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Risks of cataract surgery in solid and hematologic cancer survivors

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In this nationwide retrospective cohort study, we investigated the risk of cataract surgery among cancer survivors compared to propensity score (PS)-matched non-cancer controls. This study included 4.5 million adults in the National Health Insurance Service database who underwent health screenings between year 2011 and 2014. PS-matching at a 3:1 ratio resulted in 167,766 non-cancer controls and 55,968 patients with cancer. During a period of up to 10 years, 7703 (13.8%) patients with cancer and 24,369 (14.5%) patients in the control group underwent cataract surgery. Survival analysis showed no difference in cataract surgery risk between the overall cancer cohort and controls. Analysis by cancer types showed that solid cancers did not increase the risk of cataract surgery compared to controls, whereas hematologic cancer survivors exhibited a significantly increased risk of cataract surgery, particularly between 2 and 5 years post-index date (hazard ratio at second year, 1.81; 95% confidence interval, 1.07–3.05; $p = 0.027$). Among hematologic cancer survivors, factors significantly associated with increased cataract surgery risk included advanced age, leukemia diagnosis, bone marrow transplantation, and prolonged steroid use. This study highlights the elevated risk of cataract surgery among hematologic cancer survivors, emphasizing the need for long-term ophthalmologic follow-up in this population.

Keywords Cancer survivors, Cataract, Hematologic neoplasms

With advancements in cancer diagnosis and treatment, the 5-year relative survival for newly diagnosed cancer between 2014 and 2018 has reached 70.3%[1]. Consequently, the population of cancer survivors has surged, necessitating focused attention on their healthcare requirements. Comorbidities such as cardiovascular disease, dementia, and arthralgia are well-documented among cancer survivors[2–4].

Despite emerging studies on ocular health in cancer survivors, the available data remains limited[5,6]. Notably, cataracts are prominent among cancer survivors, alongside retinopathy, optic neuropathy, and glaucoma[5,6]. Although some studies have explored the risk of cataracts or associated factors among cancer survivors[5,7,8], uncertainties persist regarding whether the risk of cataracts requiring surgical intervention is higher among cancer survivors compared to the general population.

According to the World Health Organization, cataracts are the leading cause of blindness globally and the most common condition requiring surgery[9]. Cataracts frequently arise as a consequence of anticancer medications, prompting many clinical trials to include ophthalmic screenings for conditions such as retinopathy, corneal abnormalities, and cataract formation[10,11]. Several clinical trials have investigated the ocular side effects of antineoplastic agents, identifying an increased risk of cataracts associated with specific medications including tamoxifen[12], busulfan[13], and ibrutinib[14]. However, existing research exploring the association between cancer treatment modalities and increased cataract risk is limited, often focusing on specific subgroups such as childhood cancer survivors[7] or lacking robust control groups[8]. Also, evidence concerning the risk of cataract surgery among the overall population of cancer survivors remains limited.

In this nationwide cohort study, we leveraged the National Health Insurance Service (NHIS) database to investigate whether the risk of cataract surgery escalates among cancer survivors compared to their propensity score (PS)-matched non-cancer controls. By stratifying cataract surgery risk according to cancer type, we aimed to identify factors associated with cataracts requiring surgical intervention in cancer survivors.

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Materials and methods

Ethic statement and data source

We used the database of the Korean NHIS for policy and academic research (approval number: NHIS-2023-1-464). Under the National Health Insurance Act, the data can be used solely for research without participants' consent[15]. This study was conducted with the approval of NHIS and adhered to the tenets of the Declaration of Helsinki. The protocol was approved by the Institutional Review Board of Yonsei University Health System (approval number: 4-2022-1020). Informed consent was waived by the Institutional Review Board of Yonsei University Health System due to the retrospective nature of the study based on deidentified, routinely collected data.

Study population

This study was based on the NHIS database, accessed through the National Health Insurance Sharing Service of the Republic of Korea (https://nhiss.nhis.or.kr/). Established in 2011, the NHIS provides a comprehensive National Health Information database, including health claims data for approximately 50 million individuals[15]. However, the extensive volume of data has proven less feasible for research purposes due to inefficiencies in handling large datasets. Consequently, the NHIS now offers customized cohorts tailored to individual researchers' needs. Therefore, we requested and obtained a cohort of 4.5 million adults aged ≥ 18 years who had undergone health screenings at least once between January 1, 2011, and December 31, 2014, randomly sampled from the entire database. With the NHIS approval and support from the Korean government, we received the requested data, ensuring all patient information was anonymized to maintain confidentiality. For these sampled individuals, we constructed a comprehensive dataset encompassing their claim data between January 1, 2008, and December 31, 2021.

As in previous studies utilizing the NHIS database[16], cancer diagnoses were defined as having at least one Korean Standard Classification of Diseases-8th Revision––slightly modified from International Classification of Diseases, 10th Revision––diagnostic code between C00 and C97, along with the V193 code. In Korea, patients with cancer are registered with 'V193' codes in the national registry for cancer, ensuring strict control over their entry to receive large medical expense reductions. Cataract surgery was identified through specific claims codes of (1) S5119 (phacoemulsification) and S5117 (primary IOL implantation) or (2) S5111 (intra/extracapsular cataract extraction) and S5117 (primary IOL implantation) without S5121/S5122 (TPPV) on the same day.

