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Cancer incidence and the influence of immunosuppressive agents in Korean patients with systemic lupus erythematosus: a retrospective cohort study

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Abstract

Background To investigate cancer incidence and the potential influence of immunosuppressive agents in Korean systemic lupus erythematosus (SLE) patients.

Methods We conducted a retrospective analysis utilizing data from the Korea Healthcare Bigdata Linked Platform, which integrated the National Central Cancer Registry and National Health Insurance Service databases covering the period 2008–2017. Incidence rates (IRs) per 10,000 person-years (PYs) for site-specific cancers of SLE patients were calculated using ICD-O-3 codes. Multivariable logistic regression analysis was utilized to assess the association between immunosuppressive agents and cancer development in SLE patients.

Results A total of 10,013 predominantly female (91%) Korean SLE patients with a mean age of 36.9 ± 15.2 years were included. During a follow-up of 62,268.5 PYs, 368 patients developed cancer. The IRs per 10,000 PYs for total, solid, and hematologic cancers were 59.07, 54.09, and 5.78, respectively. The most prevalent cancers (measured in IRs per 10,000 PYs) were thyroid (17.01, 95% CI 13.78–20.25), breast (8.67, 95% CI 6.36–10.98), stomach (4.49, 95% CI 2.83–6.16), colorectal (4.17, 95% CI 2.57–5.78), and cervical (3.85, 95% CI 2.31–5.39). Approximately half (50.8%) of SLE patients with cancer were diagnosed at the localized Surveillance, Epidemiology, and End Results (SEER) stage. No statistically significant association was found between immunosuppressive agents and cancer development (Odds Ratio 1.03, 95% CI 0.80–1.34).

Conclusion Our study shows that Korean SLE patients using immunosuppressive agents are not significantly more likely to develop cancer. Further research with extended observation is warranted to corroborate these findings.

Keywords Systemic lupus erythematosus, Cancer, Incidence rate, Immunosuppressive agents

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Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease marked by chronic inflammation, often associated with comorbidities that contribute to increased mortality [1]. Cancer ranks among the leading causes of death in SLE patients, with multiple studies demonstrating an elevated risk compared with the general population [2, 3]. An international cohort study revealed a heightened overall cancer risk in SLE patients, while other investigations reported the risk was approximately 1.8 times greater than in the general population [4, 5]. Despite acknowledging an increased cancer risk in SLE, previous studies have not consistently identified risk estimates for specific cancer types [6]. A Chinese cohort study highlighted an increased risk of hematologic cancer in SLE patients, particularly among the elderly [7]. A study from Sweden showed that SLE patients had a three-to-four-fold increased risk of non-Hodgkin lymphoma [8], while a study from Denmark, reported that SLE patients had a higher incidence of lung cancer [9]. Cervical cancer was also a concern among female SLE patients, particularly when associated with human papillomavirus (HPV) infection [10].

While SLE has been established as an independent risk factor for cancer development, it is crucial to understand the diverse risk factors contributing to cancer in SLE patients. Several studies have proposed determinants such as age, gender, comorbidities, and medication [11]. However, the influence of medications on cancer risk in SLE remains contentious, with one study showing glucocorticoids having no significant association with cancer, and hydroxychloroquine potentially reducing cancer risk [12]. Another study suggested that cyclophosphamide may contribute to hematologic cancers, particularly lymphoma [13], while a study in Sweden found that immunosuppressive agents were not a significant factor for elevated cancer risk [14].

Building on our previous study, which confirmed an increased cancer risk among Korean SLE patients compared with the general population [15], this study aims to analyze the incidence patterns of various cancers, including those affecting the female reproductive system. Using data from national healthcare registries, we also investigate the association between immunosuppressive therapies and cancer risk in Korean SLE patients.

