



Medical costs in the peridiagnosis period of various biopsy-confirmed kidney diseases in South Korea

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Background: In-depth investigation is imperative to scrutinize medical costs associated with the periods before and after biopsies for diverse kidney diseases in South Korea. Long-term epidemiological data, including follow-up information, is essential for comparing risks linked to various kidney diseases and their adverse outcomes.

Methods: Patients diagnosed with glomerulonephritis (GN), tubulointerstitial nephritis (TIN), and acute tubular necrosis (ATN) at Seoul National University Hospital between 2012 and 2018 were included. We linked the prospective cohort data of biopsy-confirmed kidney disease patients (KORNERSTONE) from our study hospital to the national claims database of Korea, covering both medical events and insured costs. We analyzed medical costs during the periods before and after kidney biopsies, categorized by specific diagnoses, and delved into adverse prognostic outcomes.

Results: Our study involved 1,390 patients with biopsy-confirmed GN, TIN, and ATN. After diagnosis, monthly average medical costs increased for most kidney diseases, excluding membranous nephropathy, Henoch-Schönlein purpura, and amyloidosis. The most substantial yearly average medical cost increase was observed in the ATN, acute TIN (ATIN), and chronic TIN (CTIN) groups. Costs rose for most kidney disease categories, except for amyloidosis. Higher myocardial infarction, stroke, and death rates were noted in CTIN, ATIN, and ATN compared to other types, with lupus nephritis displaying the highest end-stage kidney disease progression rate.

Conclusion: In South Korea, medical costs for the majority of GN, TIN, and ATN patients increased following kidney biopsy diagnosis. This current data provides valuable epidemiological insights into the medical costs and prognosis of various kidney diseases in the country.

Keywords: Acute tubular necrosis, Glomerulonephritis, Medical cost, National Health Insurance Service, Postdiagnosis, Prediagnosis, Tubulointerstitial nephritis

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Introduction

Glomerulonephritis (GN), tubulointerstitial nephritis (TIN), and acute tubular necrosis (ATN) are disease categories with a significant socioeconomic burden worldwide [1–3]. These are a major cause of chronic kidney disease, severely affecting patients' quality of life and increasing the risk of kidney failure. Prompt treatment strategies for these diseases have been extensively researched because early management may prevent disease progression [2,4,5].

However, limited research has focused on the medical costs associated with these diseases before and after the diagnosis [6]. Given the rapidly aging population in South Korea, the proportion of unemployed or elderly patients with these diseases has increased, leading to a growing medical cost burden on the National Health Insurance Service (NHIS) [7]. Consequently, understanding the current economic burden on the health insurance system for these kidney diseases is crucial for preparedness in addressing future national medical cost challenges, with a specific focus on individual diseases and the time periods before and after the diagnosis [8–10]. Moreover, data on the major health outcomes including cardiovascular events, end-stage kidney disease (ESKD), and mortality can provide valuable epidemiological information to estimate the future socioeconomic burden associated with these diseases [11,12].

This study aimed to provide a comprehensive summary of the medical costs incurred by the health insurance system for GN, ATN, and TIN, as well as to gather epidemiological data on the associated major health outcomes. Leveraging the NHIS system of South Korea, which provides access to complete claims data that can be linked to in-hospital electronic health records, we connected data from a tertiary hospital, specifically from the largest biopsy-confirmed kidney disease prospective cohort known as Korea Renal Biobank Network System Toward Next-Generation Analysis (KORNERSTONE) [13], with the claims data. Our hypothesis revolved around the potential differences in medical fees before and after definitively diagnosing various kidney diseases, and their impact on major health outcomes.

Methods

Ethical considerations

This multicenter prospective cohort study focusing on various glomerular diseases in South Korea was reviewed and approved by the Institutional Review Board of Seoul National University Hospital in Korea (No. 2105-100-1219). The linkage and the use of the NHIS database was approved by the government organization (NHIS-2022-9-007). This study was conducted in accordance with the principles of the Declaration of Helsinki. Participants from the KORNERSTONE prospective cohort provided written informed consent to participate.

Study setting and population

KORNERSTONE, supported by the Korea Disease Control and Prevention Agency, is a prospective multicenter biobank for glomerular diseases in South Korea [13]. From this biobank, we identified patients with biopsy-confirmed kidney disease from one of the nation's largest tertiary hospitals, Seoul National University Hospital. Most study participants had primary GN, such as immunoglobulin A nephropathy (IgAN) and membranous nephropathy, whereas some had secondary kidney diseases, such as TIN or amyloidosis. We included patients with biopsy-confirmed kidney disease diagnosed between 2012 and 2018.

