Prevalence, Predictors, and Consequences of Late Nephrology Referral at a Tertiary Care Center

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Abstract. Despite improvements in dialysis care, mortality of patients with end-stage renal disease (ESRD) remains high. One factor that has thus far received little attention, but might contribute to morbidity and mortality, is the timing of referral to the nephrologist. This study examines the hypothesis that late referral of patients to the nephrologist might lead to suboptimal pre-ESRD care. Clinical and laboratory data were obtained from the patient records and electronic databases of New England Medical Center, its affiliated dialysis unit (Dialysis Clinics, Inc., Boston), and the office records of the outpatient nephrology clinic. Early (ER) and late (LR) referral were defined by the time of first nephrology encounter greater than or less than 4 mo, respectively, before initiation of dialysis. Multivariate models were built to explore factors associated with LR, and whether LR is associated with hypoalbuminemia or late initiation of dialysis. Of the 135 patients, 30 (22%) were referred late. There were no differences in age, gender, race, and cause of ESRD between ER and LR patients. However, there were significant differences in insurance coverage between these two groups. In the multivariate analysis, patients covered by health maintenance organizations were more likely to be referred late (odds ratio = 4.5) than patients covered by Medicare. Compared to ER, LR patients were more likely to have hypoalbuminemia (56% *versus* 80%), hematocrit <28% (33% *versus* 55%), and predicted GFR <5 ml/min per 1.73 m^2 (17% *versus* 40%) at the start of dialysis, and less likely to have received erythropoietin (40% *versus* 17%) or have a functioning permanent vascular access for the first hemodialysis (40% *versus* 4%). It is concluded that late referral to the nephrologist is common in the United States and is associated with poor pre-ESRD care. Pre-ESRD care of patients treated by nephrologists was also less than ideal. The patient-, physician-, and system-related factors behind this observation are unclear. Meanwhile, pre-ESRD educational efforts need to target patients, generalists, and nephrologists.

The prevalence and incidence of end-stage renal disease (ESRD) are increasing, and ESRD treatment consumes a significant proportion of health care resources in the United States. The prevalence of ESRD has more than doubled in the past decade, with a corresponding annual increase of 10% in the overall prevalence (1). The annual cost of treating ESRD patients is $14.5 billion, and is constantly increasing (2). Despite the considerable resources committed to the care of ESRD patients and improvement in the overall quality of dialysis therapy, the mortality among dialysis patients remains high. The mean remaining life span is only 9.3 yr for patients beginning dialysis at age 40 and 4.3 yr for patients beginning dialysis at age 59 (3).

Several investigators have demonstrated that increasing age, white race, male gender, nonrenal comorbidity, presence of malnutrition, and inadequate delivered dose of dialysis are independent predictors of mortality among dialysis patients (1,4–6). However, despite increasing attention to modifiable factors such as increased dose of dialysis and use of more biocompatible dialyzers, mortality among dialysis patients remains high (2). This has led to a search for other modifiable factors that could improve ESRD outcomes. Among factors that have received scant attention, but may significantly affect the morbidity and mortality of dialysis patients, are the timing and quality of care before initiation of dialysis (pre-ESRD care). Optimal pre-ESRD care involves early detection of progressive renal disease, intervention to retard its progression, prevention of uremic complications, attenuation of comorbid conditions, adequate preparation for ESRD therapy, and timely initiation of dialysis (7). However, it is not known whether patients referred to a nephrologist early receive better pre-ESRD care than those who are referred late. Theoretically, timely referral of patients with chronic renal failure (CRF) to a nephrologist is likely to result in an improved clinical condition and better preparation for initiation of dialysis. Indeed, data from Europe (8–11) and South America (12) have shown that delayed referral is a significant problem, and is associated with a higher prevalence of uremic complication at the initiation of dialysis, with increased hospitalizations and higher cost of care. However, there is limited information available regarding

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the patterns of timing of referral in the United States, and the effects of late referral on ESRD outcomes. The purpose of this study was to examine the prevalence, predictors, and consequences of late referral at an academic medical center.

Materials and Methods

Patients

The study population consisted of all incident patients more than 18 yr of age who began dialysis at the New England Medical Center (NEMC) between October 1, 1992 and December 31, 1997. Patients were identified using records of the annual dialysis facility survey, which is managed and administered by Dialysis Clinics, Inc. (DCI).

