Opportunities for Improving the Care of Patients with Chronic Renal Insufficiency: Current Practice Patterns

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Abstract. There are between 2 and 13 million Americans with chronic kidney disease (CKD). Recent reports suggest that their treatment is currently suboptimal. To further investigate this issue, patterns of practice for the treatment of patients with CKD who were enrolled in a large health maintenance organization in New Mexico were analyzed. Among the >200,000 patients who were enrolled in the health maintenance organization between 1994 and 1997, a cohort of 1658 patients who exhibited at least two gender-specific, elevated creatinine concentrations (Cr), separated by at least 90 d, were identified. The proportions of patients with Cr values of <2.0, 2.0 to 2.9, 3.0 to 3.9, and ≥4.0 mg/dl were 73, 17, 3, and 7%, respectively. The majority of patients were treated by a primary care physician until Cr values reached 3.0 mg/dl, at which time a nephrologist was consulted. Care tended to be transferred to the nephrologist when the Cr reached 4.0 mg/dl. Only 7.4% of patients received erythropoietin (EPO). Use of EPO increased as Cr increased. EPO was unlikely to be prescribed unless the patient had visited a nephrologist. Fewer than one half of all patients with CKD and fewer than 20% of patients with CKD with Cr values of ≥4.0 mg/dl received an angiotensin-converting enzyme inhibitor (ACEI). Nephrologists were not more likely to prescribe ACEI than were primary care physicians. Diabetic patients were more likely to receive ACEI than were nondiabetic patients, but ACEI use was quite low even among diabetic patients with CKD. The average number of hospitalizations per patient-year increased as Cr increased and was more than twice as high for patients with Cr values of ≥4.0 mg/dl, compared with those with Cr values of <2.0 mg/dl. The reasons for hospitalization were more likely to be related to comorbidities than to CKD itself, however. There are many opportunities to improve the care of patients with CKD. Better adherence to practices known to be of clinical benefit for patients with CKD not only will improve patient outcomes but also may reduce the costs of care. Providers, policy-makers, and payers should view CKD as a major public health problem and initiate innovative programs to address this growing patient population.

Although little work has been performed to estimate the prevalence of chronic kidney disease (CKD), recent analyses suggest that the size of this patient population is large (1,2). On the basis of an analysis of a large health maintenance organization (HMO) database, we previously estimated that there are >9 million Americans with elevated serum creatinine concentrations (Cr) and >2 million with moderate CKD (Cr of ≥2.0 mg/dl) (2). Early identification of such patients could facilitate (*1*) timely introduction of therapies to slow the progression of CKD, (*2*) identification and management of the comorbidities commonly associated with CKD (*e.g.*, diabetes mellitus and heart disease), (*3*) management of common complications of CKD (*e.g.*, anemia and renal osteodystrophy), and (*4*) smooth transitions to renal replacement therapy when necessary (3,4).

Unfortunately, the majority of studies published to date have revealed that patients with CKD are not routinely being identified early in their clinical courses and are not being treated with attention to the issues outlined above (5–11). Those reports are limited, however, by the study of small numbers of patients or reliance on clinical practice patterns at one or a few medical centers. In addition, those reports did not address the types and volumes of health care resources being used in the treatment of those patients.

We report here the patterns of practice for the treatment of patients with CKD at a large, integrated, staff- and network-model HMO in New Mexico. Because an extensive database, with considerable patient-specific information, was available for analysis, we were able to gain insights into the health care resources used by patients with CKD, including their patterns of hospitalization, use of various types of outpatient providers, and use of outpatient prescription medications.

Materials and Methods

Patient Population

We obtained 1994 to 1997 enrollment, inpatient and outpatient encounter, billing, and laboratory data, as well as outpatient prescrip-

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tion claims data, for all people enrolled in this large staff-model HMO for whom at least one elevated Cr value was measured in the laboratory of the HMO between January 1, 1994, and December 13, 1997. Cr values of >1.2 mg/dl for women and >1.4 mg/dl for men are above the upper limit of the normal range defined by this laboratory. Details on the study population and the prevalence of CKD in different subgroups are reported elsewhere (2). Because each enrollee was assigned a unique identification number and because all encounters and claims related to a given enrollee included that unique identification number, as well as the date of service, we were able to longitudinally evaluate all inpatient and outpatient utilization data for the patients for whom we received data.