Patients with any diagnosis or surgical history related to the following conditions during the washout period between January 1, 2008, and December 31, 2010, were excluded: (1) any 'C' codes during the washout period; (2) cataract surgery during the washout period; (3) diagnosis of pseudophakia or aphakia at baseline; (4) surgery for after cataract; (5) diagnosis of traumatic cataract; (6) diagnosis of uveitis, scleritis or episcleritis, and glaucoma; (7) trans pars plana vitrectomy; and (8) retinal detachment surgery including scleral buckling/encircling. Additionally, patients diagnosed with cancer from January 1, 2015, to December 31, 2021, in the control group were excluded to ensure that the control group remained cancer-free during the study period. Patients who died within 1 year from the index date in the cancer group were also excluded (Supplementary Fig. S1).

Subsequently, 64,261 individuals diagnosed with cancer between January 1, 2011, and December 31, 2014, and 3,467,377 individuals without a cancer diagnosis between January 1, 2008, and December 31, 2021, underwent an initial 1:max40 PS-matching for age and sex to align index dates. For the cancer group, the index date was set as the date of the first cancer diagnosis, whereas for the control group, it was set as the date of cancer diagnosis for the matched patients with cancer. Additional exclusions were made for 267,398 patients who: (1) received cataract surgery; (2) received a diagnosis of pseudophakia or aphakia; (3) underwent surgery for after cataract; (4) were diagnosed with traumatic cataract; (5) were diagnosed with uveitis, scleritis or episcleritis, and glaucoma; (6) underwent trans pars plana vitrectomy or other reattachment surgery for retinal detachment between January 1, 2011, and the index date; and (7) had missing values for health check-up variables.

Given the abundance of eligible controls, we aimed to enhance statistical power by employing a one-to-many propensity score matching strategy[17]. However, a substantial number of cancer patients remained unmatched under the 1:4 matching ratio, which could potentially introduce selection bias. Therefore, we adopted a 1:3 matching scheme, which allowed us to retain a larger sample size while maintaining adequate covariate balance and minimizing data loss. Notably, the 1:3 matching method has also been employed in various previous cancer studies[18–20]. Finally, 55,968 patients in the cancer group and 167,766 PS-matched patients in the control group were included in this study (Fig. 1).

Outcome measures and comorbidities

The primary outcome were the incidence and risk of cataract surgery events. Cataract surgery events were defined as occurrences of the following surgery codes on the same day with associated Diagnosis-Related Group (DRG) codes: S5119 (phacoemulsification) with S5117 (primary intraocular lens [IOL] implantation) or S5111 (intra/extra-capsular cataract extraction) with S5117 (primary IOL implantation) (Supplementary Table S1). In South Korea, since July 2012, all cases of simple cataract surgery have been processed exclusively under DRG codes, ensuring that each cataract surgery is associated with a corresponding DRG code. Cases with concurrent codes for trans pars plana vitrectomy (S5121, S5122) were excluded, as these were considered complicated cataract surgeries or instances where cataract surgery was performed as part of the trans pars plana vitrectomy procedure. According to Korean reimbursement criteria, if posterior capsular rupture occurs during cataract surgery and anterior vitrectomy is performed, it is grouped under the same DRG code as simple cataract cases without a separate trans pars plana vitrectomy code and was considered an event in this study. The additional codes for lens extraction and IOL implantation beyond those mentioned above are listed in Supplementary Table S1, and we excluded cases with any of these additional codes.