Clinical and laboratory data were obtained from the patient records and electronic databases of NEMC, its affiliated dialysis unit (DCI, Boston), and the office records of the outpatient nephrology clinic. Using a standardized form, age, gender, race, insurance status, cause of ESRD, laboratory values obtained within 24 h before initiation of dialysis, pre-ESRD erythropoietin use, presence and type of permanent access used for the first dialysis, initial dialysis modality, predicted GFR, and index of individual disease severity (IDS) at the initiation of dialysis were recorded for each patient. Predicted GFR was calculated from the equation derived from the Modification of Diet in Renal Disease (MDRD) Study, and is based on age, gender, race, and levels of blood urea nitrogen, serum albumin, and serum creatinine (13).

The IDS was calculated using the method described by Greenfield and Nelson (14), and later modified by Athienites and colleagues (15) for use in ESRD patients. The modified IDS includes the following 17 domains: ischemic heart disease, congestive heart failure, arrthymias, other cardiac disease, hypertension, cerebral vascular disease, peripheral vascular disease, diabetes mellitus, respiratory disease, malignancy, hepatobiliary disease, musculoskeletal/connective tissue disorder, gastrointestinal disease, nonvascular nervous system disease, renal/urological disease, HIV/AIDS, and ophthalmic conditions. For each of these domains, patients are assigned to one of four disease severity levels: 0, absence of coexisting disease; 1, mild comorbid condition; 2, symptomatic mild-to-moderate condition requiring medical intervention; and 3, an uncontrolled condition that causes moderate-to-severe disease manifestations during medical care. These last two levels usually denote acute conditions that require urgent medical intervention. Each patient was also assigned a global IDS score, which represented the maximum score assigned among the 17 domains.

Timing of referral was determined from office records of the nephrology outpatient clinic. If the first encounter with a nephrologist occurred more than 4 mo before initiation of dialysis, the patient was classified as an early referral (ER). A patient referred within 4 mo before initiation of dialysis was classified as a late referral (LR). Race was categorized as white and non-white (African-American and Asian). Hypoalbuminemia was defined as serum albumin <3.5 g/dl, and late initiation of dialysis was defined as initiation of dialysis at a predicted GFR <5 ml/min per 1.73 m^2. Insurance was categorized as private (private, fee-for-service), health maintenance organization (HMO), Medicare, Medicaid, and none. Patients with both private insurance and Medicare were categorized as private, and patients with both HMO insurance and Medicare were categorized as HMO. Medicare is a U.S. federal government-funded entitlement program of health care for the elderly (>65 yr), disabled, and patients with ESRD. Medicaid is a means-based program designed to provide health care to the indigent, and is administered through the states. Private health plans provide a predetermined set of health benefits to employees of a given organization for a fixed rate negotiated by the employer. These plans have traditionally been fee-for-service, whereby the plan pays the health care provider directly for services used by the beneficiary. The continuing growth of insurance premiums and the demand by employers for discounts led to the emergence of HMOs, which provide hospitals/physicians an incentive to limit the use of services, and pass on some of these savings to the employer (in the form of reduced premiums). The most extreme form of the new systems is "capitation," whereby the HMO contracts with the physician/hospital to provide complete medical coverage for a group of beneficiaries for a fixed sum.

Statistical Analyses

Univariate analyses of the differences in the clinical and laboratory variables between ER and LR were performed using the *t* test for continuous variables and χ^2 or Fisher exact test for discrete variables. To further explore which factors were independently associated with LR, we constructed a multivariate logistic regression model. Demographic characteristics that have previously been shown to affect outcomes in ESRD patients such as age (linear), gender (reference = male), race (reference = non-white), and diabetes (reference = non-diabetes) were forced into the model. In addition, the independent variables that were significantly associated with the outcome in the univariate analysis were explored in the multivariate analyses and kept in the final model if statistically warranted.

Two additional multivariate logistic regression models were built to test the hypothesis that LR is independently associated with hypoalbuminemia and delayed initiation of dialysis, after adjusting for *a priori* set of covariates. The covariates included in these models were age, gender, race, cause of ESRD, and global IDS score at the initiation of dialysis. Age was entered as linear in the GFR model and categorized as 18 to 49, 50 to 64, and 65+ yr in the albumin model, as these were the best fit for the model.

