Association Between Starting Hemodialysis for End-Stage Renal Disease and Incident Cataract Surgery: A 12-Year Nationwide Cohort Study

Tyler Hyungtaek Rim,[1] Chang-Yun Yoon,[2] Hye Won Park,[3] Eun Jee Chung[1]

[1]Department of Ophthalmology, National Health Insurance Service Ilsan Hospital, Goyang, Korea
[2]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Ophthalmology, Severance Hospital, Institute of Vision Research, Yonsei University College of Medicine, Seoul, Korea

Correspondence: Eun Jee Chung, Department of Ophthalmology, National Health Insurance Service Ilsan Hospital, No. 100 Ilsan-ro, Ilsandong-gu, Goyang 410-719, Gyeonggi-do, Korea;
eunjee95@nhimc.or.kr.

Submitted: September 26, 2015
Accepted: February 1, 2016

Citation: Rim TH, Yoon C-Y, Park HW, Chung EJ. Association between starting hemodialysis for end-stage renal disease and incident cataract surgery: a 12-year nationwide cohort study. *Invest Ophthalmol Vis Sci*. 2016;57:1112–1119. DOI:10.1167/iovs.15-18276

Purpose. To evaluate incident cataract surgery in subjects who started hemodialysis for end-stage renal disease.

Methods. A nationwide propensity score–matched cohort study was performed by using a 12-year longitudinal national health insurance database of 1,025,340 subjects. The hemodialysis cohort was composed of patients who started hemodialysis between January 2003 and December 2007 ($n = 291$). The control cohort was composed of randomly selected patients (5 per patient in the hemodialysis cohort; $n = 1467$) who were matched to the hemodialysis cohort according to a propensity score based on year of hemodialysis initiation, age, sex, residential area, household income, and frequency of medical attention. Each selected patient was followed up until 2013. Cox proportional hazard regression analysis was used to calculate the overall hazard of hemodialysis initiation in regard to incident cataract surgery after adjusting for the above factors, hypertension, and diabetes mellitus.

Results. Starting hemodialysis was associated with increased incident cataract surgery (hazard ratio [HR] = 1.79; 95% confidence interval [CI], 1.34–2.41). Diabetes mellitus (HR = 1.68; 95% CI, 1.22–2.32) also increased the incidence of cataract surgery. With respect to age, the effect size of hemodialysis for incident cataract surgery was greater among younger adults (aged <60 years; HR = 5.32; 95% CI, 3.06–9.26) than among older adults (aged ≥60 years; HR = 1.17; 95% CI, 0.79–1.72).

Conclusions. Patients who began hemodialysis for end-stage renal disease were more likely to undergo cataract surgery than control subjects, and this risk was more pronounced in younger patients.

Keywords: cataract, cataract surgery, end-stage renal disease, hemodialysis, NHIS-NSC 2002-2013, renal impairment

The number of terminal kidney failure patients is growing worldwide at an average rate of 7% per year.[1] In 120 countries, 1.479 billion patients suffered from end-stage renal disease (ESRD) and its prevalence rate was 185 per million people in 2002.[2] Renal failure can be caused by various pathologies, including acute kidney injury and chronic kidney disease. Although these diseases are classified as "renal impairment," there is a significant distinction in pathophysiology between hemodialysis-dependent and hemodialysis-independent patients with renal impairment. Therefore, the definition of renal failure is important for evaluating the association between ophthalmic disease and renal impairment; we defined renal impairment as the continuation of hemodialysis for ≥3 months, as this parameter is indicative of ESRD.

Cataracts are the leading cause of vision loss worldwide[3] even though cataract surgery is a highly cost-effective intervention.[4] Additionally, cataract identification and grading can be very subjective, resulting in high interobserver variation. Therefore, we evaluated incident cataract surgery to identify cases of severe cataracts in need of surgery. Although various risk factors for cataracts have been identified, to our knowledge, only a limited number of studies have evaluated the association between kidney function and cataracts, and the results have been contradictory.[5–15] Potential explanations for cataract development in subjects on hemodialysis include hypocalcemia,[6,16] the accumulation of toxic metabolites,[17] osmotic cataract formation resulting from water accumulation in the lens caused by the trapping of urea,[7] and oxidative stress.[18–20] The lens cortex[18] and the posterior subcapsular region[21,22] may be the most sensitive areas to oxidative stress. Recent studies appear to support an association of renal impairment with cataracts[12–15] and incident cataract surgery.[8,13,14,23] Recent, well-designed studies[9] have demonstrated that subjects with moderate or severe renal impairment (creatinine clearance < 60 mL/minute/1.73 m^2) are approximately 3-fold more likely to undergo cataract surgery relative to subjects with normal or mildly impaired renal function (creatinine clearance ≥ 60 mL/minute/1.73 m^2) in younger adults below 60 years of age. Nevertheless, a large-scale Asian nationwide cohort study on ophthalmic disorders in a population with ESRD has not been undertaken because ESRD is relatively rare. This propensity score–matched cohort study investigated the association between incident cataract surgery and the initiation of hemodialysis for ESRD by using a representative nationwide sample of 1,025,340 adults from the National Health Insurance Service National Sample Cohort 2002–2013 (NHIS-NSC 2002–2013) in South Korea.

