CLINICAL RESEARCH STUDY

Chronic Kidney Disease Prevalence and Rate of Diagnosis

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ABSTRACT

BACKGROUND: Chronic kidney disease is a major public health problem. However, no study to date has estimated the prevalence of chronic kidney disease based on the clinical guidelines established by the National Kidney Foundation and few studies have explored the rate of diagnoses by primary care providers.

SUBJECTS AND METHODS: Cross-sectional study of ambulatory patients in Rochester, NY. The purpose of this study was to estimate the prevalence of chronic kidney disease and the rate of primary caregiver diagnosis in ambulatory patients with chronic kidney disease.

RESULTS: Among the 24,492 outpatients that had at least 2 glomerular filtration rate estimates ≥3 months apart, 6895 had an estimated glomerular filtration rate < 60 mL/min/1.73 m², indicating a 28.2% period prevalence of chronic kidney disease. The rate of clinical diagnosis among those with chronic kidney disease was 26.5% (95% confidence interval, 17.9 to 35.1), suggesting that 74% of patients with chronic kidney disease are undiagnosed.

CONCLUSIONS: We demonstrate that the prevalence of chronic kidney disease is substantially higher in health-seeking individuals than in the general population. Moreover, we demonstrate that laboratory reporting of estimated glomerular filtration rate using the Modification of Diet in Renal Disease equation alone does not result in an optimal rate of clinical diagnosis. © 2007 Elsevier Inc. All rights reserved.

KEYWORDS: Chronic kidney disease; Diagnosis; Glomerular filtration rate; MDRD; Prevalence

Epidemic increases in chronic kidney disease have prompted the National Institutes of Health to include chronic kidney disease as a focus area in the Healthy People 2010 initiative. The 2010 guidelines call for reductions in: the rate of new cases of end-stage renal disease, the mortality rate related to chronic kidney disease, and kidney failure due to diabetes. 1 Recent medical evidence suggests that proper management of chronic kidney disease in the early stages can prevent death from cardiovascular disease, delay the need for dialysis, and improve patient health at the onset of dialysis. 2-7

While incidence and prevalence rates of end-stage renal disease are known, analogous rates for earlier stages of chronic kidney disease are limited. Chronic kidney disease is defined as a glomerular filtration rate (GFR) < 60 mL/min/1.73 m² of body surface area for ≥3 months. 2 According to the Third National Health and Nutrition Examination Survey (NHANES III) from 1988-1994, an estimated 8.3 million adults in the US have chronic kidney disease, indicating a prevalence of 4.7%. 8 However, kidney function is based on a single estimate of GFR, as are similar estimates from other studies. 9-13

Lack of epidemiological data on the scope of early-stage chronic kidney disease hinders the development and evaluation of early intervention programs that could reduce the burden of disease. Although early stages of chronic kidney disease are typically asymptomatic, detection can be achieved through laboratory testing. All clinical laboratories in Monroe County, New York have adopted the Modification of Diet in Renal Disease (MDRD) 4-variable equation to aid in estimating patients’ serum creatinine (S creat) -based GFR. The equation has proven most accurate in individuals with

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chronic kidney disease and been further validated by direct measurement in patients >70 years of age.\(^2,14-19\) The MDRD equation potentially enables early detection of chronic kidney disease, thus providing primary care physicians with an opportunity to delay disease progression. Few studies have attempted to estimate the rate of diagnoses of chronic kidney disease by primary care physicians. However, these studies were limited in that diagnostic decisions were based on $S_{\text{cr}}$ values alone.\(^12,20\) Two major objectives of this study were: estimation of the period prevalence of chronic kidney disease as defined by MDRD-estimated GFR $<60 \text{ mL/min/1.73 m}^2$ $\geq$3 months, and estimation of the rate of primary caregiver recognition/diagnosis of chronic kidney disease.

**METHODS AND MATERIALS**

**Study Population**

The study was conducted in Monroe County, New York, which has a population of 735,177.\(^21\) Monroe County demographics are similar to those of the US, with 51% of residents being female and 13% aged $\geq$65 years. Monroe County has a slightly higher percentage of African Americans (13.7%) compared with that in the US (12.3%), and the median age of residents is slightly older (39.1 years) than that of the US population (35.3 years).\(^21,22\)

The laboratory at Strong Health (University of Rochester) processes both inpatient and ambulatory specimens, comprising roughly one third of all tests done in Monroe County. The ambulatory specimens are collected from primary care offices throughout the County, which increases the likelihood of a representative sample.

