Duration of Dialysis and Its Relationship to Dialysis Adequacy, Anemia Management, and Serum Albumin Level

Michael V. Rocco, MD, Marjorie R. Bedinger, BA, Roger Milam, BF, Joel W. Greer, PhD, William M. McClellan, MD, and Diane L. Frankenfield, DrPH

● **An analysis of the relationship between intermediate outcomes and duration of dialysis therapy in hemodialysis patients was performed by linking Health Care Financing Administration (HCFA) Core Indicators data with data obtained from HCFA form 2728 at the initiation of dialysis therapy. Patients who recently initiated hemodialysis therapy were less likely to meet Dialysis Outcomes Quality Initiative guidelines than patients with a longer duration of dialysis therapy. For both urea reduction ratio and Kt/V, odds ratios for adequate dialysis were approximately 0.20 for a duration of dialysis therapy less than 0.5 years and 0.42 to 0.63 for a duration of dialysis therapy of 0.5 to 1.0 years compared with a duration of dialysis therapy of 2.0 years or greater. For patients with a duration of dialysis therapy less than 0.5 years (compared with ≥2.0 years), the odds ratio for a hematocrit less than 28% was approximately 3.0, that for a hematocrit 33% or greater was approximately 0.6, and that for a serum albumin level of 3.5 g/dL or greater (bromcresol green method) or 3.2 g/dL or greater (bromcresol purple method) was approximately 0.4. There was a direct relationship between glomerular filtration rate at the initiation of dialysis therapy and both serum albumin and hematocrit values. Patients administered recombinant human erythropoietin (rHuEPO) predialysis were more likely to have greater hematocrits. There also was a direct relationship between hematocrit and serum albumin level. Therefore, several actionable items in regard to attentive overall medical care can result in an improvement in the percentage of patients newly started on hemodialysis therapy who meet intermediate outcomes, including the administration of rHuEPO predialysis, correction of iron deficiency, and timely placement of a permanent dialysis access.**

INDEX WORDS: Hemodialysis (HD); Kt/V urea; urea reduction ratio (URR); serum albumin; anemia; glomerular filtration rate (GFR); erythropoietin.

PATIENTS UNDERGOING chronic dialytic therapy have a mortality rate many fold greater than that of individuals of the same age and sex without renal failure.[1] An increased risk for death in chronic dialysis patients has been associated with older age, male sex, white race, nonrenal medical comorbidities, and such modifiable risk factors as lower dose of dialysis and lower hematocrit levels.[2-6] As a result of these and other studies, the National Kidney Foundation (NKF)[7] developed guidelines suggesting minimal levels of dialysis dose and hematocrit needed to provide adequate care for chronic dialysis patients. Data from the Health Care Financing Administration (HCFA) Core Indicators Project have shown that despite improvements in the proportion of hemodialysis patients achieving an adequate dose of dialysis and hematocrit in recent years, the percentage of patients who did not meet NKF-Dialysis Outcomes Quality Initiative (DOQI) guidelines for dialysis dose and anemia were 20% and 41% in fall 1998, respectively.[8]

It recently was proposed that the quality of care received before the initiation of dialysis therapy may affect the morbidity and mortality of dialysis patients.[9] It is known that patients with a lower serum albumin level at the start of dialysis therapy have greater mortality and morbidity rates[2,4,10,11]; however, less is known about other parameters at dialysis therapy initiation. We tested the hypothesis that patients initiating chronic dialysis therapy were less likely to meet

From the Section on Nephrology, Wake Forest University School of Medicine, Winston-Salem, NC; Office of Clinical Standards and Quality and Office of Strategic Planning, Health Care Financing Administration, Baltimore, MD; and Renal Division and Rollins School of Public Health, Emory University School of Medicine, Emory University, Atlanta, GA.

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Address reprint requests to Michael V. Rocco, MD, Section on Nephrology, Wake Forest University School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157-1053. E-mail: mrocco@wfubmc.edu

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guidelines for dialysis adequacy, anemia, and nutrition than established dialysis patients and assessed the role of care before end-stage renal disease (ESRD) in influencing these guideline parameters.

METHODS

The Sample

Details regarding the collection of HCFA Core Indicator variables were previously published.[12] In brief, in February 1998, the 18 ESRD Network organizations provided to HCFA a listing of all patients with ESRD in their geographic area. All in-center hemodialysis patients aged 18 years or older as of September 30, 1997, and alive on December 31, 1997, were identified and eligible for inclusion in the sample. A national random sample, stratified by network, was selected from this universe of patients.

