Risks for End-Stage Renal Disease, Cardiovascular Events, and Death in Hispanic *versus* Non-Hispanic White Adults with Chronic Kidney Disease

Carmen A. Peralta,*† Michael G. Shlipak,*†‡ Dongjie Fan,§ Juan Ordoñez,‖ James P. Lash,¶ Glenn M. Chertow,†‡ and Alan S. Go†‡§

**General Internal Medicine Section, San Francisco Veterans Affairs Medical Center, Departments of †Medicine and ‡Epidemiology and Biostatistics, University of California, San Francisco, and §Division of Research, Kaiser Permanente of Northern California, ‖Division of Nephrology, Kaiser Permanente Oakland Medical Center, Oakland, California; and ¶Division of Nephrology, Department of Medicine, University of Illinois at Chicago, Chicago, Illinois*

Rates of ESRD are rising faster in Hispanic than non-Hispanic white individuals, but reasons for this are unclear. Whether rates of cardiovascular events and mortality differ among Hispanic and non-Hispanic white patients with chronic kidney disease (CKD) also is not well understood. Therefore, this study examined the associations between Hispanic ethnicity and risks for ESRD, cardiovascular events, and death in patients with CKD. A total of 39,550 patients with stages 3 to 4 CKD from Kaiser Permanente of Northern California were included. Hispanic ethnicity was obtained from self-report supplemented by surname matching. GFR was estimated from the abbreviated Modification of Diet in Renal Disease equation, and clinical outcomes, patient characteristics, and longitudinal medication use were ascertained from health plan databases and state mortality files. After adjustment for sociodemographic characteristics, Hispanic ethnicity was associated with an increased risk for ESRD (hazard ratio [HR] 1.93; 95% confidence interval [CI] 1.72 to 2.17) when compared with non-Hispanic white patients, which was attenuated after controlling for diabetes and insulin use (HR 1.50; 95% CI 1.33 to 1.69). After further adjustment for potential confounders, Hispanic ethnicity remained independently associated with an increased risk for ESRD (HR 1.33; 95% CI 1.17 to 1.52) as well as a lower risk for cardiovascular events (HR 0.82; 95% CI 0.76 to 0.88) and death (HR 0.72; 95% CI 0.66 to 0.79). Among a large cohort of patients with CKD, Hispanic ethnicity was associated with lower rates of death and cardiovascular events and a higher rate of progression to ESRD. The higher prevalence of diabetes among Hispanic patients only partially explained the increased risk for ESRD. Further studies are required to elucidate the cause(s) of ethnic disparities in CKD-associated outcomes.

J Am Soc Nephrol 17: 2892–2899, 2006. doi: 10.1681/ASN.2005101122

Progression of chronic kidney disease (CKD) to ESRD is a costly public health problem that disproportionately affects people of racial and ethnic minority groups (1–3). The crude incidence of ESRD is higher in Hispanic than in non-Hispanic white individuals (4,5). Hispanic Americans currently represent the largest minority group in the United States and are projected to be the fastest growing group in the United States by 2050 (6). Despite the growing importance of Hispanic individuals in the United States, few studies have focused on the burden of CKD in this population, but reasons for the higher incidence of treated ESRD among Hispanic individuals remains unclear. Whether the prevalence and/or severity of diabetes fully accounts for the disparity in rates of ESRD among Hispanic and white individuals is not known, despite findings that Hispanic individuals may have an increased incidence of diabetic nephropathy (7,8).

In addition to contributing to the risk for progression to ESRD, an estimated GFR (eGFR) <60 ml/min per 1.73 m^2 is independently associated with the risks for cardiovascular events and death (9). However, the influence of Hispanic ethnicity on the rates of these complications in the setting of CKD is unknown. In the general population, there are conflicting published data on the relative risks for adverse outcomes in the Hispanic population compared with non-Hispanic white individuals and other racial and ethnic groups. Despite higher rates of diabetes and obesity among Hispanic individuals, some studies have found lower rates of cardiovascular death in Hispanic individuals than in non-Hispanic white individuals, giving rise to the term "Hispanic paradox" (10–12), whereas others have observed higher rates in Hispanic individuals (13). Understanding disparities in the complications of CKD by ethnicity may provide important insights into the development of novel prevention strategies in the United States.

In this study, we investigated the associations between Hispanic ethnicity and the risk for adverse outcomes among a large

Received October 26, 2005. Accepted July 25, 2006.

Published online ahead of print. Publication date available at www.jasn.org.

Address correspondence to: Dr. Alan S. Go, Division of Research, Kaiser Permanente of Northern California, 2000 Broadway Street, 3rd Floor, Oakland, CA 94612-2304. Phone: 510-891-3553; Fax: 510-891-3606; E-mail: alan.s.go@kp.org

ISSN: 1046-6673/1710-2892

cohort of patients with an eGFR of 15 to 59 ml/min per 1.73 m^2 (14). We hypothesized that the incidence of ESRD would be higher in Hispanic than in non-Hispanic white patients with CKD and that this excess risk would be explained only partially by differences in rates of diabetes. Furthermore, we hypothesized that Hispanic ethnicity would not be an independent predictor of cardiovascular events and death in the setting of CKD after adjustment for other known confounders.