To examine the effect of year of initiation of dialysis, a dichotomous variable before or during 1994 ($\leq$1994) and after 1994 ($>$1994) was explored in each of the multivariate models. Two-way interactions between year of dialysis and insurance in the model evaluating LR, and year of dialysis and LR in the models evaluating hypoalbuminemia and delayed initiation of dialysis were explored. Statistical analyses were performed using the SAS system for Windows, version 6.12 (SAS Institute, Inc., Cary, NC).

Results

Patient Characteristics

Information regarding the timing of referral was available in 153 of the 155 patients who began dialysis at NEMC between 1992 and 1997. Of these, 105 (68%) were ER to the nephrologist, 18 (12%) were LR due to irreversible acute renal failure (ARF), and the remaining 30 (20%) were LR due to causes other than ARF. Since irreversible ARF is an unavoidable cause of LR, often occurs in the hospital setting, and is often associated with significant morbidity, the analysis was restricted to 135 patients: 105 ER and 30 non-ARF late referrals. The median follow-up with a nephrologist before the initiation of dialysis was 25 mo and 1 mo for the ER and LR patients, respectively.

Predictors of Late Referral to the Nephrologist

Among the 135 patients included in the analysis, 30 (22%) were referred late and 105 were referred early to the nephrologist. Differences in demographic and clinical characteristics of patients with ER and LR are shown in Table 1. There were

Table 1. Demographic and clinical characteristics of patients referred to the nephrologist at a tertiary care center[a]

Characteristic	Late Referral[b] (n = 30)	Early Referral[c] (n = 105)	P Value
Mean age ± SD (yr)	55 ± 17	61 ± 15	0.08
Gender (female)	46%	53%	0.50
White race	53%	54%	0.52
Insurance			0.04
Medicare	20%	45%	
private	23%	28%	
HMO	33%	15%	
Medicaid	17%	8%	
none	7%	4%	
Diabetes mellitus as cause of ESRD	40%	36%	0.70
IDS score			
zero to one	10%	8%	
two	56%	55%	0.80
three	33%	37%	

[a] HMO, health maintenance organization; ESRD, end-stage renal disease; IDS, individual disease severity.
[b] Late referral, <4 mo before initiation of dialysis.
[c] Early referral, >4 mo before initiation of dialysis.

no significant differences between the two groups with reference to age, gender, cause of ESRD, and IDS score. Similarly, there were no significant differences in the different comorbidity domains between the two groups. However, there were significant differences in insurance coverage between these two groups. In a multivariate logistic regression model, after controlling for age, gender, race, and cause of ESRD, patients who belonged to HMOs had a significantly higher odds of LR to a nephrologist (odds ratio [OR] = 4.5; 95% confidence interval [CI], 1.3 to 14.6) compared with Medicare patients. Although the likelihood of LR was higher for Medicaid (OR = 4.1; 95% CI, 0.9 to 17.7) and uninsured patients (OR = 3.2; 95% CI, 0.4 to 23.4) compared to Medicare patients, these differences were not statistically significant. The odds of LR for patients covered by HMOs compared to Medicare was higher after 1994 (OR = 5.1) than ≤1994 (OR = 3.2). However, this difference was not statistically significant.

Consequences of Late Referral to the Nephrologist

Table 2 shows the clinical and laboratory characteristics at the start of dialysis among LR and ER patients. Patients in the LR group had significantly lower serum albumin and calcium, and higher serum creatinine levels at the time of initiation of dialysis than ER patients. Permanent vascular access was attempted before initiation of dialysis in 58 and 7% of patients in the ER and LR groups, respectively. A permanent vascular access was used for the first hemodialysis in 40% of ER (80% arteriovenous fistula and 20% arteriovenous graft) and 4% and LR patients. Mean predicted GFR was not significantly different between the two groups. However, patients in the LR group were more likely to start dialysis at predicted GFR <5 ml/min per 1.73 m^2 (late initiation of dialysis). Similarly, patients in the LR group were more likely to have a hematocrit <28% and less likely to have received erythropoietin during the pre-ESRD period compared to patients in the ER group.