Data Collection

In June 1998, a one-page data collection form was sent to ESRD facilities providing care to selected patients. Clinical information in selected patients' medical records was abstracted for each patient in the sample who was undergoing in-center hemodialysis during October, November, and December 1997. Patient information collected included sex, age, race, Hispanic ethnicity, years on dialysis therapy, and primary cause of ESRD. Clinical information used to assess the quality of care provided included the following variables: patient height, predialysis and postdialysis blood urea nitrogen levels and weights (in kilograms) to calculate urea reduction ratio (URR) and Kt/V values, dialysis session length, dialyzer code (to determine dialyzer ultrafiltration coefficient), hematocrits, hemoglobin level, prescribed weekly recombinant human erythropoietin (rHuEPO) dose (in units per kilogram) at the time the hematocrit was drawn, transferrin saturation, serum ferritin concentration, iron prescription practice, serum albumin level, and laboratory method used to determine serum albumin value (bromcresol green [BCG] or bromcresol purple [BCP]). Completed forms were returned to the appropriate network office, where data were reviewed and entered into a computerized database (Epi Info version 6.04; Centers for Disease Control and Prevention, Atlanta, GA).[13] Data were forwarded to HCFA for aggregation and analysis.

Data for these patients were linked to data obtained from HCFA form 2728, which is completed by the dialysis facility for each patient at the initiation of dialysis therapy. Data on height, weight, sex, race, and serum creatinine level at the initiation of dialysis therapy were used to calculate glomerular filtration rate (GFR) by the Modification of Diet in Renal Disease (MDRD) formula.[14] Data on the use of predialysis rHuEPO and hematocrit and serum albumin values at the initiation of dialysis therapy were also obtained from this form.

Data Analysis

Kt/V values were calculated according to the Daugirdas II formula.[15] For this report, percentage, mean ± SD, and median values were derived from available reported data over the 3-month study period. Associations of measures with categories of years on dialysis therapy were tested by chi-square, hierarchical analysis of variance, and two-tailed Student's *t*-test analyses, with *P* less than 0.05 considered significant. For these analyses, racial categories were restricted to white and black groups only because of the low numbers in other racial groups.

Logistic regression analyses stratified by age group (<65 and ≥ 65 years) were conducted on the following intermediate outcome measures: mean URR of 65% or greater, mean Kt/V of 1.2 or greater, mean hematocrit less than 28%, mean hematocrit of 33% or greater, and mean serum albumin level of 3.5 and 3.2 g/dL or greater (BCG and BCP laboratory methods, respectively). The following variables were entered into each logistic regression model in a forward stepwise manner: sex, age (years), race (black and white only), Hispanic (yes or no), years on dialysis therapy as a categorical variable (<0.5, 0.5 to 1, 1 to 2, and >2 years, with >2 years as the referent category), mean postdialysis weight in kilograms, diabetes mellitus listed as primary cause of ESRD (yes or no), and network as a categorical variable. Multivariate regression was performed to determine the effect of sex, age (years), race (black and white only), diabetes listed as the primary cause of ESRD, predialysis rHuEPO use, and GFR at the initiation of dialysis therapy on both hematocrit and serum albumin levels at the initiation of dialysis therapy. Data analyses were conducted using Epi Info, version 6.04,[13] and SPSS for Windows, version 8.0 (SSPS Inc, Chicago, IL).[16]

RESULTS

Of 7,658 patients in the 1998 hemodialysis cohort, complete data were available for 7,092 patients. Demographic and medical characteristics of this cohort are listed in Table 1, stratified by duration of dialysis therapy. Patients for whom HCFA form 2728 data were not available were more likely to be women (49% versus 45%), black (43% versus 31%), Hispanic (13% versus 11%), without diabetes (66% versus 56%), aged younger than 65 years (59% versus 49%), and have a longer duration of dialysis therapy (mean, 5.5 versus 1.5 years) than patients for whom form 2728 data were available. Those patients on hemodialysis therapy for less than 6 months were more likely to be white, older, administered predialysis rHuEPO, have diabetes mellitus as the cause of ESRD, and have a greater GFR at the initiation of dialysis therapy compared with patients on hemodialysis therapy for more than 2 years.

Intermediate outcomes reported by duration of dialysis are listed in Table 2. In general, patients who had a duration of dialysis therapy less than 6 months had poorer intermediate outcomes than

Table 1. Percentage of Patients With Selected Characteristics Stratified by Duration of Dialysis Therapy