The overall study population included all individuals 18 years of age or older as of June 1, 2003 who had at least one laboratory-estimated GFR from Strong Health between June 1, 2003 and May 31, 2004. Given the potential for renal insult and instability, inpatient estimates were excluded from the study. Individuals with missing demographic information or personal identifiers were also excluded. The study was approved by the Institutional Review Board at the University of Rochester Medical Center in accordance with Health Insurance Portability and Accountability Act guidelines.

**Data Source**

The database utilized in this study was maintained by Clinical Laboratory Services at Strong Health. The database contained patient information that was submitted on the laboratory requisition and provided on the laboratory reports to the requesting physicians. The clinical laboratory of Strong Health measured $S_{\text{cr}}$ using an enzymatic method on Vitros 950 analyzers (Ortho Clinical Diagnostics, Rochester, New York). In order to address the issue of bias among the various creatinine assay methods regarding GFR estimation,\(^23\) a correlation study of 40 patients was performed comparing $S_{\text{cr}}$ values using the Vitros 950 enzymatic method to an ADVIA 2400 blank-corrected Jaffe method (Bayer HealthCare, Tarrytown, New York). The ADVIA assay is traceable to a high-performance liquid chromatography reference method and, as per manufacturer, the re-expressed MDRD equation

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GFR = 175 \times (S_{\text{cr}})^{(-1.154)} \times (\text{age})^{-0.203} \times (0.742 \text{ if } \text{female}) \times (1.210 \text{ if African-American})
\]

is used to calculate GFRs.\(^14,24\) $S_{\text{cr}}$ is measured in mg/dL, age is measured in years. A scatter plot of assay results demonstrated excellent correlation between the methods (R-square 0.9978).

**Outcomes of Interest**

For the purpose of this study, 2 outcomes were considered. First, the period prevalence of chronic kidney disease in patients seeking ambulatory health care was estimated. Chronic kidney disease was defined, utilizing the National Kidney Foundation Kidney Disease Outcomes Initiative (KDOQI) guidelines, as MDRD estimated GFR value $<60\text{ mL/min/1.73 m}^2$ for $\geq$3 months.\(^2\) Reduced kidney function to a level of GFR $<60\text{ mL/min/1.73 m}^2$ represents 50% or more loss in normal adult kidney function.\(^2\) This level of kidney dysfunction for $\geq$3 months indicates a chronic loss rather than acute reduction. The period prevalence was determined as the ratio of the number of patients with a GFR $<60\text{ mL/min/1.73 m}^2$ for $\geq$3 months to the number of patients with estimates $\geq$3 months apart. Estimated GFR results are flagged by the laboratory as abnormal based on normal age and sex limits and are reported as abnormal to the primary care physician for further assessment of chronic kidney disease.

Second, we estimated the rate of primary caregiver recognition/diagnosis of chronic kidney disease as documented in the medical record for patients with chronic kidney disease as defined by the KDOQI guidelines. Sample size calculations for construction of a 95% confidence interval (CI) to estimate diagnostic reporting rates within $\pm$10% of the true population rate required that medical records from

**CLINICAL SIGNIFICANCE**

- Prior prevalence, defining chronic kidney disease as a single estimated glomerular filtration rate $<60$, was overstated by approximately 27%.
- The predictive value (positive predictive value) of a single estimated glomerular filtration rate $<60\text{ mL/min/1.73 m}^2$ as indicative of chronic kidney disease appears to be approximately 73%.
- Laboratory reporting of estimated glomerular filtration rate using the Modification of Diet in Renal Disease equation alone does not result in an optimal rate of clinical diagnosis, with 74% of patients going undiagnosed.
100 subjects be reviewed. With proportionate sampling by race, we randomly selected 102 patients among the 6895 who met the KDOQI definition of chronic kidney disease. The recognition/diagnosis of chronic kidney disease was defined as any written evidence in each patient’s record that the physician had diagnosed chronic kidney disease. A diagnosis was noted if the physician ordered further clinical testing for renal impairment, referred the patient to a kidney specialist, or wrote in the patient record that chronic kidney disease was present. The chart review was conducted in 2005 and included all records from 2003 through May 2005.