Health Services Received by the CKD Population

To perform these analyses, we identified a cohort of patients who satisfied our criterion for CKD (at least two gender-specific elevated Cr values measured between January 1, 1994, and December 1, 1997, separated by at least 90 d). The only additional eligibility requirement we imposed when assembling this cohort was that individuals were required to have been enrolled for at least 30 d after they satisfied our CKD criterion. As a result, patients with CKD entered our health resource analysis cohort at different time points. In addition, it should be noted that the patients with CKD who were included in this analysis might be either incident or prevalent patients. For purposes of this analysis, we considered time 0 for each patient in our cohort to be the date on which he or she satisfied our CKD criterion. Therefore, patients included in our cohort were required to have been enrolled in the HMO for at least 90 d before the start of their "health resource analysis clock" but may have been enrolled in the HMO for many years before this.

In addition, because patients satisfied our criterion for CKD at different times and because patients were enrolled in the HMO for varying lengths of time, the number of available months of observation varied for different patients in this cohort. To account for these variations in the periods of observation available for each patient in our analyses of visits to nephrologists and other types of providers and patient use of angiotensin-converting enzyme inhibitors (ACEI), we calculated an "annualized percentage" of patients who received each of these types of services. This annualized percentage was calculated as follows. Patients for whom a full 12 mo of observation were available contributed 12 mo to the denominator and 1 to the numerator if they experienced an event of interest during the first 1 yr of observation or a 0 to the numerator if they did not experience an event of interest. Patients for whom a full 12 mo of observation were not available and who did not experience an event of interest during the period of observation contributed a 0 to the numerator and the number of months of observation available to the denominator. Finally, patients for whom a full 12 mo of observation were not available but who did experience an event of interest during the period of observation contributed a 1 to the numerator and 12 mo to the denominator, because the missing months of data were irrelevant for those patients, given the parameter we were estimating. We used this approach because we were more interested in calculating an annualized percentage of patients who received a particular service than we were in estimating an annualized event rate. For example, we were more interested in estimating the proportion of patients who received an ACEI during the first 1 yr of observation than we were in estimating how many ACEI prescriptions the patients received during the first 12 mo of observation. With this approach, the range of possible values for the estimated parameter is 0 to 1 and the parameter can be interpreted as representing the proportion of patients who would be expected to have received the service of interest had there been a full 1 yr of data available for all patients. For example, an annualized percentage value of 0.88 for visits to a primary care physician (PCP) would mean that, during 1 yr of observation, it would be expected that 88% of patients would have visited a PCP.

Conventions Used in All Analyses

Age Calculations. The recorded age as of January 1, 1997, was used to assign each patient to an age category.

Age Categories. Age was categorized as <30, 30 to 39, 40 to 49, 50 to 59, 60 to 65, or >65 yr.

Definition of Elevated, Gender-Specific Cr. Elevated Cr values were defined as >1.2 mg/dl for female patients and >1.4 mg/dl for male patients.

CKD Severity Categories. Each patient in the CKD cohort was assigned to one of the following CKD severity categories: <2.0, 2.0 to 2.9, 3.0 to 3.9, or ≥4.0 mg/dl. Assignments were based on the first (earlier) of the two Cr values that defined the patient as having CKD.

Definition of Diabetes Mellitus. Patients were considered to be diabetic if they received at least one outpatient prescription drug for the treatment of diabetes mellitus (defined operationally as any of the 831 different National Drug Codes used by the National Committee on Quality Assurance to define diabetes mellitus) or had experienced at least one emergency room encounter, at least one inpatient encounter, or at least two non-emergency room outpatient encounters for the treatment of diabetes mellitus (International Classification of Disease, 9th edition, diagnosis code 250, 250.x, 357.2, 362.0, or 366.41).

Definition of Hypertension. Patients were considered to be hypertensive if they had experienced at least one inpatient or outpatient encounter with any of the following International Classification of Disease, 9th edition, diagnosis codes: 401 or 401.x (essential hypertension), 402 or 402.xx (hypertensive heart disease), 403 or 403.xx (hypertensive renal disease), 404 or 404.xx (hypertensive heart and renal disease), 437.2 (hypertensive encephalopathy), 362.11 (hypertensive retinopathy), or 405 or 405.xx (secondary hypertension).