We initially screened 1,814 patients with available data during that period, and kidney disease groups with fewer than 20 cases were excluded because of concerns related to anonymization during database linkage. Patients without health insurance records from 2012 to 2018 and those with an unclear relationship between the disease and the diagnosis date were also excluded. Ultimately, we included 1,390 GN, ATN, and TIN patients (Fig. 1).

Medical costs were calculated across all departments, and the total medical costs for each kidney disease were averaged.

Data collection: the KORNERSTONE database

We included laboratory variables obtained from the in-hospital database, such as body mass index (BMI), creatinine (mg/ dL), estimated glomerular filtration rate

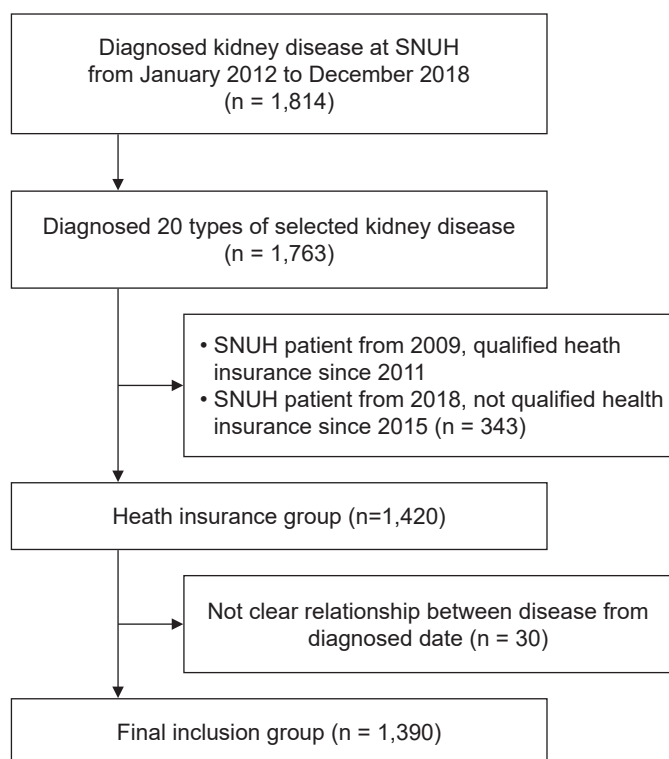


Figure 1. Inclusion criteria.

SNUH, Seoul National University Hospital.

(eGFR) calculated by the Chronic Kidney Disease Epidemiology Collaboration equation, and the random urine protein/creatinine ratio (mg/dL). Additionally, information on underlying diseases such as hypertension and diabetes mellitus was obtained. The primary diagnosis was determined by kidney biopsy, which included IgAN, focal segmental glomerulosclerosis, acute TIN (ATIN), chronic TIN (CTIN), membranous nephropathy, lupus nephritis, crescentic GN, minimal change disease, hypertensive nephropathy, diabetic mellitus nephropathy, mesangial proliferative GN, thin basement membrane disease, ATN, amyloidosis, nonspecific changes, membranoproliferative GN, and Henoch-Schönlein purpura. Using the KORNER-STONE database, we did not need to match specific billing codes for each type of kidney disease additionally.

Data collection: the National Health Insurance Service database

From the NHIS database, we collected the baseline characteristics of the study population at the time of diagnosis

of the diseases. We included age, sex, economic grade, disability status, health insurance status, and a history of hypertension, diabetes mellitus, or dyslipidemia. The economic grade was categorized into four groups based on quantiles related to health insurance fees, which were determined by individuals' income and assets. The health insurance aid status was classified into three groups based on enrollment status in the health insurance system: employed, non-employed, and aided. The aided group comprised low-income individuals registered by government organizations who had received specific medical insurance coverage.

Linkage of the databases

Following approval by the two constitutional groups, we conducted a pseudonymization process and de-identified the data in collaboration with a third-party group that generated a linkage key. The NHIS extracts relevant claims information using these keys. To preserve the de-identification of the data, we only accessed and extracted study results from the securely maintained NHIS analysis center. The detailed data flow was closely monitored by the overseeing organizations.

Outcome variables

Because the national claims database contains comprehensive claims data, health outcomes can be identified using established definitions. Adverse prognostic outcomes examined in this study included myocardial infarction (MI), stroke, death, and progression of kidney dysfunction to ESKD. We defined MI based on the International Classification of Diseases 10th revision codes I21 or I22, and stroke was defined as I63 or I64, confirmed through brain magnetic resonance imaging or brain computed tomography imaging [14]. ESKD was defined as the need for maintenance kidney replacement therapy, including dialysis or transplantation. Mortality outcomes were identified from the death registry, which collects information from death certificates.