Materials and Methods

Study Sample and Characterization of Renal Function

Assembly of the Kaiser Permanente Renal Registry was described previously (9). Briefly, the source population were members of Kaiser Permanente of Northern California, a large, integrated health care delivery system with >3.1 million members in the San Francisco and greater Bay Area. The registry included patients who were 20 yr or older; had one or more outpatient serum creatinine measurements found in the health plan laboratory database between January 1, 1996, and December 31, 2002; and had no evidence of maintenance dialysis or kidney transplant before the date of their qualifying serum creatinine test.

For this analysis, we identified the subset of Kaiser Permanente Renal Registry (from a total of 1,120,295 participants in the original registry) members who self-identified as Hispanic or non-Hispanic white and had National Kidney Foundation CKD stages 3 and 4 at study entry, defined as a baseline eGFR of 15 to 59 ml/min per 1.73 m^2 using the abbreviated Modification of Diet in Renal Disease (MDRD) estimating equation (15) and serum creatinine values (mg/dl) calibrated to the MDRD core laboratory (9). We used a modified National Kidney Foundation classification (15) to define severity of CKD at baseline: eGFR 45 to 59 ml/kg per 1.73 m^2 (stage 3a), 30 to 44 ml/kg per 1.73 m^2 (stage 3b), and 15 to 29 ml/kg per 1.73 m^2 (stage 4) (9). Changes in eGFR were estimated during follow-up using measures of serum creatinine concentration that were found in a health plan laboratory database and were not associated with an acute hospitalization because they were more likely to reflect stable kidney function. All eligible Hispanic patients were included, and a random sample of eligible non-Hispanic white patients were included at a ratio of approximately 2:1 for white to Hispanic patients.

The study was approved by the Kaiser Foundation Research Institute's institutional review board. Given the nature of the study, the need for informed consent was waived.

Patient Characteristics and Longitudinal Medication Use

Race or ethnicity was identified by self-report supplemented by surname matching for Hispanic patients (16). Only patients who were considered Hispanic or non-Hispanic white were included in our analysis. An individual's primary language was assigned on the basis of the self-reported preferred language that was found in health plan databases.

Socioeconomic status was assigned on the basis of 2000 US Census block data, which corresponds approximately to the level of city blocks or neighborhoods. Low income was defined as those who lived in a block where income is less than $35,000 per year. Low education was defined as living in a block or neighborhood where >25% of people who were 25 yr or older had less than a 12th-grade education (9).

Coexisting illnesses were identified on the basis of validated methods using pharmacy data, hospitalization discharge diagnoses, ambulatory care diagnoses, laboratory values, and regional cancer registry data as described previously (9). These diagnoses include coronary disease, ischemic stroke or transient ischemic attack, heart failure, peripheral arterial disease, diagnosed hypertension, known dyslipidemia, chronic liver disease, chronic lung disease, systemic cancer, and diagnosed dementia. Assessment of proteinuria was based on laboratory database entries of outpatient urine dipstick results of 1+ or higher (approximately 30 mg/dl or higher) in the absence of a concomitant urinary tract infection (9). The severity of proteinuria was classified as 1+, 2+, 3+, or 4+ by urine dipstick. Diabetes was identified on the basis of a longitudinal health plan diabetes registry that was validated previously for its completeness and accuracy within the Kaiser membership (17). The diabetes registry included patients with pharmacy prescriptions for diabetes medications or supplies, abnormal glycosylated hemoglobin values, or any diagnosis of diabetes or diabetic complication during an inpatient or ambulatory visit (17).

We ascertained information on receipt of medications during follow-up that may affect the outcomes of interest. These included angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, hepatic 3-hydroxy-3-methylglutaryl–CoA reductase inhibitors (statins), β blockers, calcium channel antagonists, and diuretics. Baseline medication use was defined as a filled prescription found in the outpatient pharmacy database within 120 d before a patient's index date. Time-dependent use of these medications was assigned by examination of information on estimated day supply for consecutive filled prescriptions found in the pharmacy database during follow-up. These methods were validated previously to estimate longitudinal medication use (18).

Follow-Up and Clinical Outcomes

The first determination of eGFR during the study period was used as the index date, and patients were followed until the development of ESRD; death; disenrollment from the health plan; or the end of follow-up on December 31, 2002. Disenrollment from the health plan was defined as having more than a 90-d gap in membership without evidence of interim use of medical services found in health plan databases.

The primary outcomes of interest were incident ESRD, cardiovascular events, and death from any cause. Incident ESRD was defined as initiation of maintenance hemodialysis or peritoneal dialysis, obtaining a kidney transplant, or progression to an eGFR <15 ml/min per 1.73 m^2. We identified patients who were receiving maintenance hemodialysis, peritoneal dialysis, or kidney transplant from a comprehensive health plan ESRD treatment registry (9). A cardiovascular event was defined as an acute hospitalization for an acute coronary syndrome (*e.g.*, myocardial infarction, unstable angina), heart failure, ischemic stroke or transient ischemic attack, or peripheral arterial disease using relevant validated *International Classification of Disease, Ninth Revision* codes found in hospital discharge and billing claims databases, which were validated previously (9). All-cause mortality was determined by using the California Automated Mortality Linkage System (19), health plan databases, and Social Security Administration records through December 31, 2002.