Definition and Severity of Anemia. Patients were considered to be anemic if they exhibited at least two hematocrit (Hct) values that were below the normal range for the laboratory (<42.0% for male patients and <36.0% for female patients), separated by at least 30 d. We examined the severity of anemia by classifying anemic patients into the following three categories, on the basis of the lowest Hct value observed for each patient: Hct of <30%, Hct of 30 to <33%, or Hct of ≥33% but less than the lower limit of the gender-specific normal range.

Statistical Analyses

We used a $\chi 2$ test and a Wilcoxon-type test for trend developed by Cuzick (12) to evaluate the association between the prevalence of diabetes mellitus and/or hypertension and the severity of CKD. These analyses were performed separately for patients who were <65 yr of age and for those who were ≥65 yr of age. $P < 0.05$ was considered to be statistically significant.

To understand the factors that determine the costs of caring for patients with CKD, we performed multivariate regression analysis using actual charges as the dependent variable and patient characteristics as independent variables. Before performing this regression analysis, we calculated the average monthly charges for each patient and examined the distribution of this variable. Because total charges per patient per month were not normally distributed and because failure to account for the skew in the data would lead to biased estimates of SEM, we used a natural logarithmic transformation of the

charges variable. The transformed variable was much more normally distributed.

We next created a dummy variable for each independent variable, *i.e.*, age (categories as described above), gender, presence or absence of diabetes mellitus, presence or absence of hypertension, and Cr (categories as described above). The transformed dependent variable, *i.e.*, the natural logarithm of total charges per patient per month, was then estimated using linear regression. We excluded 21 patients (1.3% of the sample) for whom charge data were missing. Our reference group was male subjects <30 yr of age with neither diabetes mellitus nor hypertension but with CKD (according to our definition) and Cr values of <2.0 mg/dl.

Because this model predicts the natural logarithm of charges, rather than actual charges, the predicted values must be retransformed to obtain estimated charge values. Simple retransformation of the estimated values for the natural logarithms of charges yielded biased and inconsistent estimates. Therefore, we used the Duan transformation algorithm, *i.e.*, predicted charges, based on the coefficient estimates from the initial model, multiplied by a smearing factor, defined as the mean of the exponential residuals. This method yielded consistent parameter estimates and minimized retransformation bias. With this analysis, we determined the incremental monthly charges generated by various patient groups, compared with those for male patients <30 yr of age with CKD but with neither diabetes mellitus nor hypertension, with a Cr value of <2.0 mg/dl.

Results

Characterization of the CKD Cohort

A total of 1658 patients satisfied the eligibility criteria for inclusion in our health resources analysis cohort. Overall, there was at least 1 yr of observation after entry into the cohort for 1001 of the 1658 patients (60%). There were 221 patients for whom we had at least 2 yr of observation after entry into our cohort and 29 patients for whom we had at least 3 yr of observation. The median observation time for patients in the cohort was 15 mo, and the total patient-months of observation were 25,810. Approximately one half (48.7%) of the patients were female, and 73.4% of the patients were ≥65 yr of age. Of the 1658 patients, 73% exhibited Cr values of <2.0 mg/dl, 17% exhibited values of 2.0 to 2.9 mg/dl, 3% exhibited values of 3.0 to 3.9 mg/dl, and 7% exhibited values of ≥4.0 mg/dl.

Table 1 provides information on the prevalence of diabetes mellitus and hypertension in the CKD cohort. Approximately one quarter of the patients with CKD exhibited evidence of diabetes mellitus, approximately three quarters exhibited evidence of hypertension, and approximately one quarter exhibited evidence of both diabetes mellitus and hypertension. The prevalence of diabetes mellitus was similar among male and female patients with CKD. The prevalence of hypertension was slightly greater among female patients with CKD than among male patients with CKD. There was a significant association between any given level of elevated Cr and the prevalence of diabetes mellitus, hypertension, or both, except for hypertension among patients ≥65 yr of age.