	Duration of Dialysis (y)				
	<0.5	0.5-1	1-2	2+	All Patients
No. of patients*	848 (12)	965 (14)	1,503 (21)	3,759 (53)	7,092 (100)
Sex (%)					
Men	54	54	52	53	53
Women	46	46	48	47	47
Age (y)					
Mean ± SD†	61.7 ± 14.4	62.8 ± 14.4	62.0 ± 15.2	59.1 ± 15.6	60.51 ± 15.3
Median	64	66	64	61	63
Age group (y)†					
18-44	15	13	15	20	17
45-64	37	35	35	38	37
65+	48	52	50	43	46
Race (%)†					
White	62	54	54	47	51
Black	27	32	32	42	37
Other/unknown	12	14	13	11	12
Ethnicity (%)					
Hispanic	11	12	11	12	12
Primary cause of ESRD (%)†					
Diabetes mellitus	48	48	43	33	39
Hypertension	22	24	26	30	27
Glomerulonephritis	9	9	11	16	13
Other/unknown	20	18	20	22	21
Postdialysis body weight (kg)					
Mean ± SD	72.9 ± 20.3	71.3 ± 17.5	73.2 ± 19.2	71.5 ± 19.6	72.0 ± 19.3
Median	70.1	69.4	70.8	68.3	69.1
Baseline GFR†‡					
Mean ± SD	7.8 ± 3.4	7.5 ± 3.5	6.8 ± 2.5	6.7 ± 2.8	7.1 ± 3.0
Median	7.2	6.8	6.4	6.4	6.7
Prescribed EPO pre-ESRD§ (%)	28	25	26	24	26

Abbreviation: EPO, erythropoietin.
*Expressed as number (percent).
†$P < 0.001$ for comparison among categories of duration of dialysis therapy.
‡GFR calculated from information on HCFA Form 2728 using the MDRD formula[14] (n = 2,533).
§Obtained from data on HCFA Form 2728 (n = 3,749).

patients with a duration of hemodialysis therapy greater than 6 months.

Dialysis Adequacy

NFK-DOQI guidelines recommend that patients receive a dose of dialysis equal to a URR of 65% or greater and a Kt/V urea of 1.2 or greater.[7] A URR of 65% or greater was present in only 43% of patients who had a duration of dialysis therapy less than 6 months compared with 68% to 78% among patients with a duration of dialysis of 6 months or greater ($P < 0.001$). Similar findings were observed for Kt/V urea values calculated by the Daugirdas II formula. A Kt/V urea of 1.2 or greater was present in only 49% of patients who had a duration of dialysis therapy less than 6 months compared with 75% to 85% among patients with a duration of dialysis therapy of 6 months or greater ($P < 0.001$). For both URR and Kt/V urea values, the percentage of patients meeting NKF-DOQI guidelines increased as duration of dialysis therapy increased. The difference in dialysis dose was not related to the prescribed time on dialysis because the median length of the dialysis session was 210 minutes for all four categories of duration of dialysis therapy. However, as duration of dialysis therapy increased, patients were more likely to undergo dialysis using a dialyzer with an ultrafiltration coefficient of 20 mL/mm Hg/h or greater

Table 2. Comparison of Selected Adequacy of Dialysis Clinical Measures for Adult In-Center Hemodialysis Patients by Duration of Dialysis Therapy

	Duration of Dialysis (y)			
Intermediate Outcome Measure	<0.5	0.5-1	1-2	>2
Dialysis adequacy				
URR*† (%)	63.0 ± 9.1	67.3 ± 8.0	68.8 ± 7.0	69.0 ± 6.6
Patients with URR ≥ 65%† (%)	43	68	76	78
Kt/V*†	1.21 ± 0.29	1.36 ± 0.26	1.41 ± 0.26	1.42 ± 0.25
Patients with Kt/V ≥ 1.2† (%)	49	75	80	85
Patients dialyzed with KUf ≥ 20 mL/mm Hg/h† (%)	44	49	51	52
Median dialysis session length (min)	210	210	210	210
Anemia management				
Hematocrit*† (%)	31.7 ± 4.0	33.2 ± 3.1	33.4 ± 3.0	33.5 ± 3.5
Patients with hematocrit ≥ 33%† (%)	41	58	60	59
Hemoglobin*† (g/dL)	10.2 ± 1.3	10.8 ± 1.1	10.9 ± 1.1	10.8 ± 1.2
Transferrin saturation*† (%)	23.9 ± 13.4	28.1 ± 12.3	30.1 ± 13.9	30.1 ± 13.8
Serum ferritin* (ng/mL)	282 ± 271	442 ± 426	550 ± 492	542 ± 467
Weekly rHuEPO dose*† (U/kg/wk)	210 ± 127	197 ± 148	181 ± 131	193 ± 145
Patients prescribed‡ (%)				
IV rHuEPO†	84	88	86	87
SC rHuEPO†	13	11	12	10
IV iron only†	50	52	52	46
Oral iron only†	24	26	24	26
Both IV and oral iron	9	12	9	9
Serum albumin				
Serum albumin by BCG method*† (g/dL)	3.56 ± 0.46	3.77 ± 0.40	3.86 ± 0.43	3.88 ± 0.39
Serum albumin by BCP method*† (g/dL)	3.39 ± 0.59	3.58 ± 0.44	3.63 ± 0.48	3.62 ± 0.45
Mean serum albumin level ≥3.5 g/dL by BCG method or ≥3.2 g/dL by BCP method (%)†	63	81	86	87

Abbreviations: IV, intravenous; SC, subcutaneous; KUf, dialyzer ultrafiltration coefficient.
*Expressed as mean ± SD.
†$P < 0.001$ for comparison among groups of duration of dialysis therapy.
‡Prescribed at least once during the study period (October to December 1997).