Statistical analysis

We presented descriptive information on medical costs

using data from the NHIS Center. In terms of major health outcomes, we provided epidemiological statistics, including total outcomes during the follow-up period and person-year incidence rates. Cox regression analysis was performed for a basic comparison of health outcome risks. A multivariable model was constructed, adjusting for age and sex to account for confounding effects related to basic demographic information. Statistical analyses were performed using SAS version 9.4 (SAS Institute). All medical costs are presented in US dollars (\$), calculated at a currency exchange rate of \$1 to 1,296.50 Korean won as of November 19, 2023.

Results

Baseline characteristics

The baseline patient characteristics are summarized in [Table 1](#). The largest patient group had IgAN ($n = 432$), followed by those with membranous nephropathy ($n = 146$), focal segmental glomerulosclerosis ($n = 90$), minimal change disease ($n = 89$), and lupus nephritis ($n = 87$). The majority of the patients were aged 40 to 60 years. Approximately 50% of the patients were classified as unemployed, and the low-income grade was most frequently observed. Before renal biopsy diagnosis, approximately half of the patients had a history of hypertension. The status of kidney function parameters varies depending on the specific diagnosis.

Medical costs of glomerulonephritis patients

Crescentic GN had the lowest monthly and yearly average medical costs, whereas ATN had the highest medical costs, both individually and within the categorized groups ([Figs. 2, 3](#); [Supplementary Table 1](#), available online).

In general, the average insurance burden on medical costs increased after the establishment of a diagnosis for most of the included kidney diseases except for membranous nephropathy, Henoch-Schönlein purpura, and amyloidosis. These three disease types showed decreased medical costs after the diagnosis.

Specifically, the medical costs related to ATN were the highest before and after the diagnosis (\$353.7 and \$482.5, respectively), whereas crescentic GN had the lowest medi-

cal costs before and after the diagnosis (\$112.7 and \$151.7, respectively). The most significant difference in pre- and postdiagnosis medical costs was observed in patients diagnosed with ATIN ([Fig. 2](#)), as the costs increased substantially after the diagnosis.

When grouped within similar disease categories and analyzed by the annual health insurance medical costs, annual medical costs increased in most categories of kidney diseases, except for amyloidosis. The annual medical costs associated with CTIN, ATIN, and ATN sharply increased annually (\$2,754.52, \$3,514.17, and \$4,769.91, respectively) after establishment of the diagnosis by kidney biopsy.

However, amyloidosis patients had the highest pre-diagnostic yearly medical costs among the categorized GN groups. However, after the diagnosis, medical costs decreased every year (\$3,792.92, \$2,762.46, and \$2,079). Crescentic GN exhibited the lowest pre- and postdiagnosis yearly medical costs (\$1,343.55 and \$1,991.96 before the diagnosis, \$2,077.84 after the diagnosis), while lupus nephritis medical costs increased after the diagnosis but declined after 2 years ([Fig. 3](#)).

Adverse outcomes in glomerulonephritis patients

Adverse prognostic outcomes for the categorized groups of kidney diseases yielded diverse results ([Table 2](#)). The group comprising CTIN, ATIN, and ATN patients had the highest rates of MI or stroke and death, with an incidence rate of 0.027 per 1,000 for MI or stroke and 0.018 for death. The highest incidence of ESKD was observed in the focal segmental glomerulosclerosis group, with an incidence rate of 0.047 per 1,000. Conversely, the crescentic GN group had the lowest prevalence of MI or stroke, with an incidence rate of 0.010 per 1,000. The lowest mortality risk was observed in patients diagnosed with membranous nephropathy, with an incidence rate of 0.006 per 1,000. The lowest incidence was observed in patients diagnosed with amyloidosis, with an incidence rate of 0.017 per 1,000. These results remained consistent even after adjusting for age and sex between the groups (Model 2). The crescentic GN and minimal change disease groups exhibited lower incidence rates of MI or stroke and death compared to those observed in the reference group. The membranous nephropathy group also showed a lower incidence of death than that observed in the reference group. The amyloidosis

Table 1. Baseline characteristics of all GN patients from 2012 to 2018 (n = 1,390)

