Risk for Progression to ESRD: Further Evidence from Population-Based Studies

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Editors Note: The classification of degrees of renal dysfunction into stages of chronic kidney disease (CKD) and the consequent appreciation of its high prevalence, around 10% in most population studies, has transformed clinical nephrology from its traditional focus on ESRD prevalent in the late 20th century to a new and much broader approach in the early 21st century. The recognition of the striking association of CKD with cardiovascular disease has made the prevalence, around 10% in most population studies, has transformed clinical nephrology from its traditional focus on ESRD prevalent in the late 20th century to a new and much broader approach in the early 21st century. The recognition of the striking association of CKD with cardiovascular disease has made the prevalence, around 10% in most population studies, has transformed clinical nephrology from its traditional focus on ESRD prevalent in the late 20th century to a new and much broader approach in the early 21st century. The recognition of the striking association of CKD with cardiovascular disease has made the prevalence, around 10% in most population studies, has transformed clinical nephrology from its traditional focus on ESRD prevalent in the late 20th century to a new and much broader approach in the early 21st century. The recognition of the striking association of CKD with cardiovascular disease has made the

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tudies that compare the prevalence and the outcomes of diseases between population groups are standard epidemiologic tools that are used to identify population-to-population variations in disease patterns, which, in turn, suggest testable genetic, environmental, behavioral, and social system hypotheses that might explain the observed differences. Cardiovascular disease epidemiology is especially rich in these comparative studies, and notable examples include the Pooling Project Research Group report, the Seven Countries Heart Study, the Ni-Ho-San Heart Study, and the World Health Organization Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) heart study (1–4). The growing availability of population-based disease registries that capture information on the incidence and outcomes of stage 5-D chronic kidney disease (CKD) offer a similar opportunity for studying the epidemiology of ESRD.

The essential observation from comparative studies that use ESRD registry data is the wide population-to-population variability in ESRD occurrence that has engendered a growing awareness that as yet unidentified risk factors must exist to account for the four- to fivefold variation in incidence rates for ESRD (5). Recent studies from national and regional ESRD registries that illustrate this approach have demonstrated substantial heterogeneity in the rise in all-cause (6) and diabetes-ESRD (7) incidence rates across European countries; the potential role of regional differences in hypertension, diabetes, and vascular disease in the variations in ESRD occurrence (8); and variations in the risk for diabetic ESRD between European and non-European populations.

The study by Hallan et al. in this issue of JASN (9) uses this approach in a novel way to address the problem of population-to-population variations in risk for ESRD. They asked the conceptually straightforward question of how much of this variability might be attributed to differences in the prevalence of earlier stages of kidney disease. They report the results from a population-based cross-sectional study that was conducted in Norway from 1995 to 1997 and examined the prevalence of CKD and risk for progression to ESRD compared with white individuals in the United States.

Their analyses not only used national ESRD registry data to estimate ESRD incidence rates of the two populations but also used results from a large health survey in central Norway and the United States National Health and Nutrition Examination Surveys to estimate prevalence rates for CKD in the two populations. Serum creatinine levels were calibrated to the same standard in both countries, and the GFR was estimated by the Modification of Diet in Renal Disease (MDRD) equation. These estimates, in turn, were used to calculate ESRD incidence rates for individuals with stages 3 to 4 CKD within the respective populations.

There was no significant difference in the prevalence of CKD when comparing Norwegians with US white individuals. In contrast, the risk for incident ESRD among US white individuals with stages 3 to 4 CKD was 2.5-fold greater compared with that of Norwegians. This finding remained significant after adjustment for age, gender, and diabetes. These disparities persisted among both populations with and without diabetes, older and younger individuals, and within both genders.

The observations by Hallan et al. (9) are consistent with similar ecologic studies within the US population that suggest that certain populations may have a greater rate of progression to ESRD (10), and they bring attention to the factors that may explain differences in ESRD incidence. Factors that are discussed by the authors include potential misclassification of incident ESRD as a result of incomplete capture of incident ESRD cases because of differences in acceptance rates, misestimation of prevalent CKD attributable to the MDRD equation, and differences in survival rates or risk for progression to ESRD among individuals with the same degree of CKD.

A provocative possibility that is raised by their observations is that...
differences in health care access and systems between Norway and the United States might be a major contributor to the differences in ESRD. Health care is free for all Norwegians, and clinical parameters that indicate quality of predialysis care were included in the current report. These differences manifest as earlier nephrology referral and a significantly greater number of predialysis nephropathy visits compared with US white patients. Norwegians also were more likely to receive a renal transplant than to initiate dialysis compared with US white patients. An increased frequency of erythropoietin administration, higher levels of serum albumin and hemoglobin at the time of dialysis initiation, and the presence of early arteriovenous fistula creation were found among Norwegian compared with US white patients.

Also, important socioeconomic differences that are found between Norwegians and US white patients may contribute to the observed differences in progression to ESRD. Fewer Norwegians were below the poverty level, none was without health insurance, and fewer lacked functional literacy. The presence of poverty is associated with an increased risk for proteinuria and CKD (11,12).

A life-course approach to the initiation and progression of CKD (13) is useful in generating hypotheses as to how differences in access to health care and less poverty might modify the development and progression of kidney disease. It is possible that socioeconomic factors and access to health care may contribute to differences in early life exposures that influence fetal development and low birth weight (14), as well as childhood growth patterns that contribute to the emergence of chronic diseases such as hypertension (15,16) and diabetes (17,18) that initiate and promote progressive kidney injury. Similarly, population-to-population differences during early adulthood in the detection and management of risk factors that are associated with progression to ESRD later in life, including diabetes, hypertension, dietary protein consumption, smoking, and nephroprotein exposure, likely are influenced by differences in access to health care and less poverty.

It should be emphasized that these and other possibilities are not explanations for the results reported by Hallan et al. (9) but are testable hypotheses that arise from this important ecologic study. Although this study extends findings from previous analyses, further study is needed to address disparities in health care access, quality of care, and clinical outcomes that are observed among different ethnic populations to identify mechanisms for these differences and develop effective interventions.

References

1. Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events: Final report of the pooling project. The pooling project research group. J Chronic Dis 31: 201–206, 1978