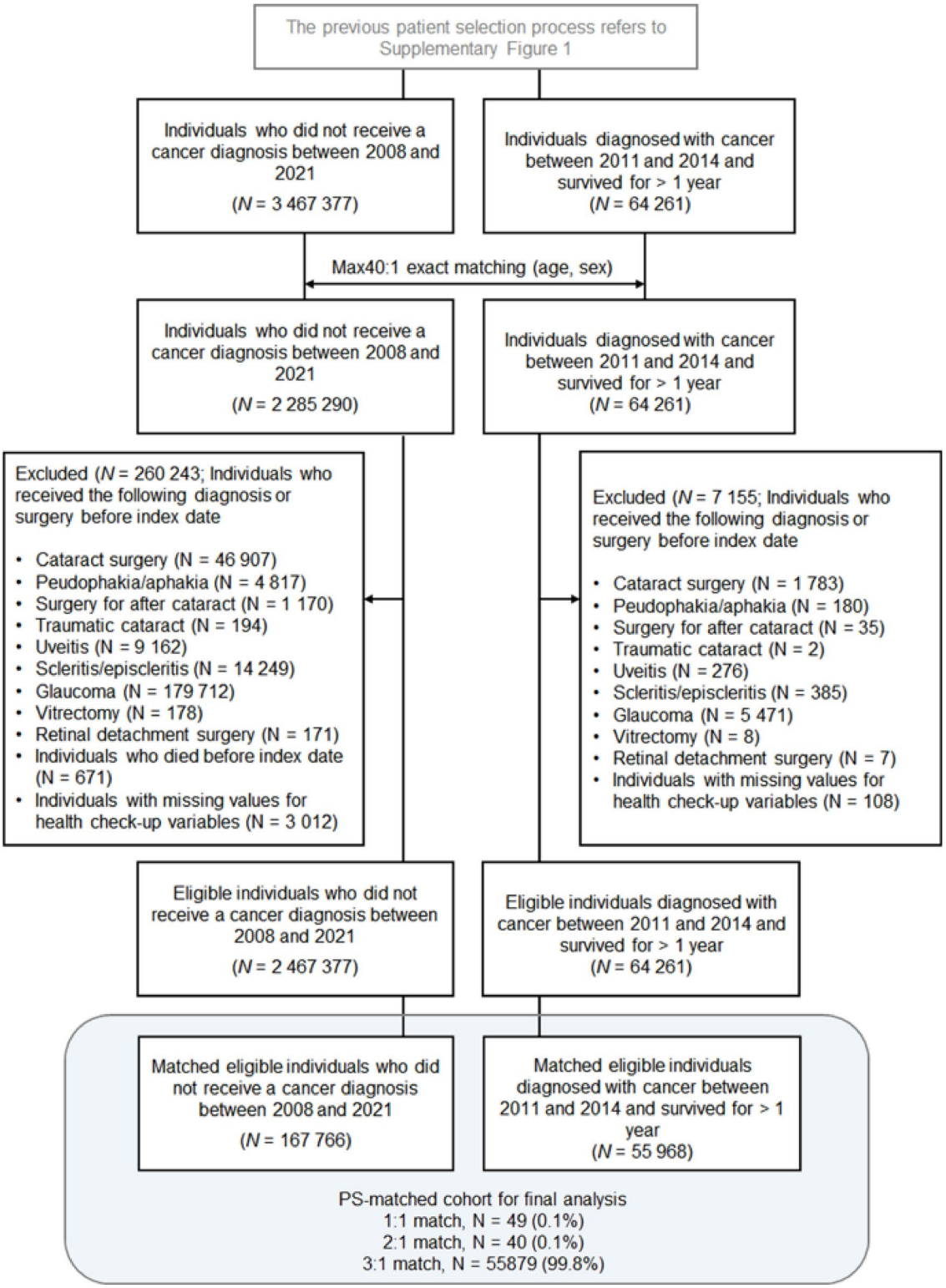

Fig. 1. Flowchart of the study population. The previous patient selection process refers to (Supplementary Fig. S1).

Data on body mass index, fasting glucose, total cholesterol, and socioeconomic status were obtained from the health checkup records closest to the index date. Comorbidities were established based on one inpatient or two outpatient records of the diagnostic codes in the medical claims database, and prescription medication information was gathered using medical claim records (Supplementary Table S1).

The cancer diagnosis served as the exposure variable. The index date was defined as the date of the first cancer diagnosis, with the index date for the matched control group set as the date of cancer diagnosis for the matched patients with cancer. Annual risk estimates were calculated for each year following the index date. Patients were censored at the date of endpoint events, their death, 10 years post-index date, or December 31, 2021, whichever came first.

Subgroup analysis

Subgroup analysis divided patients into those with hematologic cancer and those with solid cancer, with further analysis conducted within the solid cancer subgroup based on cancer type. Patients diagnosed with two or more types of solid cancer between 2011 and 2014 were categorized separately as having multiple cancers.

Given the importance of age in cataract development, subgroup analysis was also performed for patients aged 65 and older and those under 65. Lastly, risk factors, including age, sex, total body irradiation (TBI) therapy, steroid therapy, and cancer subtypes for the occurrence of cataracts requiring surgery, were determined within the hematologic cancer subgroup.

Statistical analysis

Descriptive statistics characterized baseline characteristics and comorbidities. Continuous variables were expressed as means ± standard deviations, and categorical variables were reported as frequencies (percentages). The cumulative incidence of cataract surgery was determined using the Kaplan–Meier method. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the subgroups were computed using Cox proportional hazards models, with the unexposed group as the reference. A multivariate-adjusted analysis was performed after considering the variables listed in (Table 1).

All tests were two-tailed, with statistical significance set at $p < 0.05$. Statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc, Cary, NC, USA), SPSS software (version 25.0; IBM Corp, Armonk, NY, USA), and R (version 3.5.3; R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population and baseline characteristics

The demographic characteristics of the matched control group and patients diagnosed with any type of cancer, solid cancer, and hematologic cancer at the index date are detailed in (Table 1), Supplementary Tables S2, S3, respectively. Notably, 141 individuals were diagnosed with both solid and hematologic cancer on the same date, resulting in the sum of the solid and hematologic groups being less than the total number of cancer cases by this number. All standardized mean differences were below 0.1, indicating successful PS matching and absence of major imbalances.