Method

Data sources

This nationwide cohort study utilized the Korean Healthcare Bigdata Linked Platform, which integrates data from the National Health Insurance Service (NHIS), the Health Insurance Review & Assessment Service (HIRA), and the Korea Central Cancer Registry (KCCR) for the period between 2003 and 2017. The NHIS serves as a single-payer healthcare system covering the majority of citizens, with only a small percentage relying on the Medical Aid program. The database contains comprehensive demographic information, medical claims, and prescription records, forming a robust foundation for healthcare research [16]. The HIRA manages health claim data sourced from the NHIS, providing a detailed database encompassing individual beneficiary profiles, in-hospital treatments, disease records, out-of-hospital prescriptions, and information on nursing institutions—an abundance of data that will enable comprehensive analyses of healthcare utilization patterns and treatment outcomes [17]. Established in 1980 by the Korean Ministry of Health and Welfare, the KCCR plays a pivotal role in tracking cancer developments for effective national cancer control strategies by using the International Classification of Disease for Oncology (ICD-O-3) system, ensuring accurate identification of cancer cases based on hospital discharge records. The KCCR supports national cancer control strategies by providing reliable data on cancer trends [18].

Study population and study design

Retrospective cohort of prevalent SLE patients

A retrospective cohort study was conducted on 10,013 SLE patients between 2008 and 2017. Patients aged 10–79 years were recruited who met both the ICD-10 code (M32.0) and the rare intractable disease code (V136). Inclusion criteria required patients with SLE to fulfill the classification criteria of the 1997 update of the 1982 American College of Rheumatology Revised Criteria [19], while individuals diagnosed with cancer within five years preceding the SLE diagnosis were excluded. Incidence of cancer was defined as the initial claims for cancer occurrence in KCCR. Neither patients lacking cancer claims in KCCR nor those solely diagnosed with cancer through the NHIS were included (Fig. 1). We calculated incidence rates (IRs) of cancer per 10,000 person-years (PYs) and estimated IRs for total cancer and specific cancer types among the patients. All cancers were described by Surveillance, Epidemiology, and End Results (SEER) staging as either Localized, Regional, Distant, or Unknown Status.

Case–control study between SLE patients with and without cancer during observation

Within the SLE cohort, we conducted a case–control study, matching SLE patients with cancer (case group) to those without cancer (control group). The case group comprised patients with an initial cancer diagnosis during the observation period, while controls, comprising cancer-free patients with SLE, were