Subjects and Methods

Database

This nationwide propensity score–matched cohort study design was reviewed and approved by the Institutional Review Board of the National Health Insurance Service Ilsan Hospital, Gyeonggi-do, Korea. This study adhered to the tenets of the Declaration of Helsinki. All citizens in Korea are obligated to enroll in the Korean National Health Insurance Service (KNHIS), and nearly all of the data in the health insurance system are centralized to a large database. This database contains reimbursement records from all medical facilities, including hospitals, private clinics, and public centers in South Korea. Claims are accompanied by data regarding diagnostic codes, procedures, prescription drugs, personal information about the patient, information about the hospital, the direct medical costs of both inpatient and outpatient care, and dental services. All charges to the KNHIS are claimed via the Korean electronic data interchange (KEDI) codes provided by all medical providers (e.g., the KEDI code for "hemodialysis" is O7020, and that for "surgery for cataract or lens-phacoemulsification" is S5119). This study used the NHIS-NSC 2002–2013 data, which were released by the KNHIS in 2015. This sample includes 1,025,340 nationally representative randomly selected subjects, representing approximately 2.2% of the entire population included in the KNHIS in 2002. Proportionate stratified random sampling was used based on a total of 1476 strata (2 categories for sex, 18 categories for age group, and 41 categories for income).

Hemodialysis Cohort Definition

The hemodialysis cohort included patients who claimed any procedures or materials for hemodialysis, based on the KEDI codes related to inpatient or outpatient care between January 2003 and December 2007. The KEDI codes for hemodialysis are presented in Supplementary Table S1. We excluded subjects who had claims for hemodialysis in 2002 to exclude patients with chronic conditions and to ensure that the hemodialysis cohort included only subjects with new episodes. Additionally, we excluded subjects with a diagnosis of kidney transplant failure and rejection (Korean Classification of Disease [KCD] code T86.1) or kidney transplant status (KCD code, Z94.0) between 2002 and 2007 as well as those who had received a renal transplant (KEDI code R3280xxx) in this period; the treatments associated with these codes would likely include the use of immunosuppressants, which can cause cataracts, and these patients may have had greatly improved renal function after transplant. A previous study has shown that a small portion (1.5%–5.6%) of patients who received renal replacement therapy for more than 90 days subsequently recovered sufficient renal function to stop dialysis.[24–27] Hemodialysis is usually performed in three sessions per week; therefore, we only included patients with more than 36 hospital visits (~90 days) for hemodialysis, based on the KDEI codes, to produce a cohort of patients who underwent hemodialysis for ESRD.

Definition of Incident Cataract Surgery

Incident cataract surgery included only routine cataract surgery; claims of "surgery for cataract or lens-phacoemulsification" (KEDI code S5119) and "intraocular lens implantation-primary" (KEDI code S5117) on the same day were considered simple cataract surgery in the absence of other operations, such as partial vitrectomy. Incident cataract surgery was defined as the first cataract surgery in either the right or left eye.

Independent Variables

Cox regression models were adjusted for hypertension, diabetes mellitus, age, sex, household income, geographic location, and amount of medical attention (i.e., number of hospital visits). The groups were stratified into two age subgroups (<60 years and ≥60 years) for subgroup analysis. Comorbidities that may be associated with an increased risk of cataracts, such as hypertension and diabetes mellitus, were diagnosed on the basis of the Korean Standard Classification of Diseases.[28,29] We defined these comorbidities as any diagnoses between 2003 and 2013. To reduce surveillance bias (more frequent medical attention is associated with higher rates of cataract detection and recommendation for cataract surgery), the amount of medical attention received within the 2 years before enrolment was counted (0–9; 10–19; 20–29; 30–39; 40–49; or ≥50 visits) and matched between groups.

Study Sample

We included patients who began hemodialysis before their cataract surgery based on the visit date, which was considered the index date. Eligible patients who began hemodialysis between 2003 and 2007 were identified after excluding potential preexisting cases of hemodialysis, renal transplant, or incident cataract surgery. These cases were considered new incident cases of hemodialysis ($n = 291$). We selected 1467 patients (5 per patient in the hemodialysis cohort) from the database of 1,025,340 patients who were matched to the hemodialysis patients according to the propensity score based on year of hemodialysis initiation, age, sex, residential area, household income, and frequency of medical attention.