($P < 0.001$). Data on blood flow rates or dialysis access type were not collected for this cohort of patients.

Anemia

NKF-DOQI guidelines recommend that hematocrit be maintained at 33% or greater.[17] A hematocrit of 33% or greater was found in only 41% of patients who had a duration of dialysis therapy less than 6 months compared with greater than 58% for patients with a duration of dialysis therapy of 6 months or greater ($P < 0.001$). In addition, 16% of patients who had a duration of dialysis therapy less than 6 months had a hematocrit less than 28% compared with 6% or less of patients who had a duration of dialysis of 6 months or greater ($P < 0.001$). A further improvement in hematocrit levels was not observed when duration of dialysis therapy was greater than 6 months.

Although there were statistically significant differences in rHuEPO and iron administration among the four categories of dialysis duration, these differences were not clinically significant (Table 2). Of note, approximately one quarter of patients, regardless of duration of dialysis therapy, were administered iron by only the oral route. There were both clinically and statistically significant differences in the percentage of patients with iron deficiency by dialysis therapy duration groups. Patients with a duration of dialysis therapy less than 6 months were less likely to have a transferrin saturation level of 20% or greater (51%) or a serum ferritin concentration of 100 ng/mL or greater (67%) than patients with a duration of dialysis therapy of 6 months or greater (69% to 73% for transferrin saturation; $P < 0.001$; 79% to 84% for serum ferritin level; $P < 0.001$). Finally, both a low serum ferritin

concentration (<100 ng/mL) and low transferrin saturation (<20%) were seen in 14% of patients with a duration of dialysis therapy less than 6 months compared with less than 7% in patients with a duration of dialysis therapy of 6 months or greater ($P < 0.001$).

Serum Albumin Levels

NKF-DOQI guidelines recommend that serum albumin level be maintained at 4.0 g/dL or greater by the BCG method.[18] Patients who had a duration of dialysis therapy less than 6 months had a lower serum albumin level (3.56 ± 0.46 g/dL for the BCG method) than patients with a duration of dialysis therapy of 6 months or greater (all mean values at least 3.77 g/dL; Table 2; $P < 0.001$). Similar findings were seen for patients who had serum albumin levels measured by the BCP method (Table 2; $P < 0.001$). There was an increase in serum albumin levels in the 6-month to 1-year category of duration of dialysis therapy compared with the category of less than 6 months, but no further improvements were seen in serum albumin levels in the two categories of longest duration of dialysis therapy. Similar differences were seen for patients with serum albumin levels measured by the BCP method.

Risk Factors for Adverse Intermediate Outcomes

Multivariate logistic regression was performed to identify variables associated with poor intermediate outcomes. Predictors of inadequate dialysis, measured by either URR or Kt/V, included shorter duration of dialysis, black race, male sex, greater postdialysis weight, use of a kidney with a lower ultrafiltration coefficient, shorter dialysis session length, and lower serum albumin level (Table 3). Odds ratios for adequate dialysis consistently increased toward 1.0 as duration of dialysis therapy lengthened. For both URR and Kt/V, odds ratios for adequate dialysis were approximately 0.20 for a duration of dialysis therapy less than 0.5 years and 0.42 to 0.63 for a duration of dialysis therapy of 0.5 to 1.0 years, all statistically significant compared with the referent group with a duration of dialysis therapy of 2 years or more. For patients aged 65 years or older, lower hematocrit was also a predictor of inadequate dialysis, measured by either Kt/V or URR. For patients aged younger than 65 years, decreasing age was also a predictor of inadequate dialysis (Table 3).

Predictors of hematocrit less than 28% in patients of all ages included shorter duration of dialysis therapy, black race, lower serum albumin level, and greater mean weekly rHuEPO dose (Table 4). The odds ratio for hematocrit less than 28% was 2.8 to 3.2 for a duration of dialysis therapy less than 0.5 years and was not significantly different from 1.0 for all other categories of duration of dialysis therapy. For patients aged younger than 65 years, predictors also included greater serum ferritin level and greater postdialysis weight. For patients aged 65 years and older, predictors also included lower Kt/V.