Risks of cataract surgery in cancer survivors

During 10 years from the index date, among the 55,968 patients with all cancer types, 7,703 (13.8%) underwent cataract surgery, whereas in the control group of 167,766 individuals, 24,369 (14.5%) underwent cataract surgery. In a univariate analysis, no significant difference was observed in the risk of cataract surgery between the cancer cohort and the matched control group (HR 1.00, 95% CI 0.97–1.02, $p = 0.850$). However, the multivariate-adjusted analysis indicated a trend toward slightly increased cataract surgery risk among patients with cancer compared to non-cancer controls, though this was not statistically significant (HR 1.02, 95% CI 1.00–1.05, $p = 0.067$) (Fig. 2A). When stratified by cancer type, the solid cancer group did not exhibit an increased risk of cataract surgery in univariate and multivariate-adjusted analyses (Fig. 2B). Conversely, the hematologic cancer group showed a significantly increased risk of cataract surgery in both univariate (HR 1.43, 95% CI 1.13–1.68, $p < 0.001$) and multivariate-adjusted analyses (HR 1.61, 95% CI 1.37–1.89, $p < 0.001$) compared to their matched non-cancer control group (Fig. 2C).

A stratified analysis by age in the entire cohort revealed that the risk of cataract surgery was similar between the non-cancer group and the cancer group for individuals under 65 years of age (Supplementary Figure S2A). However, for those over 65 years, an increased risk of cataract surgery in the cancer group was observed in the univariate analysis (HR 1.04, 95% CI 1.00–1.07, $p = 0.045$). Additionally, a trend towards increased risk, though not statistically significant, was noted in the multivariate-adjusted analysis (HR 1.03, 95% CI 1.00–1.07, $p = 0.075$) (Supplementary Figure S2B).

Risk of cataract surgery in solid and hematologic cancer survivors

Subgroup analysis of the multivariate-adjusted risk of cataract surgery by cancer site did not reveal a significant increase in cataract surgery among the 14 solid cancer subgroups compared to the matched control group (Supplementary Figure S3). Notably, the increased cataract surgery risk was confined to the hematologic cancer group.

The multivariate-adjusted risk of cataract surgery, stratified by year post-index date, is illustrated in (Fig. 3). Over the 10-year post-index date, no significant difference in annual cataract surgery risk was observed between solid cancer and matched non-cancer control groups, except for a significant increase in the 8th year (Fig. 3A). However, a significant increase in the adjusted HR for cataract surgery was seen in the hematologic cancer group during the 2nd (HR 1.81, 95% CI 1.07–3.05, $p = 0.027$), 3rd (HR 1.69, 95% CI 1.08–2.65, $p = 0.021$), 4th (HR 1.83, 95% CI 1.15–2.91, $p = 0.011$), and 5th year (HR 1.61, 95% CI 1.02–2.53, $p = 0.041$) following the index date (Fig. 3B).

	Group 1 (non-cancer group) *N* = 167,766	Group 2 (cancer group) *N* = 55,968	SMD
Age (years)			< 0.001
< 40	13,531 (8.07%)	4,527 (8.09%)	
40–64	110,541 (65.89%)	36,900 (65.93%)	
≥ 65	43,694 (26.04%)	14,541 (25.98%)	
Sex			< 0.001
Male	78,483 (46.78%)	26,192 (46.80%)	
Female	89,283 (53.22%)	29,776 (53.20%)	
Body mass index (kg/m^2)	23.84 (3.13)	23.89 (3.18)	0.018
Fasting glucose (mg/dL)	100.07 (23.89)	100.32 (23.66)	0.011
Total cholesterol (mg/dL)	193.13 (37.41)	193.03 (38.71)	0.003
Smoking			0.024
Non-smoker	111,439 (66.43%)	36,837 (65.82%)	
Former smoker	31,492 (18.77%)	10,364 (18.52%)	
Current smoker	24,835 (14.80%)	8,767 (15.66%)	
Alcohol consumption			0.009
None	108,176 (64.48%)	35,897 (64.14%)	
1–2/wk	38,992 (23.24%)	13,214 (23.61%)	
≥ 3/wk	20,598 (12.28%)	6,857 (12.25%)	
Household income percentiles			0.022
0–30% (highest)	74,927 (44.66%)	25,597 (45.74%)	
30–70%	48,503 (28.91%)	15,961 (28.52%)	
70–100% (lowest)	44,336 (26.43%)	14,410 (25.75%)	
Residence			0.003
City	78,140 (46.58%)	25,984 (46.43%)	
Rural	89,626 (53.42%)	29,984 (53.57%)	
Systemic diseases			
Hypertension	58,471 (34.85%)	19,804 (35.38%)	0.011
Diabetes	33,532 (19.99%)	11,426 (20.42%)	0.011
Dyslipidemia	59,795 (35.64%)	20,255 (36.19%)	0.011
Chronic kidney disease	1,357 (0.81%)	465 (0.83%)	0.002
Hyperthyroidism	5,556 (3.31%)	1,945 (3.48%)	0.009
Hypothyroidism	8,185 (4.88%)	2,808 (5.02%)	0.006
Chronic liver disease	53,437 (31.85%)	17,939 (32.05%)	0.004
Autoimmune diseases	15,676 (9.34%)	5,246 (9.37%)	0.001
Average follow-up (years)	8.20 (2.11)	7.83 (2.51)	

Table 1. Baseline clinicodemographic characteristics of the 3:1 PS-matched non-cancer control and cancer group. *Values are presented as number (percentage) or mean ± standard deviation. PS = propensity score. SMD = standardized mean difference.