Statistical Analysis

Descriptive statistics of the study population are presented. Propensity score matching was performed; we estimated the propensity scores by performing a logistic regression to predict hemodialysis occurrence considering sociodemographic factors such as age, sex, residential area, and household income, as well as year of hemodialysis occurrence and frequency of medical attention. Matching was performed by using the greedy macro with the estimated propensity score; an 8-to-1 digit greedy matching algorithm was used to identify a unique matched control for each patient in the hemodialysis cohort according to the propensity score. Using this algorithm, if a match could not be found, the algorithm then proceeded sequentially to the next highest digit match (8→1 digit) of the propensity score to make "next-best" matches. Once a match was made, the match was not considered again. To identify the hazards associated with incident cataract surgery, hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated by using univariate and multivariate Cox proportional hazard regressions. The multivariate model adjusted for hypertension, diabetes mellitus, age, sex, residence, household income, and frequency of medical attention. The proportional hazards assumption was assessed by a Cox model with Schoenfeld residuals, and the assumption was not violated overall or in any subgroup. The person-years for each group and incidence rate per 1000 person-years were calculated. The overall cataract surgery–free rate was described by using a Kaplan-Meier curve for each year of the 11-year follow-up period. The follow-up period started on the first date of hemodialysis for the cases and on randomly selected visit dates in years matched to the start of hemodialysis for the individuals in the control cohort. The follow-up period ended at the first date of incident cataract surgery or at the last follow-up date until 2013. A significance level of 0.05 was selected. The statistical packages SAS for Windows version 9.4 (SAS Institute, Inc., Cary, NC, USA) and Stata/MP version 14.0 (StataCorp, College Station, TX, USA) were used to perform the analyses in this study.

Results

Table 1 displays the characteristics of the hemodialysis and control cohorts. Overall, the hemodialysis subjects were more likely to undergo cataract surgery (23.4% vs. 12.5%, $P < 0.001$). As compared with the control cohort, cataract surgery was more commonly performed on younger patients (<60 years old) in the hemodialysis cohort but was similarly performed on older patients (≥60 years old) in the hemodialysis cohort ($P <$ 0.001 and 0.574, respectively). The patients in the hemodialysis cohort were more likely to exhibit hypertension ($P <$ 0.001) and diabetes mellitus ($P < 0.001$) than those in the control cohort. No significant difference in the year of enrolment, age, sex, residential area, household income, or frequency of medical attention was detected between the two groups, as these variables were used for matching.

Table 2 displays the HRs for incident cataract surgery, based on the univariate and multivariate Cox regression models. After adjusting for sociodemographic factors, frequency of medical attention, and comorbidities including hypertension and diabetes mellitus, subjects who began hemodialysis were significantly more likely to undergo incident cataract surgery (HR = 1.79; 95% CI, 1.34–2.41) as based on multivariate Cox regression analysis. Diabetes mellitus (HR = 1.68; 95% CI, 1.22–2.32) was associated with new incident cataract surgery. With respect to the sociodemographic characteristics, increasing age, female sex, and higher frequency of medical attention were significantly associated with incident cataract surgery.

Table 3 displays the results of subgroup analysis according to age in which the patients were stratified into two subgroups, younger than 60 years and 60 years or older, followed by multivariate Cox regression after adjusting for possible confounders, including hypertension and diabetes mellitus, age group at 5-year intervals, sex, residential area, household income, and frequency of medical attention. Among both younger (aged <60 years) and older adults (aged ≥60 years), the subjects who began hemodialysis were more likely to undergo cataract surgery than the corresponding control subjects (HR = 5.32; 95% CI, 3.06–9.26 and HR = 1.17; 95% CI, 0.79–1.72, respectively). However, this difference between groups of older adults was not significant. The predictive value of hemodialysis for cataract surgery was significantly different between age groups, based on the interaction effect evaluated with the multivariate model ($P < 0.001$).

During the 11-year follow-up period (median, 7.1 years), a total of 11,973 person-years were examined, including 1799 person-years for the hemodialysis cohort and 10,174 person-years for the control cohort. Survival analysis revealed 37.8 (95% CI, 29.8–47.9) cases of cataract surgery per 1000 person-years in the hemodialysis cohort and 18.0 (95% CI, 15.6–20.8) cases of cataract surgery in the control cohort. Based on subgroup analysis, there were 5.1 cases of incident cataract surgery in the control cohort and 32.1 in the hemodialysis cohort in the <60-year-old subgroup; there were 37.0 cases in the control cohort and 46.5 cases in the hemodialysis cohort in the ≥60-year-old subgroup. The Figure displays the Kaplan-Meier survival curves for the cataract surgery–free rate, which differed between the hemodialysis and control cohorts. In the subgroups stratified according to age (<60 years and ≥60 years), notable differences in the rates of cataract surgery were detected from the beginning of the follow-up period in the younger subgroup (aged <60 years). In older adults (aged ≥60 years), a difference in the rates of cataract surgery was also detected from the beginning of the follow-up period; however, this difference was not significant after the 5-year follow-up period.