Patients of all ages with an adequate hematocrit level (≥33%) had a longer duration of dialysis therapy, greater mean serum albumin and transferrin saturation values, lower mean rHuEPO levels, and were prescribed intravenous iron. The odds ratio for a hematocrit of 33% or greater was approximately 0.6 for a duration of dialysis therapy less than 0.5 years and was not significantly different from 1.0 for all other categories of duration of dialysis therapy. For patients aged younger than 65 years, predictors also included increasing age, male sex, decreasing weight, increasing Kt/V urea, and lower serum ferritin concentration; whereas for patients aged 65 years and older, predictors also included white race.

Serum albumin levels of 3.5 g/dL or greater by the BCG method or 3.2 g/dL or greater by the BCP method were less likely to be found in patients with shorter duration of dialysis therapy, increasing age, lower hematocrit, lower Kt/V, lower postdialysis weight, and diabetes mellitus as the cause of ESRD (Table 5). Odds ratios for these serum albumin levels were approximately 0.4 for a duration of dialysis therapy less than 0.5 years and not significantly different from 1.0 for all other groups of duration of dialysis therapy. For patients aged younger than 65 years, predictors also included female sex.

Predictors of Intermediate Outcomes at the Initiation of Dialysis Therapy

Multivariate regression was performed to determine predictors of adequate serum albumin levels (Table 6) and hematocrit at the initiation of dialysis therapy (Table 7). These analyses were restricted to patients who had data available from

Table 3. Multivariate Logistic Regression Analyses for Predictors of Adequate Dialysis

Variable	Age < 65 y		Age ≥ 65 y	
	URR ≥ 65% (n = 2,924)	Kt/V ≥ 1.2 (n = 2,928)	URR ≥ 65% (n = 2,462)	Kt/V ≥ 1.2 (n = 2,455)
Duration of hemodialysis (y; ≥2 y = referent)				
<0.5	0.22 (0.17-0.30)*	0.16 (0.12-0.22)*	0.19 (0.14-0.25)*	0.17 (0.12-0.23)*
0.5-0.99	0.52 (0.40-0.68)*	0.42 (0.32-0.55)*	0.63 (0.47-0.84)†	0.62 (0.45-0.86)†
1.0-1.99	0.83 (0.66-1.05)	0.63 (0.49-0.82)*	0.95 (0.73-1.3)	0.86 (0.64-1.2)
Age (increase of 1.0 y)	1.01 (1.01-1.02)*	1.01 (1.00-1.02)†	NS	NS
Race (black)	0.80 (0.66-0.98)‡	0.77 (0.63-0.93)†	0.64 (0.51-0.80)*	0.70 (0.55-0.90)†
Sex (women)	3.2 (2.6-3.9)*	3.1 (2.5-3.9)*	2.4 (1.9-3.0)*	1.9 (1.5-2.4)*
Diabetes mellitus as cause of ESRD	0.82 (0.68-0.99)‡	NS	NS	NS
Postdialysis weight (increase of 1.0 kg)	0.96 (0.95-0.96)*	0.96 (0.95-0.96)*	0.97 (0.96-0.98)*	0.96 (0.96-0.97)*
Network (Network 18 = referent)	5, 10, 13, 17§	NS	NS	NS
KUf (mL/mm Hg/h; 1-9 = referent)				
10-19	1.3 (0.99-1.80)	1.03 (0.77-1.40)	1.30 (0.94-1.80)	1.46 (1.02-2.10)‡
20+	1.5 (1.2-1.8)*	1.4 (1.1-1.7)†	1.6 (1.3-2.0)*	1.7 (1.3-2.2)*
Mean dialysis session length (increase per 1.0 min)	1.02 (1.01-1.02)*	1.02 (1.02-1.03)*	1.02 (1.01-1.02)*	1.02 (1.01-1.02)*
Mean hematocrit (increase of 1.0%)	NS	NS	1.05 (1.02-1.09)†	1.04 (1.01-1.08)‡
Serum albumin ≥ 3.5/3.2 g/dL‖	1.7 (1.3-2.2)*	1.6 (1.2-2.1)*	1.5 (1.2-2.0)†	1.6 (1.2-2.1)†

NOTE. Values expressed as odds ratio (95% confidence interval).
Abbreviation: NS, not significant; KUf, dialyzer ultrafiltration coefficient.
*$P < 0.001$.
†$P < 0.01$.
‡$P < 0.05$.
§These networks had odds ratios significantly less than 1.0.
‖Serum albumin level of 3.5 g/dL or greater by BCG method or 3.2 g/dL or greater by BCP method.