The initial estimation of GFR in 2003-2004 was determined using enzymatic $S_{cr}$ values and the original MDRD formula:

$$GFR = 186 \times (S_{cr})^{(-1.154)} \times (age)^{(-0.203)} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$$

These estimated GFR values were reported to the primary physician and used for the selection of chronic kidney disease patients to estimate the rate of diagnosis. The estimated GFR values were re-expressed using the re-expressed MDRD formula with no change in chronic kidney disease prevalence.

### Statistical Analysis

Descriptive statistics are presented as percentages, or means with standard deviations. A mean GFR for each individual was the basis for calculation of the group mean. Differences between groups for categorical and continuous variables were examined using chi-squared tests or Student’s t-tests, respectively. Statistical significance was ascribed to 2-sided $P$ values $< .05$. Data were normally distributed; analysis was performed using SAS Windows, version 9.1 (SAS Institute Inc., Cary, NC).

### RESULTS

The initial dataset contained 100,176 unique patients. A total of 9321 patients were excluded due to missing personal identifiers, or demographic information. Additionally, 7879 patients were excluded from the sample due to inpatient status. The final study sample consisted of 82,976 unique patients with 170,581 observations. The cohort demographics were as follows: 56% was female, 82% was Caucasian, mean age was 56.2 ± 17.1 years, and the mean estimated GFR was 77.1 mL/min/1.73 m² ± 21.54.

### Prevalence of Chronic Kidney Disease

Among the 82,976 outpatients who had $S_{cr}$ measured, 17,827 had at least one GFR $< 60$ mL/min/1.73 m². If we define chronic kidney disease (CKD) as a single GFR $< 60$ mL/min/1.73 m², this would indicate a period prevalence of 21.5%. However, using the KDOQI guidelines definition of CKD as a GFR $< 60$ mL/min/1.73 m² for ≥3 months, we found that the prevalence was higher. Among the 82,976 outpatients, 24,492 had at least 2 estimates ≥3 months apart. Among these, 6895 had at least 2 GFR $< 60$ mL/min/1.73 m² ≥3 months apart, indicating a 28.2% period prevalence of chronic kidney disease. The age-specific prevalence ranged from a low of 3.7% among those 18-39 years of age to a high of 51% among those >70 years of age. Based on the 24,492 outpatients, the positive predictive value of a single GFR $< 60$ mL/min/1.73 m² as indicative of chronic kidney disease appears to be ~73%.

The demographic characteristics of the outpatient population with and without CKD are outlined in Table 1. The Figure illustrates estimated GFR distribution. The mean estimated GFR was significantly different in those with CKD (45.15 mL/min/1.73 m²) compared with those without chronic kidney disease (80.04 mL/min/1.73 m²) ($P < .001$) (Table 1). Age was also significantly different, with a mean age of 71.4 ± 14.0 years among those with CKD compared with 54.8 ± 16.6 years among patients without CKD ($P < .001$). Among those with chronic kidney disease, 79% were ≥60 years of age. The racial and sex distributions were significantly different ($P < .001$). Caucasians and Native Americans in this sample of health-seeking individuals were disproportionately more likely to have CKD, as were females (9.0%) compared with males (7.4%) ($P < .001$).

### Diagnosis of CKD

To assess the rate of chronic kidney disease diagnoses by primary care providers, we conducted thorough chart re-
views on a random sample of 102 subjects selected from the 6895 subjects identified as having CKD (Table 2). The rate of clinical diagnosis of CKD documented in the patient’s medical record was 26.5% (95% CI, 17.9 to 35.1), suggesting that 74% of patients are undiagnosed. As shown in Table 2, patients with a clinical diagnosis of CKD (n = 27) had significantly lower GFR (33.16 vs 55.15), and a higher prevalence of anemia (56% vs 23%), hypertension (93% vs 63%), and diabetes (59% vs 29%), compared with those without a clinical diagnosis of CKD (n = 75). However, the prevalence of cardiovascular disease was not significantly different between the 2 groups (52% vs 40%) (P = .286).

Table 3 describes the distribution of GFR by diagnosis.

DISCUSSION

We demonstrate that the prevalence of chronic kidney disease, defined by a GFR <60 mL/min/1.73 m² for ≥3 months, was 28.5% in 24,492 health-seeking subjects having multiple GFR measures available. Consistent with previous reports, our study reveals that the prevalence of CKD was higher among women, Caucasians, and the elderly.8,11 Furthermore, we estimate that 74% of patients with CKD do
not have a documented diagnosis of CKD in their medical record.