Discussion

In this study, we examined 1758 sociodemographically matched subjects who were extracted from a nationwide database of 1,025,340 randomly selected subjects. We found that patients who began hemodialysis due to ESRD exhibited a higher likelihood of incident cataract surgery during an 11-year follow-up period after adjusting for the presence of hypertension and diabetes. Interestingly, the effect size (based on the HR) of starting hemodialysis for incident cataract surgery was greater among patients younger than 60 years (HR = 5.32) than among patients 60 years or older (HR = 1.17).

To the best of our knowledge, there have been only four previous well-designed longitudinal epidemiologic studies evaluating the association between kidney function and incident cataracts. First, the Beaver Dam Eye Study (BDES) involved a 5-year follow-up period[12] and concluded that abnormal renal function is not associated with incident cataracts. Second, the Blue Mountain Eye Study involved a 5-year follow-up period[13] and reported that moderate or severe renal impairment increases the risk of incident cataract surgery (odds ratio [OR] = 2.75; 95% CI, 1.06–7.14). However, the authors of the latter study have found that creatinine levels are not associated with incident cataract subtypes. The authors emphasize that younger subjects who have moderate or severe renal impairment (creatinine clearance < 60 mL/minute/1.73 m^2) exhibit an increased risk of incident cataract surgery relative to older adults. Third, the 15-year follow-up of the BDES[14] indicates that cystatin C is associated with cortical cataracts (OR = 1.24; 95% CI, 1.09–1.41) and posterior subcapsular opacity (OR = 1.24; 95% CI, 1.02–1.50) after controlling for various confounders. Moreover, the blood urea nitrogen/creatinine ratio is associated with posterior subcapsular opacity (OR = 1.22; 95% CI, 1.03–1.54). The researchers also report a similar association of kidney variables with cataract surgery and posterior subcapsular cataracts. The authors suggest that the relative risk of cataract surgery is greater among patients with posterior subcapsular cataracts. Fourth, a methodologically similar study using data from a health insurance database in Taiwan[15] has reported that subjects with chronic kidney disease are more likely to have cataracts than control subjects (OR = 1.24; 95% CI, 1.18–1.31). However, the diagnoses of chronic kidney disease and cataracts were obtained from the International Classification of Disease codes, and their accuracy could not be ascertained. In summary, these recent well-designed epidemiologic studies support an association between renal impairment and incident cataracts.

An association between incident cataract surgery and kidney function has also been reported in previous studies.[8,13,14,23] The association between ESRD and incident cataract surgery found in the present study may not necessarily represent an effect on incident cataracts. Patients with ESRD

Table 1. Characteristics of the study population: control cohort (n=1467) and hemodialysis cohort (n=291)

	Control Cohort, No. (%)	Hemodialysis Cohort, No. (%)	*P* Value
Variables			
Cataract surgery			
All ages			<0.001
No event	1284 (87.5)	223 (76.6)	
Event	183 (12.5)	68 (23.4)	
Age <60 y			<0.001
No event	742 (96.0)	119 (77.3)	
Event	31 (4.0)	35 (22.7)	
Age ≥60 y			0.574
No event	542 (78.1)	104 (75.9)	
Event	152 (21.9)	33 (24.1)	
Hypertension			<0.001
No	606 (41.3)	20 (6.9)	
Yes	861 (58.7)	271 (93.1)	
Diabetes mellitus			<0.001
No	770 (52.5)	56 (19.2)	
Yes	697 (47.5)	235 (80.8)	
Variables used for matching			
Year			
2003	254 (17.3)	50 (17.2)	>0.999
2004	260 (17.7)	52 (17.9)	
2005	265 (18.1)	53 (18.2)	
2006	291 (19.8)	58 (19.9)	
2007	397 (27.1)	78 (26.8)	
Age group, y			0.996
<50	409 (27.9)	83 (28.5)	
50–59	364 (24.8)	71 (24.4)	
60–69	444 (30.3)	88 (30.2)	
≥70	250 (17.0)	49 (16.8)	
Sex			0.761
Male	856 (58.4)	167 (57.4)	
Female	611 (41.7)	124 (42.6)	
Residence*			0.972
Seoul (metropolitan)	368 (25.1)	74 (25.4)	
2nd area	316 (21.5)	62 (21.3)	
3rd area	228 (15.5)	48 (16.5)	
4th area	555 (37.8)	107 (36.8)	
Household income			0.998
0–30%	365 (24.9)	72 (24.7)	
30–70%	547 (37.3)	109 (37.5)	
70–100%	555 (37.8)	110 (37.8)	
Frequency of medical care use			
0–9	240 (16.4)	48 (16.5)	0.999
10–19	170 (11.6)	33 (11.3)	
20–29	320 (21.8)	66 (22.7)	
30–39	284 (19.4)	54 (18.6)	
40–49	254 (17.3)	50 (17.2)	
≥50	199 (13.6)	40 (13.8)	