HCFA form 2728 (n = 3,749). Patients were more likely to have a serum albumin level of 3.5 g/dL or greater by BCG method or 3.2 g/dL or greater by BCP method if they had a greater GFR at the initiation of dialysis therapy, greater body weight, greater hematocrit level, or cause of ESRD other than diabetes mellitus. Similarly, patients were more likely to have a hematocrit of 33% or greater if they had a greater GFR at the initiation of dialysis therapy, greater serum albumin level, rHuEPO prescribed pre-ESRD, white race, or male sex.

DISCUSSION

Results from this study show that patients on hemodialysis therapy for less than 6 months were much less likely to achieve NKF-DOQI guidelines for dose of dialysis, anemia management, and serum albumin levels than patients with a longer duration of dialysis therapy. In addition, factors that are actionable by physicians' predialysis were important variables that influenced both serum albumin level and hematocrit. Serum albumin levels were likely to be greater in patients with greater hematocrits and GFRs at the initiation of dialysis therapy. Hematocrits were likely to be greater in patients administered erythropoietin predialysis and who had greater GFRs at the initiation of dialysis therapy. Finally, patients with a duration of dialysis therapy less than 6 months had, on average, lower iron stores than patients with a duration of dialysis therapy of at least 6 months.

These findings underscore the importance of appropriate pre-ESRD care in ameliorating morbidity and mortality in chronic dialysis patients,

Table 4. Multivariate Logistic Regression Analyses for Intermediate Outcomes in Anemia

	Age < 65 y		Age ≥ 65 y	
Variable	HCT < 28% (n = 2,868)	HCT ≥ 33% (n = 2,907)	HCT < 28% (n = 2,489)	HCT ≥ 33% (n = 2,475)
Duration of hemodialysis (y; ≥2 y = referent)				
<0.5	2.8 (1.9-4.1)*	0.62 (0.47-0.82)*	3.2 (2.0-5.1)*	0.58 (0.44-0.76)*
0.5-0.99	1.1 (0.70-1.8)	1.02 (0.80-1.3)	1.2 (0.69-2.1)	1.01 (0.79-1.3)
1.0-1.99	0.83 (0.55-1.3)	1.04 (0.85-1.3)	0.92 (0.53-1.6)	0.98 (0.80-1.2)
Age (increase of 1.0 y)	0.98 (0.97-0.99)*	1.01 (1.01-1.02)*	NS	NS
Race (black)	1.7 (1.3-2.3)*	NS	2.0 (1.4-3.0)*	0.80 (0.66-0.96)†
Sex (women)	NS	0.74 (0.63-0.87)*	NS	NS
Diabetes mellitus as cause of ESRD	NS	NS	NS	NS
Postdialysis weight (increase of 1.0 kg)	1.01 (1.00-1.02)‡	0.99 (0.99-1.0)‡	NS	NS
Network (Network 18 = referent)	NS	1, 2, 6, 8-11, 13-15§	NS	6, 8, 9-11, 13-15§
Mean Kt/V (increase of 1.0)	NS	1.41 (1.00-1.97)†	0.37 (0.18-0.75)‡	NS
Mean transferrin saturation (increase of 1.0%)	NS	1.02 (1.01-1.02)*	NS	1.02 (1.01-1.03)*
Mean serum ferritin concentration (increase of 1.0 ng/mL)	1.0004 (1.0002-1.0007)‡	0.9997 (0.9995-0.9999)‡	NS	NS
Mean weekly rHuEPO dose (increase of 1.0 U/kg/wk)	1.004 (1.003-1.005)*	0.997 (0.996-998)*	1.004 (1.003-1.005)*	0.998 (0.997-998)*
Prescribed IV iron	NS	1.2 (1.1-1.5)‡	NS	1.3 (1.1-1.6)‡
Serum albumin ≥ 3.5/3.2 g/dL‖	0.30 (0.22-0.42)*	1.7 (1.4-2.2)*	0.40 (0.27-0.59)*	1.9 (1.5-2.3)*

NOTE. Values expressed as odds ratio (95% confidence interval).
Abbreviation: NS, not significant; IV, intravenous.
*$P < 0.001$.
†$P < 0.05$.
‡$P < 0.01$.
§These ESRD Networks had odds ratios significantly less than 1.0.
‖Serum albumin levels of 3.5 g/dL or greater by BCG method or 3.2 g/dL or greater by BCP method.