Factors associated with cataract surgery in hematologic cancer survivor

Due to the confirmed increase in the risk of cataract surgery within the hematologic cancer group, contributing factors were analyzed and are presented in (Table 2). We examined known risk factors for cataracts and factors associated with hematologic cancer treatment. Both univariate and multivariate analyses revealed that age (adjusted HR 1.11 per year, 95% CI 1.09–1.13, $p < 0.001$), leukemia (adjusted HR 1.50, 95% CI 1.11–2.03, $p = 0.008$), and a history of bone marrow transplantation (BMT) (adjusted HR 2.42, 95% CI 1.54–3.79, $p < 0.001$) were significantly associated with increased cataract surgery risk. While hypertension (multivariate HR 1.41 (1.02–1.94), $p = 0.038$) was associated with significant increase in risk of cataract surgery, other comorbidities including diabetes, dyslipidemia, chronic kidney disease and autoimmune disease showed no significant associations with risk of cataract surgery among hematologic cancer survivors (all p-value > 0.05) (Table 2). Short-term use of systemic steroids for < 6 months did not significantly increase the risk of cataract surgery compared to patients not treated with steroids (adjusted HR 0.94, 95% CI 0.68–1.30, $p = 0.702$), whereas prolonged use for ≥ 6 months substantially elevated the risk (adjusted HR 1.84, 95% CI 1.27–2.66, $p = 0.001$). Although TBI demonstrated a high HR, statistical significance was not reached (adjusted HR 1.78, 95% CI 0.61–5.15, $p = 0.288$) (Table 2).

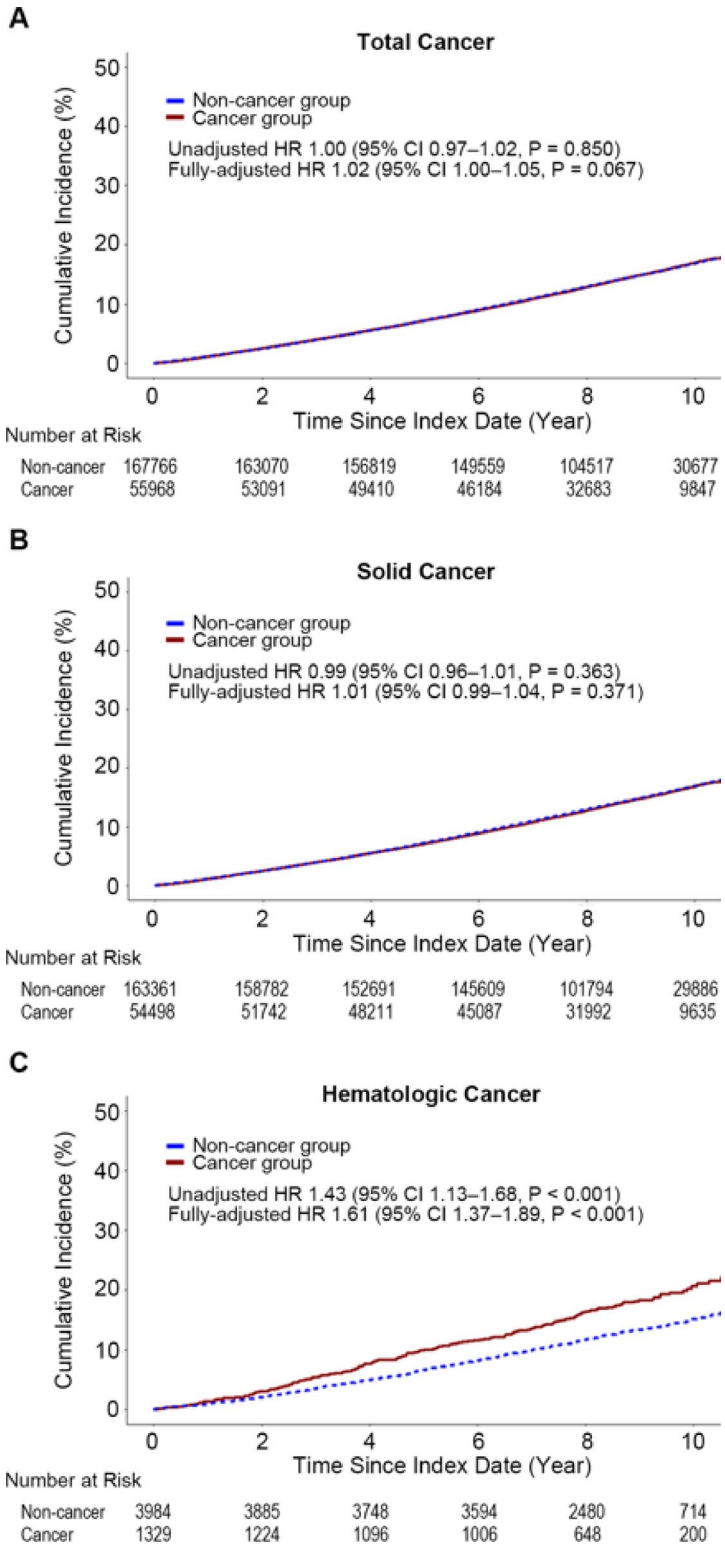

Fig. 2. Kaplan–Meier curves of the cumulative incidence of cataract surgery in the 3:1 PS-matched non-cancer control group and the (**A**) any type of cancer group, (**B**) solid cancer group, and (**C**) hematologic cancer group. PS = propensity score. HR = hazard ratio. CI = confidence interval. *HRs were adjusted for variables listed in (Table 1).