may receive more medical care, and these frequent visits may result in increased cataract surveillance and incident cataract surgery. To control for this surveillance bias, we matched the frequency of medical attention between the two cohorts. Therefore, we believe this bias to be minimal. Despite this bias, cataract surgery involves an ophthalmologist's recommendation based on the likelihood of improvement in vision. In addition to the importance of evaluating the association between incident cataracts or cataract subtypes and renal impairment, it is important to assess whether patients on hemodialysis for ESRD have operable cataracts and whether they might benefit from cataract surgery.

Table 2. Univariate and Multivariate Cox Regression Analyses of the Overall Incidence of Cataract Surgery During the 11-Year Follow-up Period (n = 1758)

	Univariate Cox Analysis			Multivariate Cox Analysis		
Variables	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Cohort						
Control	1 (ref)			1 (ref)		
Hemodialysis	2.10	1.59–2.78	<0.001	1.79	1.34–2.41	<0.001
Hypertension						
No	1 (ref)			1 (ref)		
Yes	3.55	2.51–5.01	<0.001	1.41	0.95–2.09	0.085
Diabetes mellitus						
No	1 (ref)			1 (ref)		
Yes	3.25	2.43–4.34	<0.001	1.68	1.22–2.32	0.001
Age group, y						
<50	1 (ref)			1 (ref)		
50–59	2.35	1.41–3.92	0.001	1.75	1.02–2.99	0.041
60–69	6.32	4.01–9.97	<0.001	4.12	2.51–6.77	<0.001
≥70	8.31	5.11–13.51	<0.001	5.18	3.01–8.91	<0.001
Sex						
Male	1 (ref)			1 (ref)		
Female	0.95	0.74–1.22	0.702	1.31	1.06–1.62	0.012
Residence*						
Seoul (metropolitan)	1 (ref)			1 (ref)		
Second area	0.84	0.59–1.20	0.334	0.84	0.59–1.20	0.337
Third area	0.80	0.55–1.18	0.266	0.95	0.64–1.40	0.776
Fourth area	0.77	0.56–1.05	0.095	0.76	0.56–1.05	0.101
Household income						
0%–30%	1 (ref)			1 (ref)		
30%–70%	1.31	0.93–1.85	0.126	1.18	0.83–1.67	0.366
70%–100%	1.64	1.17–2.31	0.004	1.00	0.70–1.42	0.998
Frequency of medical attention						
0–9	1 (ref)			1 (ref)		
10–19	0.98	0.52–1.85	0.941	0.93	0.49–1.76	0.815
20–29	1.97	1.21–3.21	0.006	1.20	0.72–1.98	0.485
30–39	2.23	1.36–3.66	0.001	1.34	0.80–2.24	0.272
40–49	2.44	1.48–4.02	<0.001	1.38	0.81–2.33	0.233
≥50	4.41	2.72–7.16	<0.001	1.77	1.04–2.99	0.034

* Seoul is a metropolitan area in Korea; the second area included the largest province; the third area included the second largest city as well as the second and third largest provinces; and the fourth area included other areas.

Cataract screening is generally recommended for renal transplant recipients or pancreas–kidney transplant recipients.[30,31] Young adults (aged <60 years) who started hemodialysis were 5-fold more likely to receive cataract surgery than the corresponding control subjects (Table 3). However, among older adults (aged ≥60 years), a nonsignificant difference in the incidence of cataract surgery was observed between the hemodialysis and control cohorts. This finding suggests that cataract screening might be needed in patients who begin hemodialysis, especially among young adults below 60 years of age, who may be more socioeconomically active than older adults, and among renal transplant recipients.

Study Limitations

The limitations of this study include the following: (1) the possibilities of surveillance bias and selection bias; (2) the possibility that subjects who had received cataract surgery before 2002 were included in the control cohort; (3) the inability to collect data on cataract subtypes or grades; (4) the possibility that chronic hemodialysis patients were not fully excluded in 2002; (5) the inability to collect other important health-related information, such as smoking history; (6) the possibility that in the South Korean population, differences in the medical environment, such as medical accessibility or the national insurance system, might have led to distinct results; (7) the limited analysis based on comorbidities and sociodemographic factors not considering the use of medication, such as steroids; (8) the possibility of delayed cataract surgery because of the poor general condition of the patients in the hemodialysis cohort; and (9) the possibility of a lack of consistency in defining cataract surgery and hemodialysis, based on the KEDI codes.