Statistical Analyses

All analyses were conducted using SAS statistical software version 9.2 (SAS Institute, Cary, NC). A two-sided $P < 0.05$ was considered significant. We compared baseline characteristics between Hispanic and non-Hispanic white patients using t test for continuous variables and χ^2 test for categorical variables. Age-adjusted event rates of ESRD, cardiovascular events, and death from any cause were calculated using Poisson regression with generalized estimating equations and are reported as rates per 100 person-years with associated 95% confidence intervals (CI) (9).

We examined the association between Hispanic ethnicity and outcomes using a series of nested extended Cox regression models with time-dependent covariates. For multiple or recurrent cardiovascular events, we used a sandwich estimate of the variance-covariance matrix to obtain more robust SE that accommodated the clustering of observations on patients (20). Because of a concern about being able fully to adjust statistically for the possible impact of diabetes and age on the relationship between ethnicity and adverse outcomes using standard methods, we also conducted stratified models by diabetic status and age.

Results

Study Sample and Baseline Characteristics

We identified 12,076 Hispanic and 27,474 non-Hispanic white eligible patients with stage 3 or 4 CKD at study entry defined as baseline eGFR between 15 and 59 ml/min per 1.73 m^2. At entry, Hispanic patients were younger than non-Hispanic white patients, but there were minimal differences in the distribution of baseline kidney function (Table 1). Hispanic patients had lower socioeconomic status, and nearly 17% of Hispanic patients reported having their preferred language being Spanish. Non-Hispanic white patients had a higher prevalence of comorbidities, except for diabetes and documented proteinuria, which were more common among Hispanic patients. Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers were similarly used in Hispanic and non-Hispanic patients, whereas there was slightly lower use of other medications among Hispanic patients at study entry.

Table 1. Baseline characteristics among 39,550 ambulatory non-Hispanic white or Hispanic adults with CKD from January 1, 1996, through December 31, 2002[a]

Characteristic	Total (n = 39,550)	Non-Hispanic White (n = 27,474)	Hispanic (n = 12,076)	P
Age (yr; mean [SD])	66.3 (13.9)	68.4 (13.1)	61.6 (14.5)	<0.001
Women (%)	62.3	63.7	59.1	<0.001
Serum creatinine (mg/dl; mean [SD])	1.32 (0.35)	1.31 (0.33)	1.36 (0.40)	<0.001
eGFR (ml/min per 1.73 m^2; %)				<0.001
45 to 59	80.5	80.4	80.9	
30 to 44	15.9	16.4	14.8	
15 to 29	3.6	3.2	4.4	
Low annual household income (%)	11.9	10.7	14.6	<0.001
Low education level (%)	12.7	7.5	24.6	<0.001
Spanish preferred language (%)	5.1	NA	16.6	
Medical history (%)				
coronary heart disease	14.2	16.0	10.0	<0.001
stroke or transient ischemic attack	6.1	6.9	4.3	<0.001
peripheral arterial disease	4.5	5.2	3.1	<0.001
chronic heart failure	5.8	6.7	3.5	<0.001
known any proteinuria	10.3	8.9	13.3	<0.001
1+	5.6	5.4	6.3	<0.001
2+	2.2	1.9	2.9	<0.001
3+ or 4+	2.4	1.3	4.1	<0.001
diabetes	14.6	12.1	20.3	<0.001
hypertension	41.1	41.2	40.9	0.60
dyslipidemia	34.2	33.9	35.0	0.04
chronic lung disease	20.3	21.5	17.6	<0.001
chronic liver disease	0.4	0.3	0.4	0.06
cancer	8.3	10.1	4.2	<0.001
serum albumin of 3.5 g/dl or less	3.2	3.3	2.8	0.01
diagnosed dementia	1.9	2.3	1.0	<0.001
previous hospitalizations	29.9	33.2	22.2	<0.001
Baseline medication use[b]				
ACE or ARB	16.8	16.8	17.0	0.47
diuretic	26.0	27.6	22.3	<0.001
β blocker	14.7	15.2	13.6	<0.001
calcium channel blocker	12.8	13.1	12.2	0.009
statin	8.4	8.8	7.4	<0.001

[a]ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated GFR.
[b]Within 120 d before index date.

Follow-Up

Mean follow-up was 3.83 ± 2.19 yr (range 0.003 to 7.0) with a total of 151,481 person-years of follow-up for the entire cohort. During follow-up, 18.8% of Hispanic patients and 12.7% of non-Hispanic white patients disenrolled from the health plan ($P < 0.001$). However, baseline characteristics between Hispanic and non-Hispanic white patients who disenrolled *versus* those who did not disenroll showed a similar pattern in that Hispanic patients in both groups had younger age, lower socioeconomic status, and fewer coexisting illnesses except for diabetes (data not shown).