Hospitalizations

Table 2 provides data on the average number of hospitalizations per patient-year of observation during the first 12 mo after entry into the cohort, according to the Cr category. The

Table 1. Prevalence of diabetes mellitus and/or hypertension, according to severity of CKD and age[a]

Cr Category	No. of Patients/Total No. of Patients					
	Diabetes Mellitus		Hypertension		Diabetes Mellitus and Hypertension	
	<65 Yr (n = 441)	≥65 Yr (n = 1217)	<65 Yr (n = 441)	≥65 Yr (n = 1217)	<65 Yr (n = 441)	≥65 Yr (n = 1217)
<2.0 mg/dl (n = 1203)	57/275[b] (21%)	230/928[c] (25%)	152/275[d] (55%)	722/928[e] (78%)	46/275[f] (17%)	199/928[g] (21%)
2.0 to 2.9 mg/dl (n = 289)	18/80[b] (23%)	57/209[c] (27%)	46/80[d] (58%)	173/209[e] (83%)	16/80[f] (20%)	47/209[g] (22%)
3.0 to 3.9 mg/dl (n = 53)	4/18[b] (22%)	16/35[c] (46%)	14/18[d] (78%)	31/35[e] (89%)	4/18[f] (22%)	14/35[g] (40%)
≥4.0 mg/dl (n = 113)	29/68[b] (43%)	14/45[c] (31%)	50/68[d] (74%)	38/45[e] (84%)	26/68[f] (38%)	13/45[g] (29%)
All (n = 1658)	108/441 (25%)	317/1217 (26%)	262/441 (59%)	964/1217 (79%)	92/441 (21%)	273/1217 (22%)

[a] In this and all other cohort analyses, evidence of diabetes mellitus and hypertension was ascertained as of the date the patient satisfied our criterion for chronic kidney disease (CKD). In this and all subsequent cohort analyses, the serum creatinine concentration (Cr) category was assigned on the basis of the first (earlier) of the two Cr values that defined the patient as having CKD.
[b] Pearson χ^2 coefficient for association between diabetes mellitus and Cr category = 14.450 (P = 0.002).
[c] Pearson χ^2 coefficient for association between diabetes mellitus and Cr category = 8.558 (P = 0.036).
[d] Pearson χ^2 coefficient for association between hypertension and Cr category = 10.213 (P = 0.017).
[e] Pearson χ^2 coefficient for association between hypertension and Cr category = 5.342 (P = 0.148).
[f] Pearson χ^2 coefficient for association between the presence of both diabetes mellitus and hypertension and Cr category = 15.336 (P = 0.002).
[g] Pearson χ^2 coefficient for association between the presence of both diabetes mellitus and hypertension and Cr category = 7.807 (P = 0.050).

Table 2. Hospital utilization by patients with CKD

Cr Category	Hospitalization Utilization (Average No./Patient-Yr)
All (n = 1658)	0.84
<2.0 mg/dl (n = 1203)	0.72
2.0 to 2.9 mg/dl (n = 289)	0.96
3.0 to 3.9 mg/dl (n = 53)	1.20
≥4.0 mg/dl (n = 113)	1.56

average number of hospitalizations per patient-year increased as Cr values increased and was more than twice as high for patients with Cr values of ≥4.0 mg/dl, compared with those with Cr values of <2.0 mg/dl.

The reasons for hospitalization were generally unrelated to CKD *per se*. Rather, they reflected the substantial comorbidities that were common in this patient population. Cardiovascular disease (*e.g.*, congestive heart failure, chest pain, or arrhythmias), peripheral vascular disease, infectious diseases (pneumonia or septicemia), and metabolic disorders were the most common reasons for hospitalization (data not shown).

Provider Encounters

The annualized percentages of patients who made at least one visit to a PCP or a nephrologist during the first 12 mo after entry into the cohort are presented in Table 3. Patients with CKD tended to be cared for by a PCP, without consultation with a nephrologist, until Cr values reached 3.0 mg/dl. Whereas overall 88% of patients with CKD monitored for 1 yr would be expected to visit a PCP, only 22% would be expected to visit a nephrologist. Patients whose Cr values were between 3.0 and 3.9 mg/dl were generally cared for by a PCP (82% would be expected to be seen by a PCP) as well as a nephrologist (72% would be expected to be seen by a nephrologist). When Cr values reached 4.0 mg/dl, the nephrologist would be likely to assume the care of the patient, including the primary care needs, with 80% of patients being expected to be seen by a nephrologist and only 50% being expected to be seen by a PCP. This pattern was the same for diabetic and nondiabetic patients (data not shown).