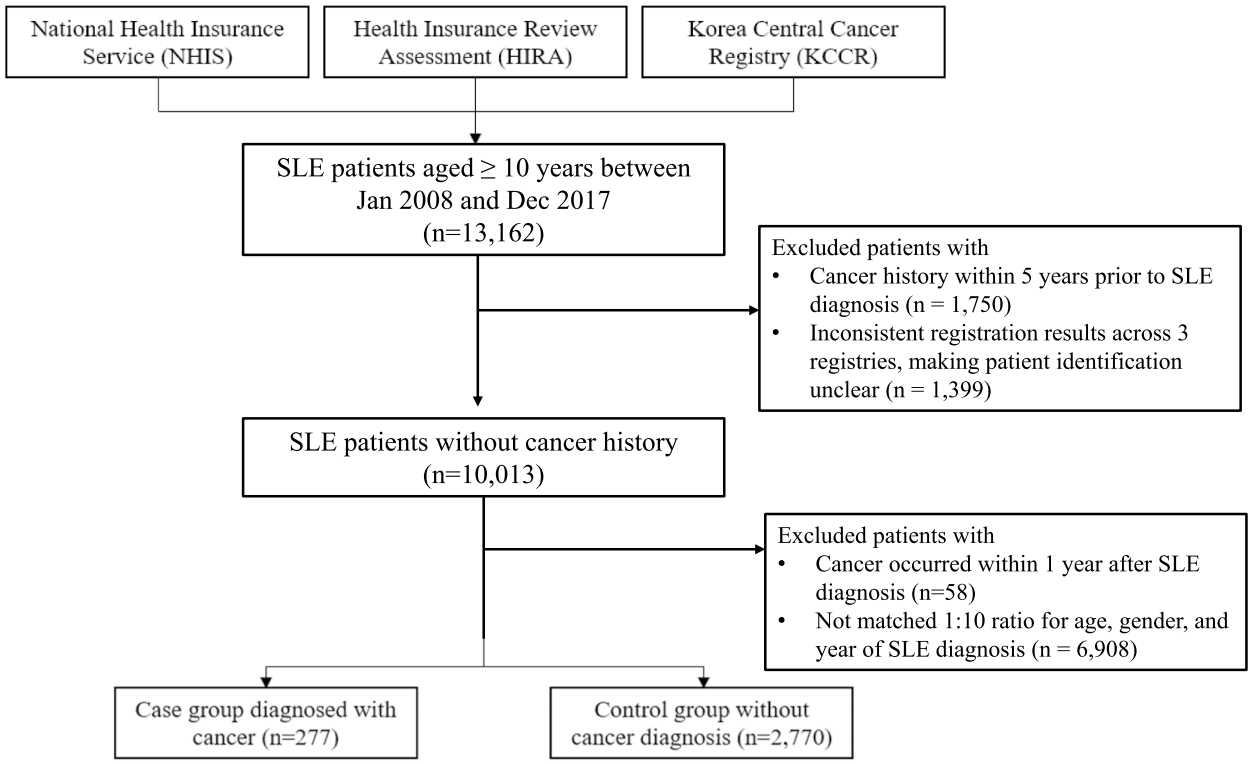

Fig. 1 Study protocol for retrospective cohort study and case–control analysis

matched based on age, sex, and the year of SLE diagnosis in a 1:10 ratio. The analysis focused on assessing the association between cancer occurrence and immunosuppressive agents in SLE within the case–control group. Patients who developed cancer within one year of SLE diagnosis were excluded from the analysis to account for lag time and accurately evaluate prior drug exposure. Exposure to immunosuppressive agents, including azathioprine, cyclophosphamide, cyclosporine, leflunomide, methotrexate, mizoribine, mycophenolate, and tacrolimus was ascertained from the claim database during the observation period.

For the sensitivity analysis, we classified patients based on their timing of exposure to immunosuppressive agents prior to cancer occurrence. Patients who had never taken immunosuppressive agents before cancer occurrence were used as the reference group. We then categorized patients into three groups: those exposed to immunosuppressive agents less than one year before cancer occurrence, those exposed between one and four years prior, and those exposed more than four years prior to diagnosis of cancer.

Statistical analysis

Baseline characteristics of the study population were presented as frequency (%) for categorical variables or mean ± standard deviation (SD) for continuous variables. IRs per 10,000 PYs were calculated by dividing the number of incident cases by the total observational period, with 95% confidence intervals (CIs). For the case–control study, Student's t-tests and Chi-squared tests were conducted for continuous and categorical variables, respectively. Univariate and multivariable logistic regression analyses were performed for the retrospective nested case–control study to assess the association between cancer occurrence and immunosuppressive agents in SLE. The odds ratio (OR) for the risk of immunosuppressive agents was calculated with 95% CI while adjusting for insurance type, income level, comorbidities (hypertension, hyperlipidemia, chronic kidney disease, and avascular necrosis), Charlson comorbidity index, and medication (nonsteroidal anti-inflammatory drugs, hydroxychloroquine, and glucocorticoids). Income level was divided into 20 quartiles, each representing 5% of the dataset. All other analyses

were performed with SAS 9.4 for Windows (SAS Institute, Inc., Cary, NC, USA).

Results

Baseline characteristics of SLE patients

The baseline characteristics of the 10,013 patients at the time of SLE diagnosis are detailed in Table 1. The cohort was 91% female, with an average age of 36.9 ± 15.2 years, Notably, 63.5% and 57.5% of the SLE patients received oral glucocorticoids and hydroxychloroquine, respectively.