Characteristic	IgAN	FSGS	CTIN	MN	LN	Crescentic GN	MCD	HTN	ATIN	Non-specific change	MPGN	Others	HSP	DMN	MesPGN	TBM	ATN	Amyloidosis
No. of subjects	432	90	49	146	87	47	89	43	55	68	46	61	17	107	20	24	15	24
Age (yr)																		
<40	58 (13.4)	13 (14.4)	6 (12.2)	21 (14.4)	9 (10.3)	9 (19.1)	16 (18.0)	3 (7.0)	8 (14.5)	8 (11.8)	5 (10.9)	7 (11.5)	2 (11.8)	11 (10.3)	2 (10.0)	3 (12.5)	3 (20.0)	4 (16.7)
40-60	224 (51.9)	56 (62.2)	23 (46.9)	68 (31.5)	48 (55.2)	29 (61.7)	51 (57.3)	19 (44.2)	25 (45.5)	40 (58.8)	21 (45.7)	33 (54.1)	11 (64.7)	54 (50.5)	11 (55.0)	11 (45.8)	5 (33.3)	15 (62.5)
≥70	150 (34.7)	21 (23.3)	20 (40.8)	57 (26.7)	30 (34.5)	9 (19.1)	22 (24.7)	21 (48.8)	22 (40.0)	20 (29.4)	20 (43.5)	21 (34.4)	4 (23.5)	42 (39.3)	7 (35.0)	10 (41.7)	7 (46.7)	5 (20.8)
Male sex	204 (47.2)	57 (63.3)	28 (57.1)	86 (39.7)	14 (16.1)	23 (48.9)	50 (56.2)	27 (62.8)	31 (56.4)	37 (54.4)	30 (65.2)	28 (45.9)	8 (47.1)	71 (66.4)	10 (50.0)	7 (29.2)	8 (53.3)	9 (37.5)
Income grade ^a																		
Q1	103 (23.8)	20 (22.2)	10 (20.4)	36 (16.4)	20 (23.0)	9 (19.1)	20 (22.5)	10 (23.3)	11 (20.0)	19 (27.9)	10 (21.7)	14 (23.0)	5 (29.4)	20 (18.7)	5 (25.0)	5 (20.8)	1 (6.7)	7 (29.2)
Q2	75 (17.4)	16 (17.8)	10 (20.4)	28 (13.0)	9 (10.3)	10 (21.3)	16 (18.0)	6 (14.0)	6 (10.9)	11 (16.2)	7 (15.2)	9 (14.8)	1 (5.9)	18 (16.8)	4 (20.0)	4 (16.7)	4 (26.7)	3 (12.5)
Q3	86 (19.9)	26 (28.9)	13 (26.5)	29 (13.0)	22 (25.3)	10 (21.3)	21 (23.6)	13 (30.2)	12 (21.8)	12 (17.6)	13 (28.3)	17 (27.9)	3 (17.6)	22 (20.6)	6 (30.0)	5 (20.8)	3 (20.0)	4 (16.7)
Q4	168 (38.9)	28 (31.1)	16 (32.7)	53 (24.3)	36 (41.4)	18 (38.3)	32 (36.0)	14 (32.6)	26 (47.3)	26 (38.2)	16 (34.8)	21 (34.4)	8 (47.1)	47 (43.9)	5 (25.0)	10 (41.7)	7 (46.7)	10 (41.7)
Insurance aid																		
