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ORIGINAL ARTICLE

End-Stage Renal Disease and Mortality Outcomes Across Different Glomerulonephropathies in a Large Diverse US Population

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Abstract

Objective: To compare renal function decline, incident end-stage renal disease (ESRD), and mortality among patients with 5 common glomerular diseases in a large diverse population.

Patients and Methods: A retrospective cohort study (between January 1, 2000, and December 31, 2011) of patients with glomerulonephropathy using the electronic health record of an integrated health system was performed. Estimated glomerular filtration rate (eGFR) change, incident ESRD, and mortality were compared among patients with biopsy-proven focal segmental glomerulosclerosis (FSGS), membranous glomerulonephritis (MN), minimal change disease (MCD), immunoglobulin A nephropathy (IgAN), and lupus nephritis (LN). Competing risk models were used to estimate hazard ratios for different glomerulonephropathies for incident ESRD, with mortality as a competing outcome after adjusting for potential confounders.

Results: Of the 2350 patients with glomerulonephropathy (208 patients [9%] younger than 18 years) with a mean follow-up of 4.5±3.6 years, 497 (21%) progressed to ESRD and 195 (8%) died before ESRD. The median eGFR decline was 1.0 mL/min per 1.73 m^2 per year but varied across different glomerulonephropathies ($P<.001$). The highest ESRD incidence (per 100 person-years) was observed in FSGS 8.72 (95% CI, 3.93-16.72) followed by IgAN (4.54; 95% CI, 1.37-11.02), LN (2.38; 95% CI, 0.37-7.82), MN (2.15; 95% CI, 0.29-7.46), and MCD (1.67; 95% CI, 0.15-6.69). Compared with MCD, hazard ratios (95% CIs) for incident ESRD were 3.43 (2.32-5.08) and 2.35 (1.46-3.81), 1.28 (0.79-2.07), and 1.02 (0.62-1.68) for FSGS, IgAN, LN, and MN, respectively. No significant association between glomerulonephropathy types and mortality was detected ($P=.24$).

Conclusion: Our findings from a real-world clinical environment revealed significant differences in eGFR decline and ESRD risk among patients with 5 glomerulonephropathies. These variations in presentation and outcomes warrant different management strategies and expectations.

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Glomerulonephropathies (GNs) account for the third most common cause of end-stage renal disease (ESRD) in the United States, accounting for 20% to 30% of the population with prevalent ESRD.[1,2] Thus, they are responsible for a large portion of the $32 billion spent annually on ESRD care in the United States.[2] In addition, mortality rates have been described to be 3- to 4-fold higher in people with GN than in people without kidney disease.[3] Overall, the incidence of GNs has increased to rates as high as 2.5 cases per 100,000 person-years in the general population.[2,4-6]

Although GNs are often referred to as a single clinical entity, the challenge lies in the fact that the term GN encompasses many different disease entities.[7] The prognoses and rates of progression to ESRD and mortality in people with different GNs are variable even within specific GN types. Morbidity and mortality are substantially higher in patients with GN than in the general population.[3,8,9] The etiology of, and histological

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variations in, specific GN subtypes lend to distinct clinical courses and renal outcomes.[6,10] Thus, there appears to be considerable variation in risk of ESRD and mortality. However, the sparse information on how people with different GNs compare in terms of renal and mortality outcomes has been based on smaller study populations from tertiary care centers and therefore may not be representative.[6,8,10-12]

We sought to overcome these potential limitations by using an electronic health record (EHR) approach to compare the rate of renal function decline, ESRD, and mortality among patients with 5 common biopsy-proven GNs (focal segmental glomerulosclerosis [FSGS], membranous glomerulonephritis [MN], minimal change disease [MCD], immunoglobulin A nephropathy [IgAN], and lupus nephritis [LN]) in a large diverse US population.

PATIENTS AND METHODS

We retrospectively identified a cohort of Kaiser Permanente Southern California (KPSC) members enrolled between January 1, 2000, and December 31, 2011. Kaiser Permanente Southern California is a prepaid integrated health system providing comprehensive care to more than 4.2 million members throughout Southern California and comprises 15 medical centers and more than 200 satellite clinics. The membership population is racially, ethnically, and socioeconomically diverse, reflecting the general population of Southern California.[13] All KPSC members have similar benefits and access to health care services, clinic visits, procedures, and co-pays for medications. Complete health care encounters are tracked using a common EHR from which study information was extracted. The Department of Research & Evaluation extracts these data for a research database. Enrollment and disenrollment information was obtained from membership records. The study was approved by the KPSC Institutional Review Board (#5815) and exempted from informed consent.

Details of the KPSC population with GN have been previously published[5] The study population included members with continuous membership between January 1, 2000, and December 31, 2011, who underwent native renal biopsy. Individual paper and EHR chart reviews were performed to identify and categorize biopsy findings and diagnoses. For individuals who underwent multiple biopsies, the first biopsy result was used. We included the 5 most common GNs in the study: FSGS, MN, MCD, IgAN, and LN. The date of renal biopsy was used as the index date (baseline) for the start of follow-up. A minimum of 6 months of continuous membership in KPSC before renal biopsy was required to reliably capture comorbidities at baseline.

Individuals who did not have a creatinine measurement within 60 days of their index date and renal transplant biopsies were excluded. Individuals actively treated with dialysis or having any history of treatment with hemodialysis, peritoneal dialysis, or renal transplant were also excluded. Individuals diagnosed with a GN other than the 5 targeted conditions or had incident ESRD before the index date were also excluded.

Renal Biopsies at KPSC

The complete renal biopsy information was obtained from biopsies performed in routine clinical practice. The indications for biopsy were clinically determined by individual practitioners and performed in both the inpatient and outpatient settings with nearly all biopsies occurring at a KPSC medical center.[14] Although 3% of renal biopsies are performed at non-KPSC facilities, all specimens are subsequently transferred to KPSC. All samples in KPSC and from non-KPSC facilities are received at the Kaiser Permanente Regional Laboratory in North Hollywood, California, for processing and preparation. Specimens are prepared separately in hematoxylin-eosin, Masson trichrome, periodic acid—Schiff, and Jones methenamine silver stains for light microscopy examination. Immunofluorescence techniques and electron microscopy are also performed on each specimen. Once prepared, all samples are sent to Kaiser Permanente Los Angeles Medical Center for review and interpretation by 2 renal pathologists. Each pathologist reviews the specimens separately, and final diagnoses are determined after a consensus is reached by the 2 renal pathologists.

Renal biopsy results were extracted by chart review performed by 4 research associates. The results were categorized on the basis of the primary diagnoses noted on the original pathology report. Both a

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