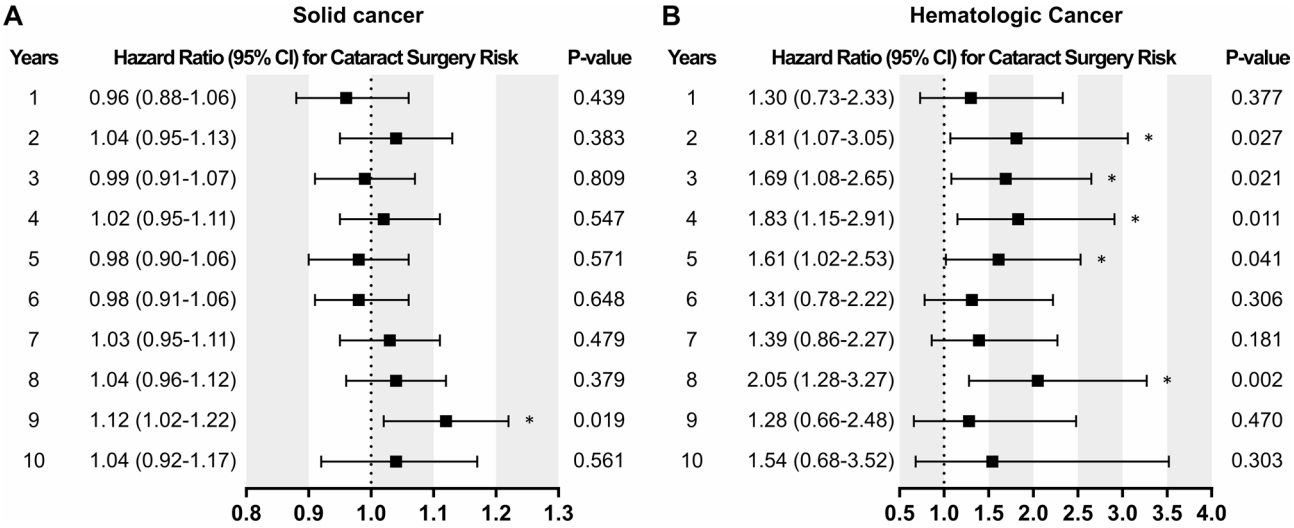

Fig. 3. Annual adjusted hazard ratios of cataract surgery in the 3:1 PS-matched non-cancer control group and the (**A**) solid cancer group and (**B**) hematologic cancer group. PS = propensity score. CI = confidence interval. * = statistically significant. *Hazard ratios were adjusted for variables listed in (Table 1).

Discussion

In this nationwide cohort study, we aimed to determine whether cancer survivors exhibit an elevated incidence of cataract surgeries. Individuals with a history of previous eye surgery, glaucoma, or uveitis were excluded, and residual risk factors were controlled using PS-matching. The overall cancer cohort did not show a statistically significant increase in cataract surgery incidence relative to the control group, with a cumulative incidence of approximately 20% over 10 years. Notably, hematologic cancer survivors experienced a marked increase in cataract surgery risk between 2 and 5 years post-diagnosis, unlike their solid cancer counterparts, who exhibited no such elevation. Similarly, a previous study on 3936 cancer survivors have also shown that among all cancer types, cataracts were reported most frequently by survivors of leukemia (both chronic, 17%; and acute, 9%), myeloma (13%), and lymphoma (7%)[8].

Subgroup analysis of solid cancers did not identify any subgroup with a significant increase in cataract surgery risk. Factors such as age, irradiation, and steroid treatment are well-established contributors to an increased risk of cataracts in patients with cancer[8]. Patients with hematologic malignancies are more likely to undergo these treatments compared to those with solid tumors, which may account for the higher incidence of cataract surgeries observed in this group. In analyzing risk factors for cataract surgery within the hematologic cancer cohort, advanced age, a history of BMT, and prolonged steroid administration were significant risk factors.

Despite extensive documentation linking glucocorticoids to posterior subcapsular cataracts, the precise mechanisms by which steroids induce cataracts remain elusive. Previous research has identified glucocorticoid receptor alpha in lens epithelial cells, implicating its activation in processes such as cell proliferation and differentiation, apoptosis, and growth factor expression[21,22]. Some studies examining the risk of cataracts associated with steroid use among cancer survivors reported no significant risk[7,8], potentially due to the absence of detailed data on steroid dosage and duration. Our study found no increased cataract surgery risk with short-term steroid use of < 6 months; however, prolonged steroid use significantly elevated the risk of cataract surgery.