Association Between Late Referral to the Nephrologist and Hypoalbuminemia at the Start of Dialysis

Hypoalbuminemia was present in 62% of the patients (80% of LR and 56% of ER) at the start of dialysis. Univariate

Table 2. Laboratory and clinical characteristics of patients referred to the nephrologist at a tertiary care center[a]

Characteristic	Late Referral[b] (n = 30)	Early Referral[c] (n = 105)	P Value
Predialysis laboratory values			
serum albumin (g/dl)	2.9 ± 0.7	3.3 ± 0.63	0.01
blood urea nitrogen (mg/dl)	110 ± 45	94 ± 38	0.08
serum creatinine (mg/dl)	9.6 ± 5.7	7.6 ± 3.6	0.02
serum sodium (mEq/L)	137 ± 5	139 ± 5	0.14
serum potassium (mEq/L)	5 ± 1.0	4.7 ± 0.7	0.17
serum bicarbonate (mEq/L)	19.3 ± 5	21 ± 5	0.08
serum calcium (mg/dl)	8.2 ± 1.3	8.7 ± 1.0	0.04
serum phosphorus (mg/dl)	6.6 ± 2.7	6.1 ± 2.6	0.37
hematocrit (%)	27 ± 9	29 ± 6	0.13
predicted GFR (ml/min per 1.73 m^2)	7 ± 4	8 ± 4	0.33
Predicted GFR <5 ml/min per 1.73 m^2	13/30 (43%)	18/102 (17%)	0.01
Predialysis EPO use	5/30 (17%)	42/104 (40%)	0.016
Permanent vascular access for the first dialysis	1/28 (4%)	41/86 (48%)	0.001
PD as initial dialysis modality	2/30 (7%)	19/105 (18%)	0.13

[a] EPO, erythropoietin; PD, peritoneal dialysis.
[b] Late referral, <4 mo before initiation of dialysis.
[c] Early referral, >4 mo before initiation of dialysis.

analysis revealed that the odds of hypoalbuminemia at the start of dialysis was greater among the LR patients (OR = 3.1; 95% CI, 1.2 to 8.2), African-Americans (OR = 2.5; 95% CI, 1.0 to 6.9), patients with an IDS score of 3 (OR = 2.7; 95% CI, 0.7 to 10.7), patients with diabetes as the etiology of ESRD (OR = 3.7; 95% CI, 1.7 to 8.4), and patients with predicted GFR <5 ml/min per 1.73 m^2 (OR = 3.2; 95% CI, 1.2 to 8.5). In a multivariate model adjusted for age, gender, race, cause of ESRD, and IDS score, patients with LR continued to have a greater likelihood of hypoalbuminemia (OR = 3.7; 95% CI, 1.3 to 10.9) at the start of dialysis. Hypoalbuminemia was less frequent after 1994. However, the odds of hypoalbuminemia were higher for LR patients in both time periods (OR 3.8 ≤1994 and 5.2 after 1994). This difference was not statistically significant.

Association Between Late Referral to the Nephrologist and Delayed Initiation of Dialysis

The predicted GFR was <5 ml/min per 1.73 m^2 at the initiation of dialysis in 24% of patients (43% of LR, 18% of ER). Univariate analysis revealed that predicted GFR <5 ml/min per 1.73 m^2 at initiation of dialysis was more likely among patients with LR (OR = 3.6; 95% CI, 1.6 to 13.7), and less likely with increasing age (OR = 0.96; 95% CI, 0.9 to 1.0) and white race (OR = 0.2; 95% CI, 0.07 to 0.5). In a multivariate model adjusted for age, gender, race, and cause of ESRD, patients with LR continued to have a greater likelihood of starting dialysis at a predicted GFR <5 ml/min per 1.73 m^2 (OR = 4.1; 95% CI, 1.4 to 11.5). Adding insurance to the model did not change the result significantly. The odds of delayed initiation of dialysis for LR were greater among those who began dialysis ≤1994 (OR = 8.4) compared to those who started dialysis after 1994 (OR = 3.2). This difference was not statistically significant.

Discussion

Our results demonstrate that: (*1*) late referral to the nephrologist is common among ESRD patients beginning dialysis at a tertiary care center in the United States; (*2*) irreversible ARF is a common cause of late referral; and (*3*) patients belonging to HMOs are more likely to be referred late compared with patients covered by Medicare. Compared to patients referred early, those referred late had a higher odds for hypoalbuminemia, hematocrit <28%, and GFR <5 ml/min. Furthermore, significantly fewer LR patients had received predialysis erythropoietin and had a functioning vascular access for the first dialysis compared to ER.