The most important limitation was the potential surveillance bias as described in the the Discussion section. However, we believe the surveillance bias to be minimal because we matched the number of medical visits between the two cohorts. We chose medical claim–based controls, who were more likely to exhibit comorbidities than the general population, which includes individuals who neither received medical care nor had a specific diagnosis. Thus, a selection bias was present. It is

Table 3. Multivariable Cox Regression of the Overall Incidence of Cataract Surgery According to Age Group During the 11-Year Follow-up Period ($n = 1758$)

	Aged <60 y (*n* = 927)			Aged ≥60 y (*n* = 831)		
Variables	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Cohort						
Control	1 (ref)			1 (ref)		
Hemodialysis	5.32	3.06–9.26	<0.001	1.17	0.79–1.72	0.432
Hypertension						
No	1 (ref)			1 (ref)		
Yes	1.77	0.80–3.89	0.156	1.07	0.69–1.66	0.762
Diabetes mellitus						
No	1 (ref)			1 (ref)		
Yes	1.79	0.94–3.41	0.074	1.53	1.07–2.20	0.020
Age group, y						
<50	1 (ref)					
50~54	1.82	0.98–3.41	0.059			
55~59	1.75	0.91–3.35	0.093			
60~64				1 (ref)		
65~69				2.02	1.38–2.95	<0.001
70~74				1.96	1.25–3.08	0.003
≥75				1.95	1.18–3.24	0.010
Sex						
Male	1 (ref)			1 (ref)		
Female	1.34	0.96–1.86	0.083	1.27	0.96–1.68	0.092
Residence*						
Seoul (metropolitan)	1 (ref)			1 (ref)		
Second area	1.55	0.69–3.46	0.287	0.74	0.49–1.11	0.144
Third area	2.03	0.93–4.42	0.075	0.65	0.39–1.09	0.104
Fourth area	1.18	0.55–2.54	0.669	0.69	0.47–0.99	0.045
Household income						
0%–30%	1 (ref)			1 (ref)		
30%–70%	1.26	0.66–2.41	0.484	1.21	0.78–1.88	0.405
70%–100%	1.04	0.49–2.21	0.909	0.97		0.870
Frequency of medical attention						
0–9	1 (ref)			1 (ref)		
10–19	1.54	0.59–4.02	0.379	0.72	0.29–1.81	0.489
20–29	1.33	0.51–3.49	0.564	0.97	0.52–1.79	0.919
30–39	2.35	0.97–5.68	0.058	0.99	0.52–1.87	0.966
40–49	2.67	1.06–6.70	0.037	0.92	0.48–1.77	0.811
≥50	7.78	3.08–19.66	<0.001	1.01	0.53–1.90	0.979

* Seoul is a metropolitan area in Korea; the second area included the largest province; the third area included the second largest city as well as the second and third largest provinces; and the fourth area included other areas.

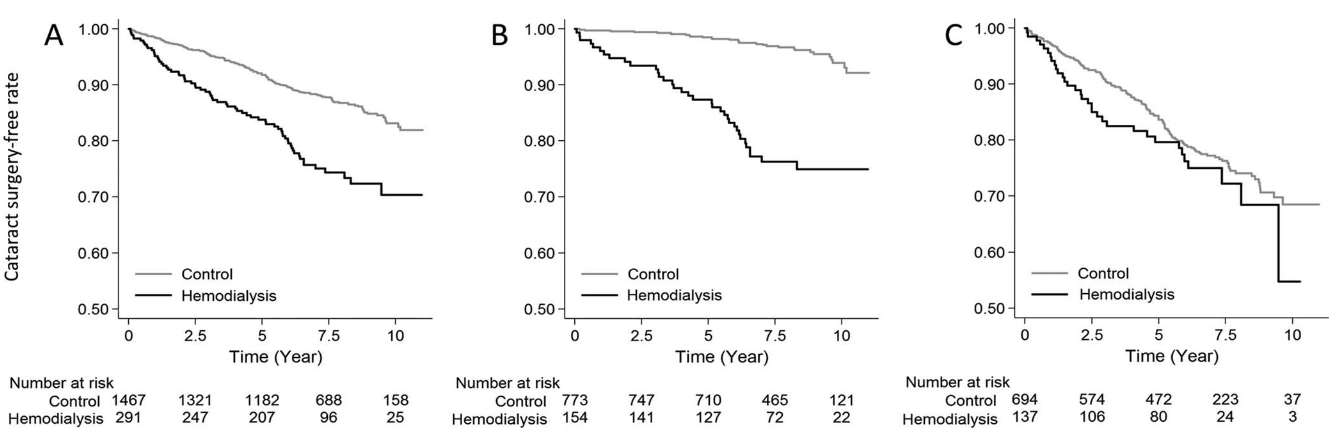

Figure. Kaplan-Meier survival curves for the hemodialysis cohort and the control cohort during the 11-year follow-up period (median, 7.2 years). The cataract surgery–free rates in all age groups (**A**), subjects aged <60 years (**B**), and subjects aged ≥60 years (**C**) are provided.