Non-employed	250 (57.9)	44 (48.9)	26 (53.1)	86 (39.7)	38 (43.7)	27 (57.4)	51 (57.3)	24 (55.8)	31 (56.4)	31 (45.6)	25 (54.3)	32 (52.5)	11 (64.7)	55 (51.4)	9 (45.0)	15 (62.5)	10 (66.7)	12 (50.0)
Employed	158 (36.6)	42 (46.7)	21 (42.9)	51 (23.5)	42 (48.3)	18 (38.3)	33 (37.1)	16 (37.2)	21 (38.2)	32 (47.1)	17 (37.0)	27 (44.3)	4 (23.5)	48 (44.9)	9 (45.0)	8 (33.3)	5 (33.3)	11 (45.8)
Aided group	24 (5.6)	4 (4.4)	2 (4.1)	9 (4.1)	7 (8.0)	2 (4.3)	5 (5.6)	3 (7.0)	3 (5.5)	5 (7.4)	4 (8.7)	2 (3.3)	2 (11.8)	4 (3.7)	2 (10.0)	1 (4.2)	0 (0.0)	1 (4.2)
Before 1 yr																		
DM	69 (15.9)	17 (18.9)	11 (22.4)	22 (15.1)	15 (17.2)	2 (4.3)	7 (7.9)	6 (14.0)	12 (21.8)	8 (11.8)	8 (17.4)	8 (13.1)	1 (5.9)	11 (10.3)	6 (30.0)	4 (16.7)	2 (13.3)	6 (25.0)
Hypertension	198 (45.8)	47 (52.2)	30 (61.2)	77 (52.7)	40 (46.0)	24 (51.1)	48 (53.9)	22 (51.2)	28 (50.9)	38 (55.9)	24 (52.2)	27 (44.3)	9 (52.9)	66 (61.7)	12 (60.0)	14 (58.3)	10 (66.7)	12 (50.0)
Dyslipidemia	126 (29.2)	26 (28.9)	18 (36.7)	57 (26.0)	32 (36.8)	16 (34.0)	35 (39.3)	14 (32.6)	24 (43.6)	23 (33.8)	17 (37.0)	21 (34.4)	5 (29.4)	35 (32.7)	7 (35.0)	8 (33.3)	9 (60.0)	10 (41.7)
Clinical measurements																		
BMI (kg/m ²)	18 ± 4	20 ± 4	18 ± 5	19 ± 3	17 ± 4	18 ± 4	20 ± 3	21 ± 4	18 ± 4	18 ± 5	19 ± 3	18 ± 3	19 ± 2	20 ± 4	20 ± 5	20 ± 2	20 ± 0	19 ± 4
Creatinine (mg/dL)	1.3 ± 1.2	1.6 ± 1.3	2.7 ± 2.4	0.9 ± 0.5	1.3 ± 1.4	4.2 ± 2.5	1.4 ± 1.5	2.3 ± 1.4	4.0 ± 2.7	0.8 ± 0.2	1.9 ± 1.7	2.1 ± 1.6	1.0 ± 0.6	1.9 ± 1.1	1.2 ± 0.6	0.7 ± 0.2	4.3 ± 3.5	1.0 ± 0.6
eGFR_EPI	78 ± 33	64 ± 33	39 ± 26	86 ± 23	82 ± 40	20 ± 20	79 ± 38	42 ± 26	22 ± 16	104 ± 25	52 ± 29	48 ± 34	85 ± 34	49 ± 28	72 ± 36	106 ± 19	23 ± 16	74 ± 27
Random_urine protein/Cr (mg/dL)	2 ± 9	3 ± 4	1 ± 1	8 ± 30	5 ± 11	3 ± 3	14 ± 25	1.6 ± 1.7	4 ± 21	0.8 ± 1.2	5 ± 6	3 ± 4	2 ± 3	5 ± 5	1 ± 1	0.5 ± 0.6	5 ± 6	8 ± 4

