributed to he-

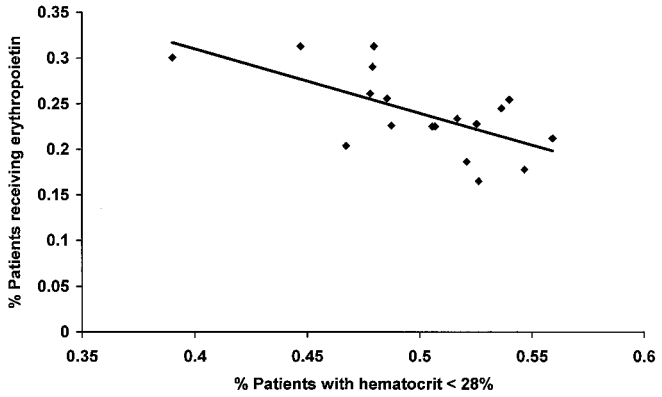

Figure 3. Correlation between proportion of patients receiving erythropoietin and prevalence of hematocrit <28% among U.S. ESRD networks ($r = -0.65$, $P = 0.004$).

modilution due to volume overload, since serum albumin levels in our study were measured before the initiation of dialysis, as opposed to after the start of dialysis in previous reports. However, among patients in whom the laboratory data were recorded after the start of dialysis, serum albumin levels were similar to those in whom they were recorded pre-ESRD. Alternatively, the higher prevalence of hypoalbuminemia observed in this study may truly reflect an increasing prevalence of malnutrition among patients starting dialysis. Indeed, the adjusted annual increases in the odds for hypoalbuminemia in the years 1996 and 1997 were 10 and 17%, respectively. This increase was observed for patients with and without employee group health insurance. These data suggest a decline in the nutritional status of patients beginning dialysis in the United States, which could reflect the popularity of low-protein diets in the 1990s to slow the progression of renal disease (31).

Correction of anemia of chronic renal failure has assumed greater clinical importance in recent years, as there are increasing numbers of older and diabetic patients entering ESRD programs in the United States (20). Between 1987 and 1994, the average age increased from 57 to 60 yr, and the proportion of diabetic patients increased from 30 to 37% (1). Concurrently, the prevalence of cardiac disease among incident dialysis patients also increased (32). Furthermore, 74% of patients have echocardiographic evidence of LVH at the time of initiation of dialysis (33). Cardiovascular disease and LVH develop in the pre-ESRD stage, and LVH in pre-ESRD patients is an important predictor of subsequent cardiac morbidity and mortality on dialysis (10,17,33,34). Consequently, correction of anemia in predialysis patients with EPO assumes great importance, as it may reduce or prevent LVH.

It is disturbing that 51% of patients had a hematocrit of <28% at the start of dialysis, and of these, only 20% had received EPO therapy before the start of dialysis. This suggests gross under-utilization of EPO among pre-ESRD patients. Because the data from the HCFA 2728 form have not been validated, misclassification of EPO use may result in the low utilization observed. However, we found a clear inverse correlation between the prevalence of EPO use and prevalence of hematocrit <28% among most ESRD networks ($r = -0.65$, $P = 0.004$), which argues against misclassification. The causes for the observed low utilization of EPO are unclear, but the high cost of EPO may be a contributing factor. However, 54% of patients beginning dialysis are already Medicare-eligible, and EPO is reimbursed by Medicare before ESRD if the serum creatinine is 3.0 mg/dl or higher and the hematocrit is <30%. Among patients with certain types of private insurance, additional requirements for reimbursement may include documentation of symptomatic anemia or symptomatic cardiac disease. However, generous reimbursement programs are available for patients who require EPO if it is not covered by insurance. Thus, economic reasons cannot fully explain the low utilization of EPO among pre-ESRD patients, and other factors such as delayed referral of patients with chronic renal failure to the nephrologist as well as the logistics of EPO therapy in the outpatient setting may have a role.

In addition to the specific causes for hypoalbuminemia and under-utilization of EPO among pre-ESRD patients, other factors may account for suboptimal pre-ESRD care among these patients. In particular, compared to Caucasians, non-Caucasian patients had a higher odds for hypoalbuminemia and low hematocrit, and lower odds for EPO use. This suggests that non-Caucasian patients may be especially vulnerable to receiving suboptimal care in the pre-ESRD stage compared with Caucasian patients. Our analysis also revealed that the likelihood of each of these indices was considerably higher among patients with nonprivate insurance or no insurance, and unemployed patients were more likely to have hypoalbuminemia and less likely to receive EPO compared to those employed. Finally, significant geographic differences in the risk of hypoalbuminemia, hematocrit <28%, and EPO use were observed among different ESRD networks, suggesting regional variations in practice patterns. Regional differences have been observed with respect to other indices of pre-ESRD care, such as placement of permanent vascular access for dialysis (35). Thus, socioeconomic and geographic conditions may influence the quality of pre-ESRD care.

Differences in the prevalence of hypoalbuminemia, uncorrected anemia, and under-utilization of EPO were also observed between patients whose initial dialysis modality was HD and PD. In general, PD patients were significantly less likely to have hypoalbuminemia or hematocrit <28%, and more likely to receive EPO than HD patients. These differences, however, may be explained by a selection bias, because PD patients were younger (mean age 56.5 *versus* 62.1), more likely to be Caucasian (69% *versus* 59%), and have private insurance (37% *versus* 22%) compared to HD patients. However, after adjusting for these and other factors, the differences between the two groups persisted, suggesting that other factors may be operative. Indeed, patients who select PD are more likely to have received pre-ESRD care by a nephrologist (36). Taken together, these data strengthen the contention that lack of specialist care by the nephrology team may partly account for the suboptimal pre-ESRD care among ESRD patients in the United States.

In conclusion, the results of this study reveal an alarmingly poor quality of pre-ESRD care among patients beginning di-

alysis in the United States. Although our analyses shed some light on the factors that could contribute to this suboptimal care, potential causes need to be investigated further. Finally, the relationship between the indices of suboptimal pre-ESRD care and morbidity, mortality, and resource utilization on dialysis needs to be established. A better understanding of these relationships is critical for improved outcomes among patients on dialysis.

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