Table 1 Baseline characteristics of the study population

Variables	SLE patients (*n* = 10,013)
Age, years	36.9 ± 15.2
-19	851 (8.5)
20–29	2,578 (25.7)
30–39	2,468 (24.6)
40–49	2,132 (21.3)
50–59	1,202 (12.0)
60–69	456 (4.6)
70–79	326 (3.3)
Sex, female	9,109 (91.0)
Payer type	
National health insurance	8,886 (88.7)
Medical aid	1,127 (11.3)
Charlson comorbidity index	1 ± 1.2
Comorbidities	
Hypertension	856 (8.5)
Diabetes mellitus	68 (0.7)
Hyperlipidemia	341 (3.4)
Chronic kidney disease	142 (1.4)
SLE-related comorbidities	
Anti-phospholipid antibody syndrome	6 (0.1)
Fibromyalgia	25 (0.2)
Avascular necrosis	76 (0.8)
Interstitial lung disease	50 (0.5)
Viral infection	
Herpes zoster	138 (1.4)
CMV	7 (0.1)
Medication[a]	
Hydroxychloroquine	5,755 (57.5)
Glucocorticoid	6,359 (63.5)
NSAIDs	2,103 (21.0)

Numerical quantitative data were presented by "mean ± SD" and categorical data were presented by "frequency (%)". [a]Medication usage in the year of SLE diagnosis

SLE systemic lupus erythematosus, *CMV* cytomegalovirus, *NSAID* nonsteroidal anti-inflammatory drug

Incidence rate of site-specific cancer in SLE patients

Among the 10,013 SLE patients, 368 developed cancer after their SLE diagnosis, resulting in an IR of 59.07 per 10,000 PYs (95% CI 53.04–65.11). Throughout a follow-up period of 62,268.5 PYs, 337 cases of solid cancers and 36 cases of hematologic cancers were observed, with respective IRs of 54.09 (95% CI 48.32–59.87) and 5.78 (95% CI 3.89–7.67) per 10,000 PYs. Thyroid cancer exhibited the highest incidence rate among solid cancers (IR 17.01, 95% CI 13.78–20.25), followed by breast (IR 8.67, 95% CI 6.36–10.98), stomach (IR 4.49, 95% CI 2.83–6.16), and colorectal cancer (IR 4.17, 95% CI 2.44–8.80). For hematologic cancers, patients with SLE exhibited a higher incidence of non-Hodgkin lymphoma (NHL), with NHL nodal (IR 2.73, 95% CI 1.43–4.03) and NHL extranodal (IR 1.93, 95% CI 0.84–3.02). Hodgkin lymphoma (HL) cases were not observed (Table 2).

Table 2 Incidence rates of site-specific cancer in Korean patients with SLE (*n* = 10,013)

Site-specific cancer	N	Incidence rate per 10,000 (n/PYs)*	95% CI
All cancer*	368	59.07	(53.04–65.11)
Solid cancer	337	54.09	(48.32–59.87)
Thyroid	106	17.01	(13.78–20.25)
Breast	54	8.67	(6.36–10.98)
Stomach	28	4.49	(2.83–6.16)
Colon and rectum	26	4.17	(2.57–5.78)
Cervix uteri	24	3.85	(2.31–5.39)
Lung	18	2.89	(1.55–4.22)
Liver	16	2.57	(1.31–3.83)
Endometrium	12	1.93	(0.84–3.02)
Kidney	8	1.28	(0.39–2.17)
Ovary	6	0.96	(0.19–1.73)
Oropharyngeal	6	0.96	(0.19–1.73)
Brain and central nervous system	5	0.80	(0.10–1.51)
Bladder	4	0.46	(0.01–1.27)
Pancreas	4	0.64	(0.01–1.27)
Gallbladder etc	3	0.48	(-0.06–1.03)
Vulva and vagina	3	0.48	(-0.06–1.03)
Prostate	1	0.16	(-0.15–0.48)
Hematologic cancer	36	5.78	(3.89–7.67)
Non-Hodgkin lymphoma _nodal	17	2.73	(1.43–4.03)
Non-Hodgkin lymphoma _ extranodal	12	1.93	(0.84–3.02)
Leukemia	4	0.64	(0.01–1.27)
Myeloma	3	0.48	(-0.06–1.03)

PY person-years, *CI* confidence interval. *The observation period for each cancer type was standardized to 62,268.5 PYs. SLE, systemic lupus erythematosus

* Five patients were diagnosed with both solid and hematologic cancer

Surveillance, Epidemiology, and End Results (SEER) staging of cancer in SLE patients

Of the 368 cancer cases, SEER staging revealed 187 localized, 104 regional, 43 distant, and 34 unknown cases. Approximately half of all SLE patients (50.8%) were diagnosed at a localized SEER stage, with only 11.7% diagnosed at a distant stage. For solid cancers, 176 cases out of 337 were localized, 100 had regional spread, and 30 had distant spread at diagnosis. The distribution of stages for hematologic cancers showed no significant differences (Table 3).