Values are presented as number only, number (%), or mean ± standard deviation.

ATIN, acute tubulointerstitial nephropathy; ATN, acute tubular necrosis; BMI, body mass index; CTIN, chronic tubulointerstitial nephritis; DM, diabetes mellitus; DMN, diabetic mellitus nephropathy; eGFR_EPI, estimated glomerular filtration rate; epidemiology collaboration calculation, mL/min per 1.73 m²; FSGS, focal sclerosis glomerulitis; GN, glomerulonephritis; HSP, Henoch-Schönlein purpura; HTN, hypertensive nephropathy; IgAN, immunoglobulin A nephropathy; LN, lupus nephritis; MCD, minimal change disease; MesPGN, mesangial proliferative GN; MN, membranous nephropathy; MPGN, membranoproliferative GN; TBM, thin basement membrane disease.

^aQ1, 0.25 quantile; Q2, 0.5 quantile; Q3, 0.75 quantile; Q4, 1 quantile.

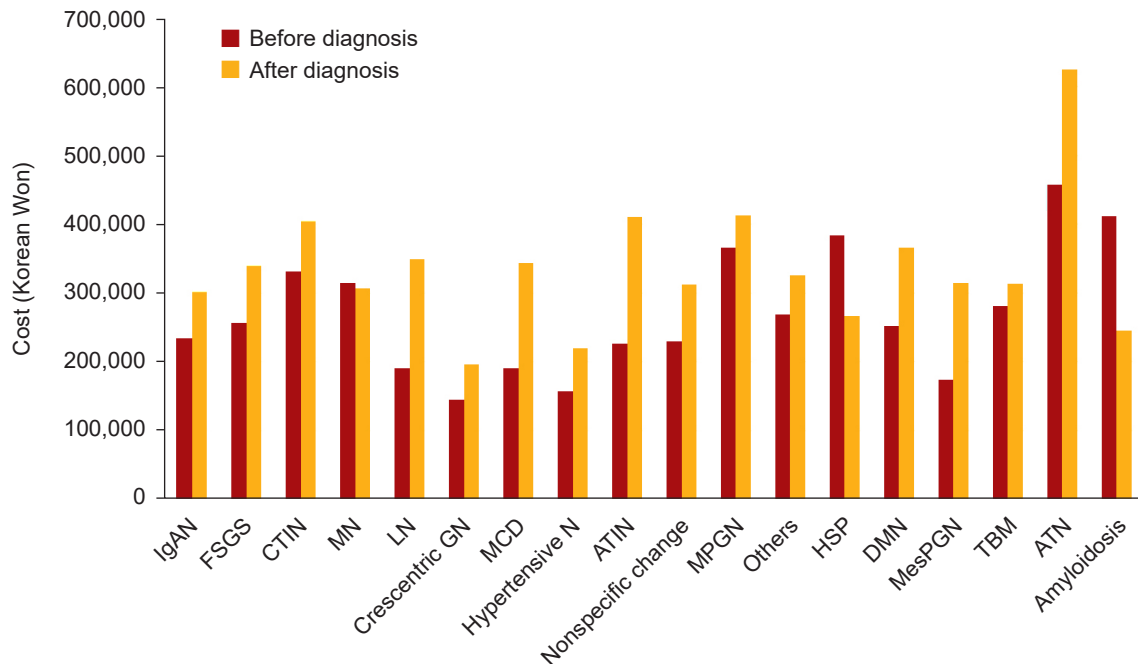


Figure 2. Outpatient and inpatient monthly average medical cost per patient. US dollar 1 equals 1,296.50 Korean won as of November 19, 2023.

ATIN, acute tubulointerstitial nephropathy; ATN, acute tubular necrosis; CTIN, chronic tubulointerstitial nephritis; DMN, diabetic mellitus nephropathy; FSGS, focal sclerosis glomerulitis; GN, glomerulonephritis; HSP, Henoch-Schönlein purpura; IgAN, IgA nephropathy; LN, lupus nephritis; MCD, minimal change disease; MesPGN, mesangial proliferative GN; MPGN, membranoproliferative GN; MN, membranous nephropathy; N, nephropathy; TBM, thin basement membrane disease.

group had the lowest incidence rate, whereas the lupus nephritis group had the highest incidence rate of ESKD. However, owing to the low incidence rates, the regression results did not reach statistical significance. For all outcomes with fewer than 10 cases for each kidney disease, it is advisable to check the confidence interval to assess the uncertainty of results.

Discussion

This study aimed to summarize the current insurance burden related to major GN, TIN, and ATN. We linked one of the largest GN cohorts in the nation, KORNERSTONE [13], with a health claims database and successfully reported the medical costs of biopsy-confirmed kidney diseases. Our study provides important information for shaping future government policies regarding the increasing insurance cost burden in South Korea, especially considering the substantial socioeconomic burden related to chronic

kidney disease.

The link between these two databases was a crucial strength of this study as it included patients with confirmatory diagnoses through kidney biopsies and offered a concise economic burden profile throughout the follow-up period. It illustrated the potential of data linkage to nationwide claims data, which has demonstrated significant strength in many recent medical publications and suggests opportunities for future research in nephrology.

In most of the 20 types of kidney diseases we studied, postdiagnosis medical costs were higher than those in the prediagnosis period. This is understandable because most kidney diseases require additional treatment after the diagnosis of the disease entity [15]. Moreover, some rapidly progressing diseases may require kidney replacement treatments, justifying high medical costs after the diagnosis. However, this may also suggest that prompt diagnoses of various GN and other kidney diseases (such as TIN and ATN) may reduce the economic burden after the confir-