Table 3. Annualized percentage of patients who visited a PCP or nephrologist, according to Cr category[a]

Cr Category	Annualized Percentage	
	PCP[b]	Nephrologist
All (n = 1658)	0.88	0.22
<2.0 mg/dl (n = 1203)	0.93	0.12
2.0 to 2.9 mg/dl (n = 289)	0.86	0.31
3.0 to 3.9 mg/dl (n = 53)	0.82	0.72
≥4.0 mg/dl (n = 113)	0.50	0.80

[a] See text for explanation. PCP, primary care physician.
[b] The type of provider was assessed on the basis of specialty-specific location-of-service codes used by the health maintenance organization.

The patterns of anemia management are of great interest and will be reported in detail elsewhere. Table 4, however, presents data on the annualized percentage of patients with CKD who made at least one visit to a nephrologist during the first 12 mo after entry into the CKD cohort, according to the presence and severity of anemia. Although there was a tendency for patients with CKD whose Cr values were ≥3.0 mg/dl to be more likely to visit a nephrologist if they were anemic than if they were not anemic, the likelihood of a patient with CKD visiting a nephrologist did not increase as the severity of anemia increased, regardless of the severity of CKD. For example, for patients with Cr values of ≥4.0 mg/dl, 76, 75, and 82% were expected to visit a nephrologist during a 1-yr period at measured Hct levels of >32.9% up to the lower limit of the gender-specific normal range, 30 to 32.9%, or <30%, respectively.

Outpatient Prescription Medications

Patients with CKD received a large number of prescription medications. The most commonly filled prescriptions were related to cardiovascular disease, diabetes mellitus, acid-peptic disease, menopause, and depression. Information was not available regarding the use of over-the-counter medications, including multivitamins, folic acid, and phosphate binders.

Erythropoietin Use

A total of 215 patients with CKD (13%) were anemic but exhibited Hct values of >32.9%, 114 patients with CKD (6.9%) exhibited Hct values of 30 to 32.9%, and 372 patients with CKD (22.4%) exhibited Hct values of <30% (Table 4). Of the 1658 patients in the cohort, 7.4% received erythropoietin (EPO) at least once during the period of observation (data not shown). The majority of patients who received EPO exhibited moderate or severe anemia; very few patients with Hct values of >32.9% received this medication. Most patients who received EPO also exhibited the most severe CKD, on the basis of Cr values. In addition, at any given Hct level, there was an increased tendency for EPO administration with increasing Cr values. Finally, it was uncommon for patients to receive EPO unless the patients had been seen by a nephrologist, even after controlling for CKD severity and Hct level. More detailed analyses of anemia and its treatment are ongoing and will be presented elsewhere.

ACEI Use

There are several noteworthy findings regarding the use of ACEI in this cohort (Table 5). First, during the first 1 yr after entry into our CKD cohort, fewer than one half of the patients with CKD we examined had at least one pharmacy claim for any ACEI/patient-yr of observation. Second, the annualized percentages of patients who received an ACEI were similar regardless of Cr level when Cr values were ≤3.9 mg/dl but decreased (to <20%) when Cr values were ≥4.0 mg/dl. Third, although the likelihood of ACEI use was higher among dia-

Table 4. Annualized percentage of patients who visited a nephrologist, according to anemia category and Cr category[a]

Cr Category	All Patients (n = 1658)	Annualized Percentage			
		Not Anemic (n = 957)	Hct of >32.9% and ≤ Low Value for Gender (n = 215)	Hct of 30 to 32.9% (n = 114)	Hct of <30% (n = 372)
All	0.22	0.13	0.26	0.33	0.39
<2.0 mg/dl	0.12	0.10	0.15	0.23	0.15
2.0 to 2.9 mg/dl	0.31	0.30	0.31	0.16	0.38
3.0 to 3.9 mg/dl	0.72	0.63	0.81	0.75	0.71
≥4.0 mg/dl	0.80	0.44	0.76	0.75	0.82

[a] See text for explanation. Hct, hematocrit.

betic patients with CKD than among nondiabetic patients with CKD, the annualized likelihood of ACEI use among diabetic patients was still low, regardless of the Cr values. Fourth, there was little, if any, difference in the likelihood of ACEI use among either diabetic or nondiabetic patients with CKD in each Cr category who visited a nephrologist, compared with those who did not visit a nephrologist. The greater likelihood of ACEI use among all patients with CKD with Cr values of >4.0 mg/dl who visited a nephrologist, compared with those who did not visit a nephrologist, is attributable to the large number of nondiabetic patients who did not visit a nephrologist, rather than to differences in the patterns of ACEI administration for nephrologists *versus* non-nephrologists.