In this study, multivariate analysis identified BMT as the most significant risk factor for cataract surgery in hematologic patients with cancer. Cataract formation in the context of BMT is likely attributed to long-term toxicity from pharmacotherapy, TBI, cranial irradiation therapy, and corticosteroid therapy for graft-versus-host disease (GVHD)[23–25]. BMT frequently necessitates high-dose chemotherapy, which can induce multiple organ dysfunction syndrome, including adrenal insufficiency or hepatic dysfunction post-transplantation[26]. Additionally, many patients experience GVHD, for which prolonged corticosteroid usage, with a median duration of 2–3 years[27], remains the mainstay of first-line treatment, either alone or in combination with other immunosuppressive agents[28]. Conditioning TBI is recognized for enhancing overall survival in patients with multi-human leukocyte antigen (HLA) mismatch[29]; however, it significantly increases the risk of cataract formation compared to chemotherapy-only regimens[30]. A study reported the incidence of cataracts among TBI recipients to be approximately 20%, rising to 40% with extended steroid use for GVHD[31].

Regarding radiotherapy, our analysis based on claim data could not specify the organs targeted by radiation, precluding assessment of cranial radiotherapy, a well-established cause of cataracts[32]. Instead, we focused on the impact of TBI. The HRs for cataract development among TBI recipients were consistent with those reported in other studies[33], although statistical significance was not achieved. Cataract development post-radiotherapy is closely related to the radiation dose and typically manifests years after exposure, with prior literature indicating a median time of 9.6 years from cancer diagnosis to cataract onset[7]. This latency period may explain the absence of statistically significant differences in this study, where follow-up extended up to 10 years post-cancer diagnosis, as considerable time is necessary for patients to undergo cataract surgery post-radiotherapy. Furthermore, TBI is

	Univariate analysis		Multivariate analysis - model 1		Multivariate analysis - model 2	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (per 1 year)	1.10 (1.09–1.12)	< 0.001	1.11 (1.09–1.12)	< 0.001	1.11 (1.09–1.13)	< 0.001
Age (categorical)						
20–39 years	Reference					
40–64 years	10.20 (2.52–41.30)	0.001				
≥ 65 years	44.10 (10.90–179.00)	< 0.001				
Sex						
Male	Reference				Reference	
Female	1.20 (0.91–1.57)	0.191			1.13 (0.78–1.64)	0.520
Body mass index (kg/m^2)						
< 25	Reference				Reference	
≥ 25	1.10 (0.83–1.45)	0.517			1.12 (0.83–1.49)	0.460
Household income percentiles						
0–30% (highest)	Reference				Reference	
30–70%	0.87 (0.63–1.22)	0.424			1.01 (0.72–1.43)	0.955
70–100% (lowest)	0.98 (0.70–1.36)	0.893			0.86 (0.61–1.21)	0.401
Residence						
City	Reference				Reference	
Rural	1.15 (0.87–1.51)	0.322			1.11 (0.83–1.47)	0.492
Smoking						
Non-smoker	Reference				Reference	
Former smoker	0.84 (0.60–1.18)	0.308			1.03 (0.67–1.59)	0.889
Current smoker	0.74 (0.50–1.10)	0.132			1.19 (0.74–1.94)	0.475
Alcohol consumption						
None	Reference		Reference		Reference	
1–2/week	0.55 (0.38–0.79)	0.001	0.91 (0.63–1.33)	0.64	0.93 (0.62–1.37)	0.699
≥ 3/week	0.72 (0.44–1.18)	0.193	0.98 (0.60–1.62)	0.95	0.98 (0.58–1.67)	0.94
Systemic diseases						
Hypertension	3.21 (2.44–4.22)	< 0.001	1.4 (1.02–1.91)	0.035	1.41 (1.02–1.94)	0.038
Diabetes	2.44 (1.83–3.24)	< 0.001	1.18 (0.85–1.62)	0.321	1.18 (0.86–1.64)	0.308
Dyslipidemia	1.83 (1.39–2.40)	< 0.001	0.87 (0.63–1.20)	0.391	0.85 (0.61–1.19)	0.339
Chronic kidney disease	2.03 (0.90–4.58)	0.087	1.02 (0.44–2.37)	0.957	1.08 (0.46–2.51)	0.866
Hyperthyroidism	1.79 (0.97–3.28)	0.061	1.85 (0.99–3.47)	0.056	1.85 (0.97–3.52)	0.063
Hypothyroidism	1.63 (0.91–2.92)	0.100			1.01 (0.55–1.87)	0.966
Chronic liver disease	1.46 (1.11–1.93)	0.007	0.93 (0.69–1.27)	0.652	0.93 (0.68–1.26)	0.628
Autoimmune diseases	1.67 (1.15–2.44)	0.008	1.23 (0.83–1.81)	0.295	1.19 (0.80–1.76)	0.383
Cancer type						
Lymphoma	Reference		Reference		Reference	
Leukemia	1.77 (1.35–2.33)	< 0.001	1.53 (1.13–2.06)	0.005	1.5 (1.11–2.03)	0.008
Bone marrow transplantation						
No	Reference		Reference		Reference	
Yes	1.63 (1.11–2.37)	0.012	2.36 (1.51–3.69)	< 0.001	2.42 (1.54–3.79)	< 0.001
Irradiation therapy						
None	Reference		Reference		Reference	
Total body irradiation	1.48 (0.55–3.98)	0.440	1.81 (0.62–5.26)	0.277	1.78 (0.61–5.15)	0.288
Systemic steroid therapy						
None	Reference		Reference		Reference	
< 6 months	1.06 (0.77–1.46)	0.731	0.92 (0.67–1.28)	0.637	0.94 (0.68–1.30)	0.702
≥ 6 months	1.91 (1.35–2.71)	< 0.001	1.82 (1.26–2.62)	0.001	1.84 (1.27–2.66)	0.001