especially in the first year of dialytic therapy. As early as 1978, it was appreciated that patients who were referred shortly before their need for dialysis therapy had greater morbidity and mortality rates than patients referred earlier in the course of renal insufficiency.[19] These initial observations have been confirmed and amplified by a number of investigators from many Western countries.[20-25] For example, referral to a nephrologist within 4 months of starting dialysis therapy (late referral) was associated with a greater degree of hypoalbuminemia, anemia, lower GFR at the initiation of dialysis therapy, and decreased likelihood of being administered predialysis rHuEPO compared with patients referred more than 4 months (early referral) before initiating dialysis therapy.[22,24,26] However, even in the early-referral group, the rate of suboptimal pre-ESRD care was high. Hypoalbuminemia was present in 56% of patients; hematocrit less than 28%, 33% of patients; GFR less than 5 mL/min at the start of dialysis therapy, 17% of patients; and presence of a functional permanent access at the time of the first hemodialysis session, 40% of patients.[22]

In addition, several investigators reported that mortality rates for hemodialysis patients were greater during the first 90 days of dialysis therapy

Table 5. Multivariate Logistic Regression Analyses for Intermediate Outcomes in Serum Albumin Levels

	Serum Albumin ≥ 3.5/3.2 g/dL*	
Variable	Age < 65 y (n = 3,526)	Age > 65 y (n = 2,903)
Duration of hemodialysis (y; 2+ y = referent)		
<0.5	0.35 (0.26-0.47)†	0.41 (0.31-0.55)†
0.5-0.99	0.82 (0.60-1.1)	0.75 (0.56-1.0)
1.0-1.99	0.80 (0.60-1.05)	1.1 (0.86-1.5)
Age (increasing age per year)	0.986 (0.976-0.996)‡	0.98 (0.96-0.99)§
Race (black)	NS	NS
Sex (women)	0.71 (0.57-0.88)‡	NS
Diabetes mellitus as cause of ESRD	0.46 (0.37-0.57)†	0.62 (0.51-0.77)†
Postdialysis weight (increase of 1.0 kg)	1.02 (1.01-1.03)†	1.02 (1.01-1.03)†
Network	1, 2, 10, 11, 16‖	1, 10, 11, 16, 17‖
Mean Kt/V (increase of 1.0 unit)	3.7 (2.5-5.7)†	2.6 (1.7-4.0)†
Mean hematocrit (increase of 1.0%)	1.14 (1.11-1.17)†	1.13 (1.10-1.17)†

NOTE. Values expressed as odds ratio (95% confidence interval).
Abbreviation: NS, not significant.
*Serum albumin level of 3.5 g/dL or greater by BCG method or 3.2 g/dL or greater by BCP method.
†$P < 0.001$.
‡$P < 0.01$.
§$P < 0.05$.
‖These ESRD Networks had odds ratios significantly less than 1.0.

than at subsequent times.[6,23,27-29] Studies by Soucie and McClellan[6] and Khan et al[28] showed that patients with an increased risk for early death had lower mean serum albumin levels. In addition, the study by Soucie and McClellan[6] showed that the presence of specific comorbid conditions, such as cancer, congestive heart failure, and myocardial infarction, was each associated with increased risk for early death. However, none of these analyses included data on either anemia or dose of dialysis. Of note, Soucie and McClellan[6] noted that the crude mortality rate in white patients was 34.9/100 dialysis-years, whereas for blacks, it was 19.2/100 dialysis-years. Similar differences in mortality rates for patients who died after the first 90 days of dialysis therapy have been reported by the US Renal Data System.[1] This racial difference in mortality rates is the most likely explanation for the decrease in percentage of white patients on

Table 6. Predictors of Serum Albumin Level of 3.5 g/dL or Greater by BCG Method or 3.2 g/dL or Greater by BCP Method at Initiation of Dialysis Therapy

	OR (95% CI)	*P*
GFR	1.04 (1.01-1.07)	<0.01
Weight (kg)	1.007 (1.003-1.012)	<0.001
Diabetes mellitus as cause of ESRD	0.44 (0.37-0.53)	<0.001
Hematocrit (%)	1.03 (1.02-1.05)	<0.001

NOTE. Analysis restricted to those patients in the sample with HCFA Form 2728 information (n = 3,749). Variables entered into the model: GFR, erythropoietin prescribed pre-ESRD (yes, no), hematocrit (%), diabetes mellitus as primary cause of ESRD versus other causes of ESRD, patient weight (kg), sex, race (black, white only), Hispanic ethnicity (yes, no), and age (years).
Abbreviations: OR, odds ratio; CI, confidence interval.

Table 7. Predictors of Hematocrit of 33% or Greater at Initiation of Dialysis Therapy

	OR (95% CI)	*P*
GFR	1.08 (1.04-1.12)	<0.001
Erythropoietin prescribed pre-ESRD	1.61 (1.28-2.03)	<0.001
Race (black)	0.61 (0.48-0.79)	<0.001
Sex (women)	0.79 (0.63-0.98)	<0.05
Serum albumin level (g/dL)	1.29 (1.11-1.50)	<0.001

NOTE. Analysis restricted to those patients in the sample with HCFA Form 2728 information (n = 3,749). Variables entered into the model: GFR, erythropoietin prescribed pre-ESRD (yes, no), serum albumin level (g/dL), diabetes mellitus as primary cause of ESRD versus other causes of ESRD, patient weight (kg), sex, race (black, white only), Hispanic ethnicity (yes, no), and age (years).

our survey as duration of dialysis therapy increased.