possible that patients previously received cataract surgery outside the study period of 2002–2013. Therefore, if someone received cataract surgery in both eyes before 2002 and was included in the control cohort, cataract surgery would not occur in these subjects during the study period. However, age should not have been a confounding factor in age-related cataract formation because age was controlled via matching. As expected, diabetes mellitus, which is a well-known risk factor for cataract formation,[28] was more prevalent in the hemodialysis cohort (Table 1). To control for this confounder, we included comorbidities in the multivariate model. Therefore, we believe the effect of comorbidities was well adjusted. Each cataract subtype exhibits distinct physiologic characteristics and etiologic factors,[32] and this variability might represent a major limitation of the present study, in which it was not possible to determine the cataract subtype. Furthermore, cataract surgery is applied to cataracts that require intervention, and the grading of cataracts may include the possibility of misclassification. Despite these biases and the impossibility of determining the cataract subtype in the included patients, cataract surgery involves an ophthalmologist's evaluation and determination of the possibility of vision improvement. Therefore, we emphasize that the higher rate of incident cataract surgery among hemodialysis patients was a result of the judgment of the ophthalmologist. We excluded medication use, such as cumulative steroid use, from the analysis because of its complexity. However, the mean cumulative steroid dose, which is one of the most important risk factors for cataract formation, between the hemodialysis and control cohorts was similar as based on our explanatory analysis (107.6 mg for the control cohort versus 101.2 mg for the hemodialysis cohort, based on dose conversion using prednisone equivalents; $P = 0.747$). Further study is needed to evaluate the association between medication use and cataract formation. Validation of the KEDI codes has not yet been performed. However, the increased cataract surgery rate in the control cohort (Fig. 1) partially shows the validity of the KEDI codes. Every claim via KEDI codes was reviewed by the Health Insurance Review and Assessment System (HIRA), and HIRA requests that medical providers resubmit and modify inappropriate claims on the basis of their own "big data" screening methods (not open to the public).

We conclude that patients who began hemodialysis exhibited a significantly higher rate of incident cataract surgery than control patients during an 11-year follow-up period after adjusting for hypertension and diabetes mellitus. Interestingly, the hemodialysis cohort exhibited an approximately 5-fold higher HR in young adults (<60 years) relative to the control cohort. Thus, it is important for both nephrologists and ophthalmologists to recommend cataract screening. In particular, we should screen hemodialysis patients younger than 60 years as well as older adults because cataracts are not common in younger adults. Otherwise, such individuals may be left in an untreated state of poor vision.

Acknowledgments

This study used the NHIS-NSC 2002–2013 (NHIS-2015-2-046), which was released by the KNHIS. The authors alone are responsible for the content and writing of the paper.

Disclosure: **T.H. Rim**, None; **C.-Y. Yoon**, None; **H.W. Park**, None; **E.J. Chung**, None