Table 2. Cox proportional hazards regression of risk of cataract surgery among hematologic cancer survivors. *Model 1 conducted multivariate risk analysis using variables with $p < 0.1$ from univariate risk analysis results, whereas model 2 performed multivariate risk analysis using all variables incorporated in the univariate risk analysis. HR = hazard ratio, CI = confidence interval.

generally administered as a conditioning regimen before allogeneic BMT in cases of HLA mismatch rather than autologous BMT[34], complicating the precise analysis due to interactions with various risk factors.

Previous studies have identified leukemia as a risk factor for cataracts compared to other hematologic malignancies[7,8]. The higher incidence of cataracts in patients with leukemia may be due to the more frequent use of BMT, high-dose steroids, and TBI. For instance, one study demonstrated that BMT was performed in 5.0–5.5% of patients with leukemia compared to 2.2–3.4% of patients with lymphoma[35]. Another study highlighted that patients with leukemia received a higher median ionizing radiation dose to the lens of the eye than individuals with other hematologic malignancies[7]. However, even after adjusting for these treatment factors, the risk of cataract surgery remained higher in leukemia than in lymphoma, underscoring the necessity for further research.

We acknowledge certain limitations of our study. Firstly, as our research relied on medical claims data rather than detailed medical records, the outcome measure was based on procedure codes for cataract surgery, which may not fully reflect clinical cataract diagnoses, specific subtypes, or severity. Also, there was lack of access to visual acuity data. Secondly, we could not specify the dosage and location of irradiation therapy, which was critical as irradiation therapy is known to show a dose-related response in cataract formation. Detailed chemotherapy regimens and dose were also not captured in the NHIS claims data. This restricts our ability to analyze treatment-specific effects. Thirdly, this study focused on adults who underwent health screenings, indicating that separate research might have been needed for pediatric populations. Fourthly, patients' family history, lifestyle factors and occupational exposure which are important factors for development of cataracts, were not included in the study as the NHIS claims database does not include detailed individual data on family history or lifestyle factors. Lastly, our study reported the incidence of cataract surgeries rather than the actual incidence of cataracts, potentially leading to underreporting. This discrepancy arose because some patients diagnosed with cataracts may not have undergone surgery due to poor general health or other socioeconomic factors.

Despite these limitations, our study represents the largest cohort dataset available, comparing the risk of cataract surgery in patients diagnosed with cancer with a non-cancer control group. Additionally, unlike previous studies that reported cataract incidence along with other ocular complications among cancer survivors, we excluded patients with combined ocular complications. Procedures like combined vitrectomy or triple operation surgery were deemed unsuitable for assessing cataract surgery and were excluded from our analysis. Furthermore, patients who underwent cataract surgery before the index date, those who underwent intraocular surgery that could induce cataracts, and patients diagnosed with conditions such as glaucoma or uveitis were excluded from our study.

In conclusion, this nationwide cohort study revealed that patients with hematologic cancer showed an increased risk of cataract surgery compared to patients without cancer, whereas those with solid cancer did not show an elevated risk. Our results suggest that hematologic cancer survivors, particularly those treated with bone marrow transplantation or long-term steroids, receive annual ophthalmologic evaluations starting within 2–5 years post-diagnosis. However, these findings pertain to the overall population of cancer survivors, and further research is necessary to delineate the specific effects of individual anticancer modalities on risk of cataract surgery. Given the prolonged latency period for cataract development after radiotherapy or high-dose steroid use, studies with longer follow-up periods are required to accurately capture the timing and progression of cataract surgery post-cancer treatment.

Data availability

The data that support the findings of this study are available from National Health Insurance System, but restrictions apply to the availability of these data, which were used under licence for the current study and so are not publicly available. Data are, however, available from the corresponding author, YJK upon reasonable request and with permission from the National Health Insurance System (https://nhiss.nhis.or.kr/bd/ab/bdaba000eng.do).

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Author contributions

H.J. drafted the article; Y.J.K. and S.W.L. conceived the idea of the project; S.K and S.W.L performed the statistical analysis and established the database; Y.J.K interpreted the data; B.H.K, C.S.L, S.H.B, and S.S.K contributed in revising the intellectual content. All authors discussed the results and contributed to the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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