ESRD in Hispanic versus *Non-Hispanic White Patients with CKD*

During follow-up, we observed 578 cases of ESRD in Hispanic and 764 cases among non-Hispanic white patients. The age-adjusted rate of ESRD was higher in Hispanic (1.22 per 100 person-years; 95% CI 1.12 to 1.32) compared with non-Hispanic white patients (0.67 per 100 person-years; 95% CI 0.62 to 0.72; $P < 0.001$; Figure 1).

After adjustment for sociodemographic characteristics, Hispanic ethnicity was associated with an almost two-fold higher risk for ESRD compared with white patients (Table 2). After adjustment for diabetic status, other clinical characteristics, and medication use, the effect was attenuated, although Hispanic ethnicity remained independently associated with a 33% higher risk for ESRD.

Cardiovascular Events in Hispanic versus *Non-Hispanic White Patients with CKD*

During follow-up, there were 3349 observed cardiovascular events in Hispanic and 11,744 cardiovascular events among non-Hispanic white patients. The age-adjusted rate of cardiovascular events was slightly lower in Hispanic (10.31 per 100 person-years; 95% CI 9.98 to 10.63) compared with non-Hispanic white patients (10.94 per 100 person-years; 95% CI 10.75 to 11.14; $P < 0.001$; Figure 1). After adjustment for sociodemographics, clinical characteristics, and medication use, Hispanic ethnicity was associated with a 19% lower risk for cardiovascular events compared with white patients (Table 2).

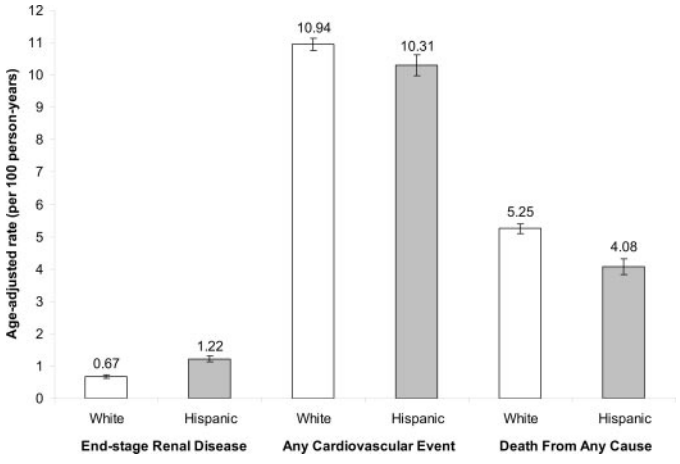

Figure 1. Age-adjusted rates of ESRD, cardiovascular events, and death from any cause in Hispanic compared with non-Hispanic white patients with chronic kidney disease (CKD).

All-Cause Mortality in Hispanic versus *Non-Hispanic White Patients with CKD*

During follow-up, 926 deaths from any cause occurred in Hispanic and 4797 deaths among non-Hispanic white patients. The age-adjusted rate of death was lower in Hispanic (4.08 per 100 person-years; 95% CI 3.84 to 4.32) compared with non-Hispanic white patients (5.25 per 100 person-years; 95% CI 5.10 to 5.39; $P < 0.001$; Figure 1). After adjustment for potential confounders and medical therapy, Hispanic ethnicity was associated with a 29% lower mortality rate compared with white patients (Table 2).

Diabetes, Hispanic Ethnicity, and Adverse Outcomes

To examine whether the association between Hispanic ethnicity and risk for adverse outcomes varied by diabetic status, we conducted stratified models by the presence or absence of diabetes. In patients with diabetes, Hispanic ethnicity was independently associated with an increased risk for ESRD (hazard ratio [HR] 1.35; 95% CI 1.16 to 1.57) but lower adjusted rates of cardiovascular adverse events (HR 0.87; 95% CI 0.78 to 0.98) and death (HR 0.68; 95% CI 0.59 to 0.78) compared with white patients. In patients without diabetes, Hispanic ethnicity was associated with an increased risk for ESRD that was of borderline statistical significance (HR 1.14; 95% CI 0.95 to 1.36) and with lower risks for cardiovascular events (HR 0.77; 95% CI 0.70 to 0.85) and death (HR 0.72; 95% CI 0.65 to 0.80; Figure 2).

Age, Hispanic Ethnicity, and Adverse Outcomes

Given that Hispanic patients in our sample were significantly younger than non-Hispanic white patients in this cohort, we evaluated whether age would significantly modify the relationship between Hispanic ethnicity and adverse outcomes in the setting of CKD by performing age-stratified models. Among the subgroup of patients who were 50 yr or older, we found that these associations remained similar to the overall findings, with increased risk for ESRD and reduced risk for cardiovascular events and all-cause mortality across the age groups for Hispanic compared with non-Hispanic white patients (Figure 3).