There also is ample evidence that patients should initiate chronic dialysis therapy when GFR declines to a level of 10 mL/min.[30] Patients who start dialysis therapy at lower levels of GFR are more likely to have hypoalbuminemia,[31] greater mortality rates,[32-34] and greater hospitalization rates.[32,33] In addition, present recommendations for dialysis adequacy recommend a dose equivalent to a GFR of approximately 10 mL/min.[7]

The lower average dose of dialysis seen in patients initiating dialysis therapy likely is secondary to the small percentage of patients with a permanent vascular access. Other studies performed in US patients have shown that more than 50% of patients required use of a temporary catheter within the first 2 months of hemodialysis therapy and less than 50% of patients had a permanent access present at the initiation of dialysis therapy.[35-38] Patients with temporary catheters have, on average, lower blood flow rates and therefore lower doses of dialysis.[37] In all new hemodialysis patients, but particularly those patients with temporary catheters, more effort should be exerted to ensure that the initial hemodialysis prescription provides an adequate dose of dialysis through using dialyzers of larger surface area and increasing time as necessary to achieve adequate dialysis. Consideration could also be given, in light of recent HCFA efforts to update several ESRD forms, to include an item on HCFA form 2728 to indicate if and when a permanent access was placed in new dialysis patients. These data could be used for quality improvement efforts to increase the timely placement of a permanent dialysis access.

Lower hemoglobin levels at the initiation of dialysis therapy may be caused by one or more factors, including iron deficiency, lack of predialysis rHuEPO therapy, and inhibition of erythropoiesis by uremic factors. We found that less than one quarter of hemodialysis patients were prescribed rHuEPO predialysis, and others have shown that rHuEPO administration was also influenced by insurance status and initial dialysis modality.[38] In addition, we found that patients in the first 6 months of dialysis therapy were more likely to be iron deficient than patients with a longer duration of dialysis therapy. This problem with iron deficiency is compounded by our observation that approximately 25% of patients were administered iron by only the oral route. The absorption of oral iron is decreased in the presence of ESRD, and it is unlikely that iron deficiency can be corrected solely by the administration of oral iron.[39]

Causes of hypoalbuminemia are complex and include both nutritional and nonnutritional factors. We have shown that serum albumin level at the initiation of dialysis therapy was inversely proportional to GFR and directly proportional to hemoglobin level. Others have shown a similar relationship between serum albumin level and either serum creatinine level or GFR at the initiation of dialysis therapy.[9,22]

There are several caveats to this analysis. First, because this is a cross-sectional and not a longitudinal analysis, results may be influenced by survival bias. Patients who initiate dialysis with poor intermediate outcomes may have greater mortality rates; therefore, they are less likely to survive and would be underrepresented in patient groups of longer durations of dialysis therapy. However, it is unlikely that this survival bias is the sole explanation for our findings because the magnitude of the difference in intermediate outcomes is much greater than the death rate during the first 6 months of dialysis. Second, we did not have information on type of dialysis access present at the initiation of dialysis therapy or at the time intermediate outcome variables were obtained. Thus, we had to rely on dialysis access findings from other studies to base our conclusions on dialysis adequacy. Because the patient sample for this study was chosen to be a representative cross-section of hemodialysis patients in the United States, it is unlikely that patterns of dialysis-access placement would have been significantly different in our patient population. Third, data in this report are from the last quarter of 1997, the time when the NKF-DOQI guidelines were released. Therefore, DOQI guidelines were not influencing clinical care at the time these data were obtained. Finally, our analysis indicates that for both dialysis adequacy and treatment of anemia, there were statistically significant differences in outcomes based on ESRD Network, indicating that regional effects on intermediate outcomes were present and suggesting that facility effects were also present.[40,41] The

design of our study did not allow us to analyze in a more formal manner these facility or center effects.

Thus, a number of actionable items can result in improved intermediate outcomes in patients during the first 6 months of dialysis therapy. These items include timely placement of a permanent dialysis access, appropriate initiation of chronic dialysis therapy, prescribing a dose of dialysis that meets NKF-DOQI guidelines at the initiation of dialysis therapy, treatment of anemia with rHuEPO and intravenous iron, and monitoring and treatment of malnutrition. Guidelines being developed by both the Renal Physicians Association and the NKF may improve awareness of these actionable items in the predialysis population.

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