Multivariate Regression Analysis of Total Charges per Patient per Month

Table 6 presents the parameter estimates, standard errors, and P values that resulted from the multivariate regression analysis of the association between patient characteristics and health care charges. It should be kept in mind that the absolute charges can vary significantly, depending on the particular payer involved and other factors, but the relative effects of various patient characteristics and levels of renal function on charges should be independent of the absolute values. After retransformation of the charges variable, the results presented in Table 7 were generated. With control for other factors, the average charges per patient per month were similar for male

Table 5. Annualized percentage of patients who received an ACEI, according to Cr category and whether they were seen by a nephrologist[a]

Cr Category	Annualized Percentage		
	All Patients	Patients Seen by Nephrologist[b]	Patients Not Seen by Nephrologist
All patients	n = 1658	n = 317	n = 1341
all (n = 1658)	0.34	0.31	0.35
<2.0 mg/dl (n = 1203)	0.36	0.38	0.36
2.0 to 2.9 mg/dl (n = 289)	0.31	0.31	0.31
3.0 to 3.9 mg/dl (n = 53)	0.43	0.42	0.45
≥4.0 mg/dl (n = 113)	0.15	0.16	0.09
Diabetic patients	n = 425	n = 109	n = 316
all (n = 425)	0.49	0.44	0.51
<2.0 mg/dl (n = 287)	0.50	0.56	0.50
2.0 to 2.9 mg/dl (n = 75)	0.59	0.57	0.60
3.0 to 3.9 mg/dl (n = 20)	0.45	0.43	0.56
≥4.0 mg/dl (n = 43)	0.28	0.28	0.29
Nondiabetic patients	n = 1233	n = 208	n = 1025
all (n = 1233)	0.29	0.24	0.30
<2.0 mg/dl (n = 916)	0.32	0.32	0.32
2.0 to 2.9 mg/dl (n = 214)	0.21	0.19	0.22
3.0 to 3.9 mg/dl (n = 33)	0.41	0.41	0.41
≥4.0 mg/dl (n = 70)	0.05	0.05	0.06

[a] See text for explanation. ACEI, angiotensin-converting enzyme inhibitor.
[b] Seen by a nephrologist within 1 yr after entry into the CKD cohort.

Table 6. Estimated coefficients and *P* values from the total-charges linear regression

Variable[a]	β-Coefficient	Standard Error	*P* Value
Intercept	3.568	0.181	0.0001
Age of 30 to 39 yr	1.964	0.256	0.0001
Age of 40 to 49 yr	2.251	0.225	0.0001
Age of 50 to 59 yr	2.462	0.216	0.0001
Age of 60 to 64 yr	2.200	0.235	0.0001
Age of ≥65 yr	2.633	0.191	0.0001
Female gender	−0.014	0.065	0.8315
Diabetes mellitus only	0.851	0.183	0.0001
Hypertension only	0.511	0.087	0.0001
Both diabetes mellitus and hypertension	0.963	0.101	0.0001
Cr level of 2.0 to 2.9 mg/dl	0.113	0.087	0.1951
Cr level of 3.0 to 3.9 mg/dl	0.736	0.183	0.0001
Cr level of ≥4.0 mg/dl	1.157	0.134	0.0001

[a] The reference group was male patients <30 yr of age with CKD but neither diabetes mellitus nor hypertension and with Cr levels of <2.0 mg/dl.

and female patients. Higher charges were noted for all age groups, compared with the reference group, with the increase being $519/mo for ages 30 to 39 yr, $720/mo for ages 40 to 49 yr, $909/mo for ages 50 to 59 yr, $680/mo for ages 60 to 64 yr, and $1095/mo for ages ≥65 yr.