Sensitivity Analyses

Because of the possible misclassification of ethnicity using surname matching, we conducted a sensitivity analysis in which we excluded patients who were identified as Hispanic by surname matching only. The multivariable results were not materially different for the outcomes ESRD (HR 1.40; 95% CI 1.22 to 1.60), cardiovascular events (HR 0.86; 95% CI 0.80 to 0.93), and death (HR 0.70; 95% CI 0.64 to 0.76). In addition, to address the issue of possible misclassification of the presence and severity of CKD, we did a sensitivity analysis in which we excluded patients with only one serum creatinine measure during the study period. The results were not materially different compared with the overall cohort for the outcomes of ESRD (HR 1.34; 95% CI 1.18 to 1.53), cardiovascular events (HR

Table 2. Multivariable association between Hispanic ethnicity and the risks for ESRD, any cardiovascular event, and death from any cause among 39,550 ambulatory white or Hispanic adults with stages 3 to 4 CKD[a]

Model Nested	Hispanic *versus* Non-Hispanic White (Adjusted HR [95% CI])		
	ESRD	Any Cardiovascular Event	Death from Any Cause
Unadjusted	1.99 (1.78 to 2.21)	0.75 (0.69 to 0.80)	0.51 (0.47 to 0.54)
+ Age, gender, income, education, and preferred language	1.93 (1.72 to 2.17)	0.84 (0.78 to 0.91)	0.76 (0.71 to 0.82)
+ Hypertension and medical history[b]	1.74 (1.55 to 1.96)	0.87 (0.81 to 0.94)	0.78 (0.72 to 0.84)
+ Diabetes and use of insulin	1.50 (1.33 to 1.69)	0.80 (0.74 to 0.86)	0.73 (0.68 to 0.79)
+ Baseline eGFR[c] and time-updated proteinuria	1.29 (1.14 to 1.48)	0.80 (0.75 to 0.87)	0.71 (0.65 to 0.77)
+ Time-varying medication use[d]	1.33 (1.17 to 1.52)	0.81 (0.75 to 0.87)	0.71 (0.65 to 0.77)

[a]CI, confidence interval; HR, hazard ratio.
[b]Includes coronary heart disease, stroke or transient ischemic attack, peripheral arterial disease, chronic heart failure, dyslipidemia, chronic lung disease, chronic liver disease, systemic cancer, serum albumin of 3.5 g/dl or less, and previous hospitalizations.
[c]Baseline Modification of Diet in Renal Disease eGFR in ml/min per 1.73 m^2.
[d]Includes ACE inhibitors, ARB, diuretics, β blockers, calcium channel blockers, and statins and are included as time-dependent covariates.

0.82; 95% CI 0.76 to 0.89), or death (HR 0.70; 95% CI 0.64 to 0.76).

Discussion

Among patients with National Kidney Foundation stage 3 or 4 CKD, Hispanic ethnicity was associated with a higher risk for progression to ESRD and lower risks for cardiovascular events and death compared with non-Hispanic white patients in this large cohort. These findings persisted after adjustment for sociodemographic characteristics, comorbidities, and longitudinal medication use. Multivariable results from models that were stratified by diabetic status or age showed similar findings. Our observations may help to explain the reported higher rates of ESRD in Hispanic individuals when compared with white individuals in the overall population, (5) despite findings of similar prevalence of CKD (21,22).

To our knowledge, this is the first longitudinal study to address the clinical complications in the Hispanic population with kidney disease in the United States. Despite the knowledge that the Hispanic population is growing faster than any other minority group in the United States and that Hispanic individuals have a large burden of chronic disease, this subgroup has been relatively understudied, particularly in the area of CKD. Our findings of increased risk for ESRD but lower risks for cardiovascular adverse events and mortality are intriguing. Even though some of this variation in outcomes was explained by differences in sociodemographic factors, diabetes, and comorbidities, the finding was robust and persisted among those without diabetes and across age

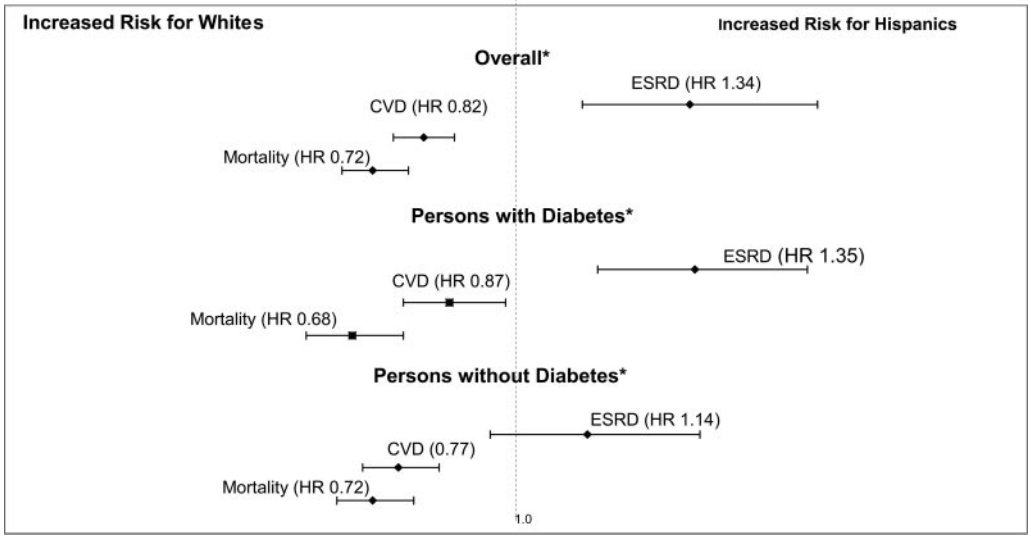

Figure 2. Multivariable risks for ESRD, cardiovascular events, and death in Hispanic compared with non-Hispanic white patients with CKD, stratified by the presence or absence of diabetes.