Our findings show that prior estimates of CKD prevalence, defined as a single GFR <60, were inflated by approximately 27%. We also demonstrate that CKD prevalence among health-seeking individuals is substantially higher than in the general population. This difference has important implications for identification and management of those with CKD. Given that a majority of the estimated 8.3 million individuals with CKD may already be seeking health care for other reasons, an increased awareness among physicians is likely to maximize detection and management of CKD.

The rate at which primary care physicians recognize chronic kidney disease and diagnose patients as such should shape the development of effective primary care physician education programs. The poor sensitivity of prior screening tools, particularly the use of $S_{cr}$ values as a marker of renal insufficiency, has been implicated in the lack of CKD diagnosis. For this reason, Strong Health implemented the MDRD equation in an effort to provide physicians with a more accurate measurement of kidney function to improve the identification of individuals with CKD.

Prior studies have estimated the rate of diagnosis; however, diagnostic decisions in these studies were based on $S_{cr}$ values. The primary care physicians in our study were making diagnostic decisions based upon estimated GFR. Despite the increased sensitivity of this method, physicians in our study were not likely to document a diagnosis of CKD, as only 26.5% of patients with chronic kidney disease had documentation of CKD in their medical record. The data also indicate a possible sex bias in recognition of CKD; evidence of clinical diagnosis was found in only 22.8% of medical records of women, compared with 34.4% of these for men (Table 2). Our findings suggest that physicians are more likely to make the diagnosis as severity of disease increases, with early stages going undiagnosed.

Akbari et al found in a limited setting that the use of estimated GFR combined with an educational intervention of physicians significantly improved the rate of CKD diagnosis in Canada. The rate of diagnosis increased 3-fold (22.4% to 85.1%) following the implementation of the educational program. It was hypothesized that the implementation of widespread reporting of laboratory GFR without the educational component would increase nephrology referrals and overwhelm specialists. Our findings indicate that, given the low rate of physician-documented diagnosis of CKD, the widespread reporting of laboratory GFR alone is unlikely to result in an increase in nephrology referrals. We are not aware of any such change in these referral trends.

The underdiagnosis of CKD is particularly worrisome given that early identification provides an opportunity to slow the progression and alter the course of disease. Several studies indicate that patients are referred to specialized nephrology care just before the need for dialysis, which is often too late. Our findings suggest that referrals during late stages of CKD may be a result of delay in the early clinical diagnosis of CKD by primary care physicians. We speculate that education of primary care physicians on CKD and increased awareness of risk factors may improve the diagnosis rate.

The lack of data on microalbuminuria is a limitation of our study. The number of individuals with a GFR >60 and microalbuminuria is unknown. As a consequence, we have underestimated the prevalence of CKD among those patients with a GFR >60. Additionally, given that our study includes only individuals seeking health care during the study period, we do not have renal function estimates for the entire catchment population. However, the size and demographic characteristics of our study cohort, and the fact that specimens were collected from primary care offices throughout the County, increase the likelihood of a representative sample. By limiting our study to outpatient $S_{cr}$ values and the use of one laboratory for estimation of GFR, we increased our confidence in the validity of the estimated GFR values.

It is very important to note that the prevalence of CKD was determined using individuals with 2 observations ≥90 days apart. It is possible that patients with 2 estimates had more medical problems, particularly hypertension and diabetes, resulting in a slightly inflated prevalence. Additionally, the patients without $S_{cr}$ measurements were likely healthier than those with measured values, and had a lower prevalence than the 28.2% of patients who had 2 or more $S_{cr}$ values. Finally, although the number of chart reviews was limited, our findings indicate that, at best, the rate of CKD diagnosis was 35.1%, which indicates a need for improvement.

In conclusion, we demonstrate that the prevalence of chronic kidney disease is substantially higher in the health-seeking population based on the National Kidney Foundation clinical definition. The notable difference in the prevalence between health-seeking individuals and the general population has important implications for identification and management of individuals with chronic kidney disease. Moreover, we demonstrate that laboratory reporting of estimated GFR using the MDRD equation alone does not result in an optimal rate of clinical diagnosis, with 74% of patients remaining undiagnosed.

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