The average charges also increased as Cr values increased. Compared with patients with CKD with Cr values of <2.0 mg/dl, monthly charges were $10 higher, $92 higher, and $185 higher for patients with Cr values of 2.0 to 2.9, 3.0 to 3.9, and ≥4.0 mg/dl, respectively. In addition, monthly charges were $114 higher for patients with diabetes mellitus, $57 higher for patients with hypertension but not diabetes mellitus, and $137 higher for patients with both diabetes mellitus and hypertension, compared with patients with neither condition.

Table 7. Effect of regressors on charges per patient per month

Patient Characteristic	Increase in Charges per Patient per Month, Relative to the Reference Group[a] ($)
Female gender	−1
Age of 30 to 39 yr	519
Age of 40 to 49 yr	720
Age of 50 to 59 yr	909
Age of 60 to 64 yr	680
Age of ≥65 yr	1,095
Diabetes mellitus only	114
Hypertension only	57
Both diabetes mellitus and hypertension	137
Cr level of 2.0 to 2.9 mg/dl	10
Cr level of 3.0 to 3.9 mg/dl	92
Cr level of ≥4.0 mg/dl	185

[a] Among patients with CKD. The reference group was male patients <30 yr of age with neither diabetes mellitus nor hypertension and with Cr levels of <2.0 mg/dl. All values are significant at $P < 0.0001$, except for female gender and Cr level of 2.0 to 2.9 mg/dl, neither of which was statistically significant.

Discussion

For a cohort of 1658 patients with CKD enrolled in a large HMO, we have characterized recent patterns of medical practice, which suggest substantial opportunities to improve care for this population. Although previous reports documented the effects of late referral of patients with CKD to nephrologists, this study provides a more complete view of the current practice patterns for these patients, including a number of aspects of care not previously well characterized. Because we used Cr levels to define CKD and did not have information regarding the prevalence of proteinuria or other urinalysis findings or regarding GFR, we likely omitted some patients with CKD from this analysis. Several findings for the patients we did identify are noteworthy. First, diabetes mellitus, hypertension, or both were significantly associated with increased Cr and were increasingly prevalent with higher Cr values. Second, the number of hospitalizations increased directly with the level of Cr, and the majority of hospitalizations were related to associated comorbidities, rather than to CKD itself. Third, in this mixed-model HMO system, although the annualized percentage of patients who visited a nephrologist during the first 1 yr of observation after entry into our CKD cohort increased as Cr values increased, nephrologists tended not to be involved in the care of patients with CKD whose Cr values were <3.0 mg/dl. Fourth, although the prevalence of anemia was high among the patients with CKD in our cohort, recombinant human EPO was used infrequently, even among patients with hemoglobin values of <10 g/dl. Finally, use of ACEI among patients with CKD was disappointingly low, particularly among patients with Cr values of ≤4.0 mg/dl. Perhaps even more disappointing was our observation that the likelihood of ACEI use was no

higher among patients with CKD who were cared for by nephrologists, even after controlling for CKD severity.

There are many opportunities to reduce hospitalizations for patients with CKD with close attention to the management of associated comorbid conditions. Cardiovascular disease is highly prevalent among patients with CKD and often leads to hospitalization (13–15). Closer attention to the management of heart disease in this population, as outlined by Meyer and Levey (16) in a recent National Kidney Foundation consensus statement, could substantially improve outcomes. In addition, several studies demonstrated that even partial correction of anemia (to a hemoglobin level of 11 to 12 g/dl) among patients with CKD can prevent left ventricular hypertrophy from developing or can lead to its regression (17–20). Both anemia and cardiovascular disease were recently demonstrated to be key predictors of nonelective hospitalizations before dialysis initiation (21).

A minority of patients received ACEI, although ACEI use was more common among diabetic patients. As discussed in a recent meta-analysis of ACEI use among patients with CKD with or without diabetes mellitus, ACEI are effective in slowing the progression of renal disease (21). A recent analysis by Golan *et al.* (22) demonstrated that the use of ACEI therapy for patients with type 2 diabetes mellitus is also cost-effective.