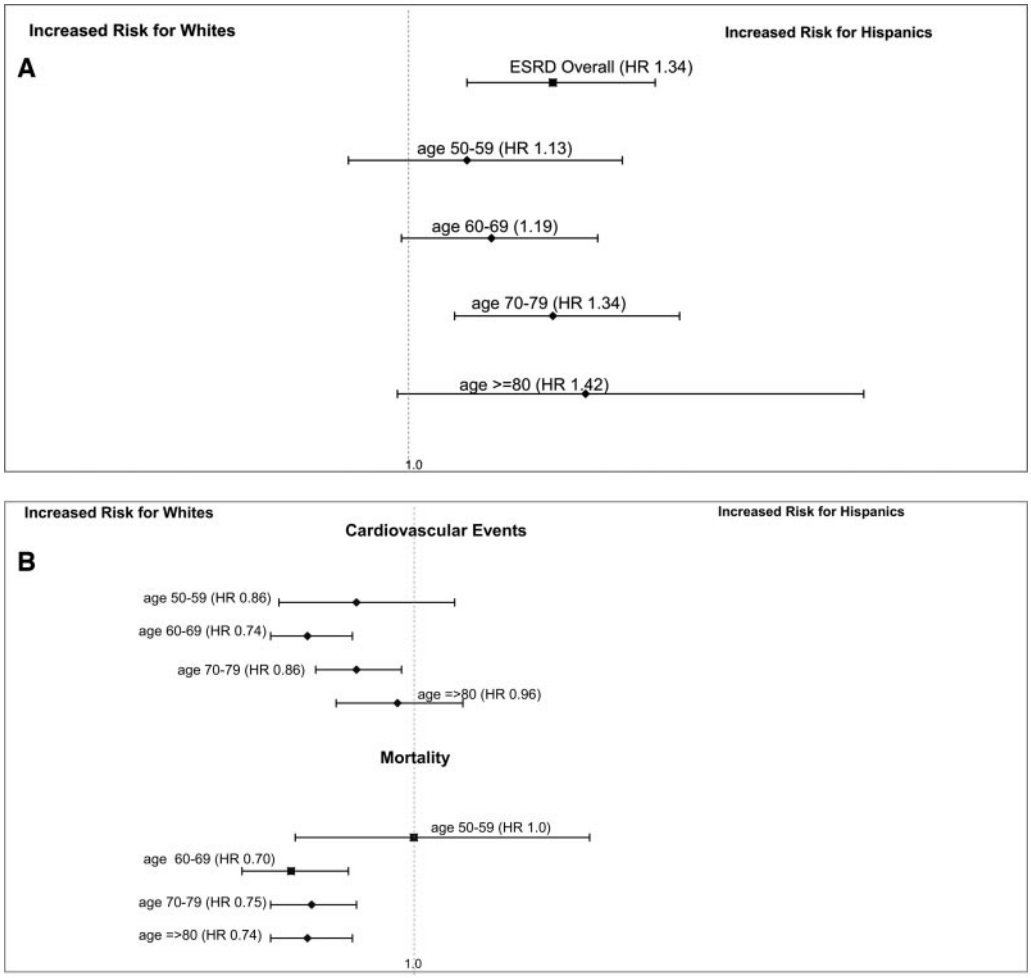

Figure 3. Risks for ESRD (A) and cardiovascular adverse events and mortality (B) for Hispanic compared with non-Hispanic white patients who had CKD and were 50 yr or older, stratified by age.

groups. Whether this residual association is due to biologic or environmental differences remains unknown.

The finding of higher rates of ESRD among Hispanic individuals warrants further exploration. Previous data show that Hispanic individuals have a higher prevalence of type 2 diabetes (23,24) and a higher risk for diabetic nephropathy compared with white individuals (7,8,25,26); however, diabetes prevalence and severity did not seem to explain fully the higher ESRD risk among Hispanic patients. Differences in severity of kidney disease and a genetic predisposition to diabetic nephropathy have been cited as possible explanations for the increased incidence of ESRD among Hispanic individuals (1,27). Hispanic patients in our cohort had a higher prevalence and severity of documented proteinuria, but adjustment for proteinuria did not explain the association between Hispanic ethnicity and risk for ESRD. Therefore, kidney disease severity alone (as measured by eGFR and dipstick proteinuria) may not account for the observed excess risk. Further studies should be conducted to elucidate the effect of biologic (*e.g.*, inflammatory factors, fat distribution, differences in endothelial function), genetic, and sociodemographic factors (*e.g.*, diet, exercise, environmental exposures) that may account for these disparities.