Among all patients beginning dialysis between 1992 and 1997, 32% had their first nephrology encounter less than 4 mo before initiation of dialysis. These results are similar to those recently reported by the United States Renal Data System (USRDS) Dialysis Morbidity and Mortality Study (DMMS) Wave 2 (1). In a representative national sample of patients who began dialysis in 1996, 31% were seen by a nephrologist for the first time less than 4 mo before start of dialysis. In contrast, among 585 patients who began dialysis at the University of Missouri Health Science Center between 1982 and 1987, 66% required dialysis within 4 mo of their first visit to the nephrologist (16). Among patients who began dialysis between 1990 and 1994 at an inner city dialysis unit in New York, 57% of patients had not received pre-ESRD care by a nephrologist (17). More importantly, among LR in our study (32%), 12% required dialysis following irreversible ARF and only 20% were LR due to causes other than irreversible ARF. Since irreversible ARF precludes ER to the nephrologist, the true prevalence of late referral was even lower (22%).

We found that the type of insurance was the only factor that was significantly associated with LR. Among patients who began dialysis at the New England Medical Center between 1992 and 1997, 10 of the 26 patients belonging to three different HMOs were referred late compared to 6 of 53 patients covered by Medicare. When adjusted for age, gender, race, and cause of ESRD, these HMO patients had a 4.5-fold greater likelihood of being referred late compared to patients covered by Medicare at our institution. Although the likelihood of LR was also higher among Medicaid (OR = 2.3) and uninsured patients (OR = 3.9) compared to the Medicare patients, this difference did not reach statistical significance. In contrast, the USRDS DMMS Wave 2 found that lack of insurance, but not coverage by HMO, was independently associated with LR (18). The association between LR and HMOs is disturbing. It is possible that in the era of managed care, pressure to contain cost influences primary care physicians' decision to refer patients to a nephrologist. However, because these results are from a single center in a state that has a substantial HMO penetration, this conclusion may not be generalizable and should be interpreted with caution. Other factors may be operative, and additional studies are needed to explore this issue.

Several investigators have reported that LR is associated with suboptimal pre-ESRD care, as manifested by advanced uremic complications and inadequate preparation for initiation of dialysis (9,12,19–21). We found that patients who were referred late were significantly more likely to have hypoalbuminemia and hypocalcemia, and less likely to have received erythropoietin and a permanent vascular access before the first hemodialysis. In addition, LR was associated with initiation of dialysis at lower levels of renal function, as documented by a higher serum creatinine and a higher proportion of patients with predicted GFR <5 ml/min per 1.73 m^2.

Hypoalbuminemia at initiation of dialysis is a strong predictor of subsequent morbidity and mortality on dialysis. Indeed, in the USRDS Case Mix Severity Study of 3,399 patients who began dialysis in 1986–1987, compared to patients with serum albumin levels of 3.5 to 4.0 g/dl, the adjusted relative risk of death among patients with serum albumin of 3.0 to 3.5, 2.5 to 3.0, and <2.5 g/dl was 1.20, 1.66, and 2.16, respectively, for hemodialysis patients and 1.09, 1.79, and 1.92, respectively, for peritoneal dialysis patients (22,23). We observed that the overall prevalence of predialysis hypoalbuminemia (60%) was similar to that recently reported in a large sample of U.S. incident dialysis patients (24). However, the prevalence of hypoalbuminemia was considerably higher among LR compared to ER patients (86% *versus* 56%). In a multivariate analysis, after controlling for age, gender, race, cause of

ESRD, and comorbidity, LR was associated with a 3.7-fold greater odds of hypoalbuminemia. The cause(s) for the strong association between hypoalbuminemia and LR are less clear. One possibility is that LR is associated with delayed initiation of dialysis, and delayed initiation of dialysis is associated with hypoalbuminemia. Indeed, as renal function declines, spontaneous dietary protein restriction occurs (25), along with multiple derangements in protein metabolism (26). Indeed, we found that patients with predicted GFR <5 ml/min per 1.73 m^2 at the start of dialysis were more likely to have hypoalbuminemia. Alternatively, the high prevalence of hypoalbuminemia among LR may be due to the lack of supervision by a qualified dietitian among these patients or a colinearity between the factors that cause hypoalbuminemia and LR. The small sample size precluded an examination of these latter possibilities.

Among patients with CRF, severe anemia is associated with left ventricular hypertrophy (LVH), left ventricular dilation, and a high cardiac output (27). LVH is an important predictor of cardiac morbidity and mortality on dialysis (28,29). Cardiovascular disease and LVH develop before ESRD (30). Hence, correction of anemia with erythropoietin during the predialysis phase is of great importance. However, among patients starting dialysis in the United States between 1995 and 1997, 51% had hematocrit $<28\%$, and only 20% of those with hematocrit $<28\%$ received erythropoietin before starting dialysis (24). LR of patients with CRF to the nephrologist could be one of the explanations for the underutilization of erythropoietin pre-ESRD. We observed that late referrals were more likely to have a hematocrit $<28\%$ (55% *versus* 33%), and less likely to have received pre-ESRD erythropoietin (17% *versus* 40%), compared to ER.