Overall, a minority of patients with CKD in our sample were seen by a nephrologist during the first 1 yr of observation after entry into our CKD cohort. Referral to the nephrologist generally occurred when Cr values were $\geq$3.0 mg/dl. This represents a GFR of $\leq$20 ml/min for most patients. A National Institutes of Health Consensus Development Conference (23) on CKD recommended that nephrologists be consulted much earlier in the course of renal disease, when Cr values reach 1.5 mg/dl for women or 2.0 mg/dl for men, so that appropriate diagnostic tests can be performed and interventions, when available, can be prescribed. Unfortunately, the experience we observed is more typical of clinical practice throughout the United States. Among a cohort of patients who underwent dialysis but were $>$65 yr of age when they developed end-stage renal disease, 81% had not been seen by a nephrologist until 3 mo before dialysis and 47% had not been seen by a nephrologist until 1 mo before dialysis (4). Although these data were for patients who began to undergo dialysis in the second half of 1987, more recent data from the United States Renal Data System Dialysis Morbidity and Mortality Study, Wave 2, indicated that the proportion of patients who reported that they had been seen by a nephrologist at least 1 yr before starting dialysis was 40 to 50% (24). Several studies have demonstrated that the late referral of patients to nephrologists increases morbidity and costs for patients with CKD (25–28). The fact that few patients in our study received recombinant human EPO unless they were seen by a nephrologist, regardless of hemoglobin levels, provides at least one explanation for the findings of these previous studies.

A similar problem exists in many other countries, with the proportion of dialysis patients who required dialysis within 1 mo after the first visit to a nephrologist ranging from 25% in Paris, France, to 42% in Oxford, United Kingdom, to 58% in Sao Paulo, Brazil (29–31). The consequences of these late referrals are devastating; patients who are referred late are more likely to present for dialysis with severe uremia, congestive heart failure, the need for temporary vascular access, malnutrition, and metabolic acidosis. Total numbers of days of hospitalization in the 12 mo after the initiation of dialysis and mortality rates are significantly higher for patients referred late (3,4).

Even if patients are referred to nephrologists, some aspects of care that have been demonstrated to be beneficial for patients with CKD are not adhered to consistently. For example, there was no evidence in our study that patients with CKD who visited a nephrologist had a higher likelihood of ACEI use than did those who did not visit a nephrologist. In addition, significant numbers of anemic patients with CKD who visited a nephrologist did not receive EPO. Our findings are consistent with practices observed in other settings. We analyzed patients with CKD being treated in a variety of settings in Boston and demonstrated that $<$40% of patients who were appropriate candidates for EPO, on the basis of the presence of CKD and Hct levels of $<$33%, actually received the drug (32). Although in some cases this may reflect inadequate resources to pay for this costly medication, this is not the explanation for many patients. Rather, the physician, whether a PCP or a nephrologist, has simply not considered it appropriate to prescribe EPO. Similarly, McClellan *et al.* (33) demonstrated that ACEI are infrequently prescribed for patients with CKD who are being discharged from the hospital. The appropriate use of EPO and ACEI could substantially improve outcomes for this patient population.

A key area of treatment for patients with CKD, *i.e.*, access to and utilization of dietitians, was not evaluated because of a lack of available data. For monitoring of nutritional status, effects of reduced-protein diets, use of appropriate multivitamins, and control of phosphorus and sodium intake, the routine availability of a trained dietitian is essential for the optimal treatment of patients with CKD.

We performed a regression analysis to gain better insight into the patient characteristics that are most important in determining the costs of care. Because the data available to us were derived from one HMO and because the data reflect charges, rather than costs, our absolute charge estimates may not be generalizable to other settings. However, the relative contributions of particular patient characteristics to charges may be more generalizable and hence of value to health plans and providers at risk for the care of such patients. Our analysis suggests that the independent effect of age on charges is much larger than the effect of either CKD severity or the presence of comorbidities (diabetes mellitus and/or hypertension). Nonetheless, substantial incremental cost is incurred when Cr values increase above 3.0 mg/dl and when diabetes mellitus or hypertension is present. Any “risk-adjusted” payment system for the care of patients with CKD should take these associations into account.

This study adds considerable new information to our understanding of how patients with CKD are being treated, and it suggests numerous opportunities to improve outcomes for this

patient population. Better adherence to practices known to be of clinical benefit not only will improve patient outcomes but also may reduce costs of care. Because of the high clinical and financial costs of end-stage renal disease programs, providers and policy-makers should view CKD as a major public health problem and should initiate innovative programs to address this growing patient population.

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