Contrary to what we observed for the outcome of ESRD, Hispanic patients with CKD had lower rates of cardiovascular events and death compared with white patients. Our finding is consistent with previous data documenting a "Hispanic paradox" of lower cardiovascular mortality despite a higher incidence of traditional cardiovascular risk factors in Hispanic individuals (11,12) and with the observation of a "Hispanic advantage" of lower death rates in national samples (11,12,28) and in populations with advanced renal disease (29). The "healthy immigrant" effect and that many Hispanic individuals may return to their country of origin once they are older and sicker have been cited as possible explanations for this apparent paradox (10–13). However, there were no material differences in the baseline characteristics of our cohort and the subset of people who disenrolled from the health plan. Ascertainment bias and misclassification in national death registries have been cited as possible explanations (30). The lower prevalence of cardiovascular disease at baseline among Hispanic patients in our cohort also may help to explain our findings. Competing risks also may explain some of the observed difference in the risk for ESRD in this cohort because lower cardiovascular morbidity and mortality may allow for a longer life span and thus

progression to ESRD. However, other biologic factors may explain the reduced cardiovascular risk for Hispanic individuals, such as differences in fat distribution, smoking habits, or lower prevalence of novel cardiovascular risk factors.

Our findings set the stage for future research on the burden of kidney disease in Hispanic individuals. Given that prevalence of CKD is similar in national samples (22) and that our study has documented higher rates of progression to ESRD, future research should focus on delineating factors that contribute to this increased ESRD risk. In addition, research efforts should focus on the explanation of lower cardiovascular morbidity and mortality in Hispanic patients with CKD, including the possible roles of novel cardiovascular risk factors, inflammatory markers, thrombogenic factors, and adipocytokines.

Our study has certain limitations. This cohort only includes Hispanic patients in northern California. Although data from the US Census Bureau show that the Hispanic population in northern California is closely representative of the overall US Hispanic population (6), our findings should be confirmed in other Hispanic subgroups. In addition, Hispanic individuals may not represent a homogeneous group. Differential incidence, severity of disease, and response to treatment have been observed in cardiovascular disease and asthma for different Hispanic subgroups, depending on national origin (31,32). Future studies that further subdivide this population using genetic admixture or country of origin might better discern the subgroups within Hispanic ethnicity that are at highest risk. Ascertaining the occurrence of death using the California death certificate registry and Social Security Administration files may be incomplete. Although our study did control for time-updated comorbidities as well as longitudinal medical therapy, we did not have information on other potential confounders such as alcohol use, smoking, BP control, dietary and physical activity patterns, and body mass index. Finally, given our study design, we cannot determine the specific mechanisms for the observed variation in outcomes.

Conclusion

Within a large cohort of patients with stage 3 or 4 CKD, Hispanic patients experienced higher rates of progression to ESRD but lower rates of cardiovascular events and death compared with non-Hispanic white patients after adjustment for potential confounders. Future studies are needed to examine potential pathways that mediate the excess ESRD risk to delineate effective prevention strategies within the rapidly growing Hispanic population.

Acknowledgments

This study was supported by National Institute of Diabetes and Digestive and Kidney Diseases grants R01 DK58411 and UO1 DK60902.

References

1. Benabe JE, Rios EV: Kidney disease in the Hispanic population: Facing the growing challenge. *J Natl Med Assoc* 96: 789–798, 2004
2. Hsu CY, Vittinghoff E, Lin F, Shlipak MG: The incidence of end-stage renal disease is increasing faster than the prevalence of chronic renal insufficiency. *Ann Intern Med* 141: 95–101, 2004
3. Hsu CY, Lin F, Vittinghoff E, Shlipak MG: Racial differences in the progression from chronic renal insufficiency to end-stage renal disease in the United States. *J Am Soc Nephrol* 14: 2902–2907, 2003
4. Pugh JA, Stern MP, Haffner SM, Eifler CW, Zapata M: Excess incidence of treatment of end-stage renal disease in Mexican Americans. *Am J Epidemiol* 127: 135–144, 1988
5. US Renal Data System: *USRDS 2004 Annual Data Report: Atlas of End-Stage Renal Disease in the United States*, Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2004
6. US Census Bureau: Available: http://www.census.gov/Press-Release/www/2002/demoprofiles.htm. Accessed September 15, 2005
7. Karter AJ, Ferrara A, Liu JY, Moffet HH, Ackerson LM, Selby JV: Ethnic disparities in diabetic complications in an insured population. *JAMA* 287: 2519–2527, 2002
8. Young BA, Maynard C, Boyko EJ: Racial differences in diabetic nephropathy, cardiovascular disease, and mortality in a national population of veterans. *Diabetes Care* 26: 2392–2399, 2003
9. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 351: 1296–1305, 2004
10. Rewers M, Shetterly SM, Hoag S, Baxter J, Marshall J, Hamman RF: Is the risk of coronary heart disease lower in Hispanics than in non-Hispanic whites? The San Luis Valley Diabetes Study. *Ethn Dis* 3: 44–54, 1993
11. Sorlie PD, Backlund E, Johnson NJ, Rogot E: Mortality by Hispanic status in the United States. *JAMA* 270: 2464–2468, 1993
12. Liao Y, Cooper RS, Cao G, Kaufman JS, Long AE, McGee DL: Mortality from coronary heart disease and cardiovascular disease among adult US Hispanics: Findings from the National Health Interview Survey (1986 to 1994). *J Am Coll Cardiol* 30: 1200–1205, 1997
13. Hunt KJ, Resendez RG, Williams K, Haffner SM, Stern MP, Hazuda HP: All-cause and cardiovascular mortality among Mexican-American and non-Hispanic white older participants in the San Antonio Heart Study: Evidence against the "Hispanic paradox." *Am J Epidemiol* 158: 1048–1057, 2003
14. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G: National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Ann Intern Med* 139: 137–147, 2003
15. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D: A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 130: 461–470, 1999
16. Stewart SL, Swallen KC, Glaser SL, Horn-Ross PL, West DW: Comparison of methods for classifying Hispanic ethnicity in a population-based cancer registry. *Am J Epidemiol* 149: 1063–1071, 1999
17. Selby JV, Ray GT, Zhang D, Colby CJ: Excess costs of medical care for patients with diabetes in a managed care population. *Diabetes Care* 20: 1396–1402, 1997