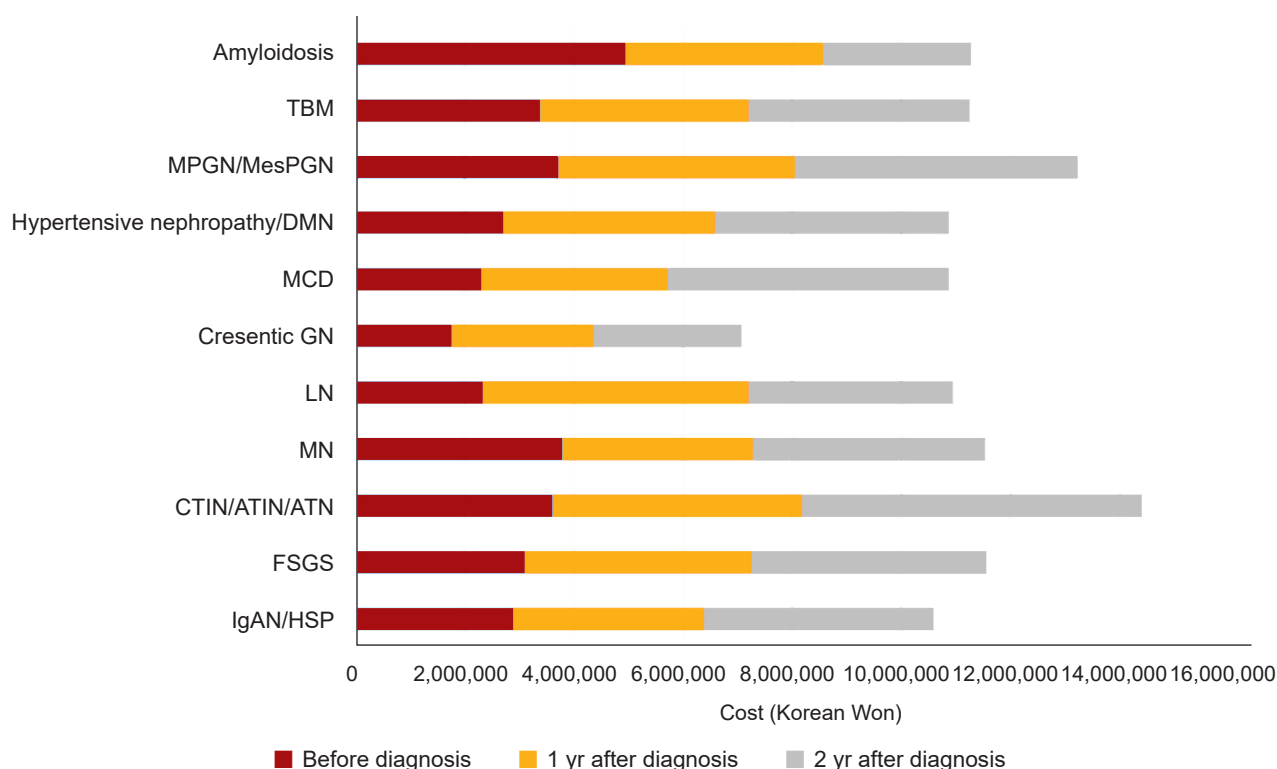


Figure 3. Average yearly medical costs per patient before and after diagnosis in the categorized group. US dollar 1 equals 1,296.50 Korean won as of November 19, 2023.

ATIN, acute tubulointerstitial nephropathy; ATN, acute tubular necrosis; CTIN, chronic tubulointerstitial nephritis; DMN, diabetic mellitus nephropathy; FSGS, focal sclerosis glomerulitis; GN, glomerulonephritis; HSP, Henoch-Schönlein purpura; IgAN, IgA nephropathy; LN, lupus nephritis; MCD, minimal change disease; MesPGN, mesangial proliferative GN; MPGN, membranoproliferative GN; MN, membranous nephropathy; TBM, thin basement membrane disease.

mation of the diagnoses. The enrolled patients had comorbidities requiring lifelong treatments, such as hypertension and diabetes mellitus. Approximately 50% and 10% of the enrolled patients were diagnosed with hypertension and diabetes mellitus, respectively, which may have influenced the expansion of medical costs.

Among the disease types, crescentic GN patients had the lowest average financial burden, whereas those diagnosed with ATN had the highest medical fees. ATN is often associated with critical medical conditions, which may explain why this disease category was associated with the highest medical costs after the diagnosis, given the impending conditions [16]. Conversely, enrolled patients in this study have baseline creatinine levels above 4 mg/dL which means many patients have already experienced irreversible loss of kidney function when crescentic GN is diagnosed [17]. Therefore, further diagnostic evaluation or

treatment beyond kidney replacement therapy was not required, resulting in the lowest total medical cost. The medical costs associated with membranous nephropathy, Henoch-Schönlein purpura, and amyloidosis were lower after the confirmatory diagnoses. These diseases often exhibit typical characteristics that allow for diagnostic confirmation or strong assumptions, even before a kidney biopsy. For example, membranous nephropathy can be diagnosed based on anti-PLA2R antibody titers, Henoch-Schönlein purpura typically presents a characteristic clinical history of lower leg purpura, and amyloidosis is likely accompanied by hematologic abnormalities or abnormal results in protein electrophoresis. Consequently, kidney biopsies for these patients might have been performed for confirmatory purposes and actual diagnostic workups or treatments might have been initiated in the prediagnosis period. This could explain the lower medical costs during the postdiag-