Optimal preparation for renal replacement therapy includes timely education and discussion of the different treatment modalities with the patient and family, timely placement of the dialysis access, and timely initiation of dialysis. We observed that the choice of initial dialysis modality was peritoneal dialysis in 18% of ER compared to only 7% of LR. These data tend to support the observations of previous investigators that late referral compromises the ability of the patient to make an informed choice of dialysis modality (reviewed in reference (7)). Likewise, LR also precludes the timely placement of a permanent vascular access. Ideally, patients who select hemodialysis should have a permanent vascular access placed several months before initiation of dialysis (31). Lack of a permanent access is almost invariably associated with hospitalization for initiation of dialysis, placement of temporary catheters, a higher likelihood of receiving an arteriovenous graft as opposed to an arteriovenous fistula, and higher morbidity and cost (32). We found that only 37% of patients had a functioning permanent vascular access for their first dialysis. Furthermore, this proportion was considerably lower among LR (4%) compared with ER (40%). The overall prevalence of a functioning permanent vascular access is similar to that reported among 1,997 patients who began hemodialysis in 1993 in the United States. In this study, only 37% of patients had a functioning access at initiation of dialysis (33). Moreover, early referral was independently associated with a 79% higher likelihood of having a permanent vascular access at initiation of dialysis (33).

The timing of initiation of dialysis has recently been a subject of intense debate in the nephrology community (34,35). Proponents of early initiation cite evidence suggesting that initiation of dialysis at low levels of GFR adversely affect nutrition, volume and BP control, resulting in poor ESRD outcomes (7). Consequently, the Peritoneal Dialysis Adequacy Work Group of the National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) recommends that dialysis be initiated when the weekly renal Kt/V urea falls below 2.0, which approximates a GFR of 10.5 ml/min (36). Interestingly, as many as 24% of patients in this study began dialysis at predicted GFR <5 ml/min per 1.73 m^2. This proportion was significantly higher among LR compared with ER (43% *versus* 17%). When adjusted for age, gender, cause of ESRD, and comorbidity, LR was independently associated with higher odds of late initiation of dialysis. Type of insurance did not affect the association between LR and delayed initiation of dialysis. These data confirm the suspicion that late referral to the nephrologist is an important cause of late initiation of dialysis.

We explored the possibility that practice patterns of patient care may have changed during the course of this study. Indeed, the odds of LR among patients covered by HMOs were greater in patients who began dialysis in 1994 compared to $\leq$1994. Furthermore, the odds of hypoalbuminemia among LR were greater among those who started dialysis after 1994. In contrast, the odds of delayed initiation of dialysis among late referrals were lower after 1994. However, due to the limited sample size, the significance of these differences could not be established.

The results of this study substantiate the hypothesis that LR to the nephrologist is an important cause of suboptimal pre-ESRD care. However, pre-ESRD care among patients treated by a nephrologist for more than 4 mo before initiation of renal replacement therapy was also less than ideal. Even among ER, 56% had hypoalbuminemia, 33% had a hematocrit $<28\%$, only 40% had received predialysis erythropoietin, only 40% had a functioning permanent vascular access for the first dialysis, and 17% started dialysis at a predicted GFR <5 ml/min per 1.73 m^2. One possibility is that the 4-mo cutoff that we and others have used to define ER may be too liberal. Optimal pre-ESRD care would probably require referral to the nephrologist at an even earlier time point in the course of progressive renal disease. The National Institutes of Health (NIH) Consensus Conference of 1993 recommends that patients with chronic renal failure be referred to a renal team when the serum creatinine has increased to 1.5 mg/dl in women and 2.0 mg/dl in men (37). The median interval between the first encounter with the nephrologist and start of dialysis was 25 mo among patients in the early referral group. Consequently, an alternative interpretation of these data could be that pre-ESRD care of patients treated by nephrologists, too, is less than ideal. The patient-, physician-, and system-related factors behind this observation are currently unclear. Meanwhile, Pre-ESRD edu-

cational efforts should target the patients, generalists, and the nephrologists.

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