18. Go AS, Hylek EM, Chang Y, Phillips KA, Henault LE, Capra AM, Jensvold NG, Selby JV, Singer DE: Anticoagulation therapy for stroke prevention in atrial fibrillation: How well do randomized trials translate into clinical practice? *JAMA* 290: 2685–2692, 2003
19. Arellano MG, Petersen GR, Petitti DB, Smith RE: The California Automated Mortality Linkage System (CAMLIS). *Am J Public Health* 74: 1324–1330, 1984
20. Therneau TM, Grambsch PM: Modeling survival data: Extending the Cox model. In: *Statistics for Biology and Health*, edited by Dietz KGM, Krickeberg K, Tsiatis A, Samet J, New York, Springer-Verlag, 2000, pp 228–229
21. Coresh J, Byrd-Holt D, Astor BC, Briggs JP, Eggers PW, Lacher DA, Hostetter TH: Chronic kidney disease awareness, prevalence, and trends among US adults, 1999 to 2000. *J Am Soc Nephrol* 16: 180–188, 2005
22. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS: Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 41: 1–12, 2003
23. Baxter J, Hamman RF, Lopez TK, Marshall JA, Hoag S, Swenson CJ: Excess incidence of known non-insulin-dependent diabetes mellitus (NIDDM) in Hispanics compared with non-Hispanic whites in the San Luis Valley, Colorado. *Ethn Dis* 3: 11–21, 1993
24. Marshall JA, Hamman RF, Baxter J, Mayer EJ, Fulton DL, Orleans M, Rewers M, Jones RH: Ethnic differences in risk factors associated with the prevalence of non-insulin-dependent diabetes mellitus. The San Luis Valley Diabetes Study. *Am J Epidemiol* 137: 706–718, 1993
25. Garza R, Medina R, Basu S, Pugh JA: Predictors of the rate of renal function decline in non-insulin-dependent diabetes mellitus. *Am J Nephrol* 17: 59–67, 1997
26. Chiapella AP, Feldman HI: Renal failure among male Hispanics in the United States. *Am J Public Health* 85: 1001–1004, 1995
27. Lindeman RD, Romero L, Liang HC, Hundley R, Baumgartner R, Koehler K, Garry P: Prevalence of proteinuria/microalbuminuria in an elderly urban, biethnic community. *Geriatr Nephrol Urol* 8: 123–130, 1998
28. Swenson CJ, Trepka MJ, Rewers MJ, Scarbro S, Hiatt WR, Hamman RF: Cardiovascular disease mortality in Hispanics and non-Hispanic whites. *Am J Epidemiol* 156: 919–928, 2002
29. Pugh JA, Tuley MR, Basu S: Survival among Mexican-Americans, non-Hispanic whites, and African-Americans with end-stage renal disease: The emergence of a minority pattern of increased incidence and prolonged survival. *Am J Kidney Dis* 23: 803–807, 1994
30. Patel KV, Eschbach K, Ray LA, Markides KS: Evaluation of mortality data for older Mexican Americans: Implications for the Hispanic paradox. *Am J Epidemiol* 159: 707–715, 2004
31. Hunt KJ, Williams K, Resendez RG, Hazuda HP, Haffner SM, Stern MP: All-cause and cardiovascular mortality among diabetic participants in the San Antonio Heart Study: Evidence against the "Hispanic paradox." *Diabetes Care* 25: 1557–1563, 2002
32. Burchard EG, Avila PC, Nazario S, Casal J, Torres A, Rodriguez-Santana JR, Toscano M, Sylvia JS, Alioto M, Salazar M, Gomez I, Fagan JK, Salas J, Lilly C, Matallana H, Ziv E, Castro R, Selman M, Chapela R, Sheppard D, Weiss ST, Ford JG, Boushey HA, Rodriguez-Cintron W, Drazen JM, Silverman EK: Lower bronchodilator responsiveness in Puerto Rican than in Mexican subjects with asthma. *Am J Respir Crit Care Med* 169: 386–392, 2004