Table 2. Adverse outcome of categorized group

Variable	Subject (n)	MI or stroke (n)	IR (per 1,000)	HR (95% CI)	Death (n)	IR (per 1,000)	HR (95% CI)	ESKD (n)	IR (per 1,000)	HR (95% CI)
IgAN/HSP	439	46	0.016	1 (Reference)	29	0.009	1 (Reference)	63	0.023	1 (Reference)
FSGS	88	10	0.020	1.31 (0.65–2.62)	5	0.009	1.02 (0.39–2.68)	21	0.047	1.89 (1.14–3.13)
CTIN/ATIN/ATN	118	18	0.027	1.84 (1.06–3.19)	12	0.018	1.92 (0.97–3.80)	24	0.040	1.68 (1.04–2.70)
MN	143	15	0.016	1.02 (0.57–1.84)	6	0.006	0.65 (0.27–1.58)	32	0.039	1.64 (1.00–2.51)
Lupus nephritis	85	9	0.018	1.24 (0.60–2.57)	5	0.009	1.09 (0.41–2.86)	19	0.044	2.10 (1.24–3.55)
Crescentic GN	47	3	0.010	0.62 (0.19–2.00)	2	0.007	0.69 (0.16–2.91)	7	0.027	1.15 (0.53–2.53)
MCD	88	8	0.014	0.87 (0.41–1.87)	5	0.009	0.90 (0.34–2.34)	18	0.037	1.55 (0.92–2.63)
Hypertensive nephropathy/DMN	146	18	0.022	1.51 (0.87–2.63)	10	0.011	1.32 (0.63–2.73)	33	0.044	1.85 (1.21–2.84)
MPGN/MesPGN	63	9	0.023	1.54 (0.75–3.16)	6	0.015	1.64 (0.67–3.97)	12	0.034	1.45 (0.70–2.69)
TBM	24	3	0.019	1.11 (0.34–3.59)	2	0.012	1.25 (0.29–5.28)	5	0.035	1.59 (0.64–3.98)
Amyloidosis	22	2	0.017	1.17 (0.28–4.86)	2	0.017	1.90 (0.45–8.04)	2	0.017	0.79 (0.19–3.23)

ATIN, acute tubulointerstitial nephropathy; ATN, acute tubular necrosis; CI, confidence interval; CTIN, chronic tubulointerstitial nephritis; DMN, diabetic mellitus nephropathy; ESKD, end-stage kidney disease; FSGS, focal sclerositis glomerulitis; GN, glomerulonephritis; HSP, Henoch-Schönlein purpura; HR, hazard ratio; IgAN, immunoglobulin A nephropathy; IR, incidence rate; MCD, minimal change disease; MesPGN, mesangial proliferative GN; MN, myocardial infarction; MPGN, membranous nephropathy; MPGN, membranoproliferative glomerulonephritis; TBM, thin basement membrane disease.

All HRs and CIs were adjusted for age and sex.

nosis period.

Also, in this study, we did not include uninsured treatment costs, and we could not analyze specific treatments for each type of kidney disease, which may have affected the medical costs.

Regarding the prognosis of the assessed kidney disease patients, we could not identify a significant difference between the investigated groups due to low statistical power. It is important to note that not only kidney outcomes but also other prognostic outcomes, such as cardiovascular events, and stroke are crucial endpoints in kidney disease patients. Therefore, future multicenter studies recruiting a larger number of patients with biopsy-confirmed kidney diseases may provide valuable nationwide prognostic information. Furthermore, these disease categories were more likely to be associated with critical conditions, including cardiovascular events, such as MI. This is because the pathophysiology of these disease categories is primarily related to renal ischemia, which can lead to cardiac ischemia and ultimately, MI. Cardiogenic and neurologic adverse events can lead to high medical costs due to long-term rehabilitation required after the treatment of acute conditions. To mitigate potential biases, we censored all events at the time of death for cause-specific hazard ratio analysis. Consequently, the impact of competing risks attributable to death is expected to be minimal.

This study had several limitations. First, some remaining kidney disease categories were not assessed in this study. Second, the patients were exclusively enrolled in a single medical center. Third, the study period was limited, which constrained our ability to investigate the temporal trends of the socioeconomic burden of the assessed kidney diseases or to assess the interaction between alterations in baseline socioeconomic status and related medical costs.

Fourthly, the sample size may be insufficient to observe statistically significant differences in patients' outcomes. Lastly, the study only includes patients who underwent kidney biopsy. Thus, common chronic kidney disease patients with metabolic disorders (e.g., diabetic or hypertensive kidney disease) may have different medical costs or prognoses than ours, as the included patients mostly had atypical clinical manifestations that required the biopsies.

In conclusion, this study provided general information on the medical costs and prognosis of GN, ATN, and TIN patients in South Korea. Notably, the postdiagnosis med-

ical costs were higher than those after the diagnosis was established. This study emphasizes the importance of understanding the total insurance burden of medical costs for kidney disease patients, and the need to prepare for the future medical costs of newly diagnosed kidney disease patients.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The data for this study are available from the National Health Insurance Service database of the Republic of Korea after approval of the organization.

Authors' contributions

Conceptualization, Methodology, Project administration, Supervision, Funding acquisition: YSS, SP
Data curation, Investigation: All authors; KORNERSTONE Study Group
Formal analysis, Validation: All authors
Writing-original draft: All authors
Writing-review & editing: All authors
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