References

1. Grassmann A, Gioberge S, Moeller S, Brown G. ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. *Nephrol Dial Transplant*. 2005;20:2587–2593.
2. Kolesnyk I, Noordzij M, Kolesnyk M, Kulyzky M, Jager KJ. Renal replacement therapy in Ukraine: epidemiology and international comparisons. *Clin Kidney J*. 2014;7:330–335.
3. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. *Br J Ophthalmol*. 2012;96:614–618.
4. Taban M, Behrens A, Newcomb RL, et al. Acute endophthalmitis following cataract surgery: a systematic review of the literature. *Arch Ophthalmol*. 2005;123:613–620.
5. Berlyne GM, Ari JB, Danovitch GM, Blumenthal M. Cataracts of chronic renal failure. *Lancet*. 1972;1:509–511.
6. Koch HR, Siedek M, Weikenmeier P, Metzler U. Cataract during intermittent hemodialysis: the influence of hypocalcemia on the development of opacities (author's translation) [in German]. *Klin Monbl Augenheilkd*. 1976;168:346–353.
7. Heyningen R, Harding JJ. Do aspirin-like analgesics protect against cataract: a case-control study. *Lancet*. 1986;327:1111–1113.
8. Harding JJ, van Heyningen R. Case-control study of cataract in Oxford. *Dev Ophthalmol*. 1987;15:99–103.
9. Miglior S, Bergamini F, Migliavacca L, Marighi P, Orzalesi N. Metabolic and social risk factors in a cataractous population: a case-control study. *Dev Ophthalmol*. 1989;17:158–164.
10. Klein BE, Klein R, Linton KL. Prevalence of age-related lens opacities in a population: the Beaver Dam Eye Study. *Ophthalmology*. 1992;99:546–552.
11. Donnelly C, Seth J, Clayton R, Phillips C, Cuthbert J, Prescott R. Some blood plasma constituents correlate with human cataract. *Br J Ophthalmol*. 1995;79:1036–1041.
12. Klein BE, Klein R, Lee KE. Renal function abnormalities and incident cataract after a five-year interval: The Beaver Dam Eye Study. *Curr Eye Res*. 1998;17:720–725.
13. Huynh SC, Kifley A, Strippoli GF, Mitchell P. Is renal impairment a predictor of the incidence of cataract or cataract surgery: findings from a population-based study. *Ophthalmology*. 2005;112:293–300.
14. Klein BE, Knudtson MD, Brazy P, Lee KE, Klein R. Cystatin C, other markers of kidney disease, and incidence of age-related cataract. *Arch Ophthalmol*. 2008;126:1724–1730.
15. Wang TJ, Wu CK, Hu CC, Keller JJ, Lin HC. Increased risk of co-morbid eye disease in patients with chronic renal failure: a population-based study. *Ophthalmic Epidemiol*. 2012;19:137–143.
16. Kazi G, Phillips C, Lambie A, Winney R. Hypocalcaemic cataract as a presenting symptom of renal insufficiency. *Postgrad Med J*. 1984;60:166–167.
17. Beiran I, Scharf J, Tamir A, Miller B. Influence of systemic diseases and environmental factors on age at appearance, location and type of acquired cataract. *Metab Pediatr Syst Ophthalmology (1985)*. 1993;17:34–37.
18. Spector A. Oxidative stress-induced cataract: mechanism of action. *FASEB J*. 1995;9:1173–1182.
19. Delcourt C, Carriere I, Delage M, Descomps B, Cristol JP, Papoz L. Associations of cataract with antioxidant enzymes and other risk factors: the French Age-Related Eye Diseases (POLA) Prospective Study. *Ophthalmology*. 2003;110:2318–2326.
20. Chung SS, Ho EC, Lam KS, Chung SK. Contribution of polyol pathway to diabetes-induced oxidative stress. *J Am Soc Nephrol*. 2003;14:S233–S236.
21. Hodge WG, Whitcher JP, Satariano W. Risk factors for age-related cataracts. *Epidemiol Rev*. 1995;17:336–346.
22. Urban RC Jr, Cotlier E. Corticosteroid-induced cataracts. *Surv Ophthalmol*. 1986;31:102–110.
23. Clayton R, Cuthbert J, Duffy J, et al. Some risk factors associated with cataract in SE Scotland: a pilot study. *Trans Ophthalmol Soc U K*. 1981;102:331–336.

Investigative Ophthalmology & Visual Science

24. Nunan TO, Stevens EA, Croft DN, Hilton PJ, Jones NF, Wing AJ. Recovery of renal function after prolonged dialysis and transplantation. *Br Med J (Clin Res Ed)*. 1983;287:248–249.

25. Sekkarie MA, Port FK, Wolfe RA, et al. Recovery from end-stage renal disease. *Am J Kidney Dis*. 1990;15:61–65.

26. Metcalfe W, Khan IH, Prescott GJ, Simpson K, Macleod AM; Scottish Renal Registry. End-stage renal disease in Scotland: outcomes and standards of care. *Kidney Int*. 2003;64:1808–1816.

27. Siddiqui S, Norbury M, Robertson S, Almond A, Isles C. Recovery of renal function after 90 d on dialysis: implications for transplantation in patients with potentially reversible causes of renal failure. *Clin Transplant*. 2008;22:136–140.

28. Rim TH, Kim MH, Kim WC, Kim TI, Kim EK. Cataract subtype risk factors identified from the Korea National Health and Nutrition Examination survey 2008-2010. *BMC Ophthalmol*. 2014;14:4.

29. Rim TH, Kim DW, Kim SE, Kim SS. Factors associated with cataract in Korea: a Community Health survey 2008-2012. *Yonsei Med J*. 2015;56:1663–1670.

30. Kasiske BL, Vazquez MA, Harmon WE, et al. Recommendations for the outpatient surveillance of renal transplant recipients: American Society of Transplantation. *J Am Soc Nephrol*. 2000; 11(suppl 15):S1–S86.

31. Becker BN, Odorico JS, Becker YT, et al. Simultaneous pancreas-kidney and pancreas transplantation. *J Am Soc Nephrol*. 2001;12:2517–2527.

32. Hiller R, Sperduto RD, Ederer F. Epidemiologic associations with nuclear, cortical, and posterior subcapsular cataracts. *Am J Epidemiol*. 1986;124:916–925.

Investigative Ophthalmology & Visual Science