Case–control study between SLE patients with and without cancer during observation

A total of 277 SLE patients diagnosed with cancer (case group) and 2770 matched cancer-free SLE patients (control group) were included. Baseline characteristics are provided in Supplementary Table 1. Comorbidities such as hypertension (40.1%), hyperlipidemia (24.9%), and chronic kidney disease (11.2%) were more prevalent in the case group.

Impact of immunosuppressive agents on cancer development in SLE patients

Table 4 details the correlations between immunosuppressive agents and cancer risk. The OR for cancer development associated with the use of immunosuppressive agents was 1.03 (95% CI 0.79–1.33), indicating no significant association between these agents and cancer development in SLE patients. None of the individual immunosuppressive agents analyzed significantly affected cancer risk. Furthermore, sensitivity analysis showed that cancer risk was not significantly influenced by the timing of exposure to immunosuppressive agents prior to cancer diagnosis (Supplementary Table 2).

Table 3 The Surveillance, Epidemiology, and End Results (SEER) staging of cancer in SLE patients ($n = 10,013$)

Stage	N (%)	Incidence rate per 10,000 (n/PYs)[a]	95% CI
All cancer	368 (100.0)	59.07	(53.04 –65.11)
Localized	187 (50.8)	30.02	(25.71 –34.32)
Regional	104 (28.3)	16.69	(13.49 –19.90)
Distant	43 (11.7)	6.90	(4.84–8.97)
Unknown	34 (9.2)	5.46	(3.62–7.29)
Solid cancer	337 (100.0)	54.09	(48.32–59.87)
Localized	176 (52.2)	28.25	(24.08–32.42)
Regional	100 (29.7)	16.05	(12.91–19.20)
Distant	30 (8.9)	4.82	(3.09–6.54)
Unknown	31 (9.2)	4.98	(3.22–6.73)
Hematologic cancer	36 (100.0)	5.78	(3.89–7.67)
Localized	14 (38.9)	2.25	(1.07–3.42)
Regional	4 (11.1)	0.64	(0.01–1.27)
Distant	14 (38.9)	2.25	(1.07–3.42)
Unknown	4 (11.1)	0.64	(0.01–1.27)

PY person-years, *CI* confidence interval

[a] The observation period for each cancer type was standardized to 62,268.5 PYs.
SLE, systemic lupus erythematosus

Discussion

Our retrospective cohort study provides valuable insights into the cancer risk profile among Korean patients with SLE by integrating data from three nationwide databases. Consistent with previous studies, our findings show that SLE patients have an increased susceptibility to thyroid cancer as well as breast, cervical, uterine, and ovarian cancer [20]. The observed SEER stage distribution at the time of cancer diagnosis revealed that over half of the cases were localized, with a substantial proportion at the regional stage. After the subsequent case–control study, our results found no significant difference in overall cancer risk between individuals who had taken immunosuppressive agents and those who had not. This study leverages a large, nationally representative cohort with comprehensive healthcare data linkage, ensuring accurate cancer diagnoses and robust clinical insights. By analyzing site-specific cancer risks and adjusting for confounding factors through multivariable models, it provides a detailed and reliable understanding of cancer risks in SLE patients.

Our study provides a comprehensive assessment of cancer risk and stage distribution in SLE patients, contributing to the growing body of evidence indicating a higher overall cancer risk in this population. Several previous studies, including our own, have reported an elevated cancer risk in SLE patients compared with the general population [15, 21, 22]. For example, we calculated an IR of 28.92 (95% CI 24.64–33.21) per 10,000 PYs for breast and reproductive organ cancers in SLE patients. However, previous studies often lacked detailed information on cancer staging and specific female-related conditions. Our current study addresses these limitations by offering a more nuanced analysis of cancer risk, particularly for cancers affecting the female reproductive system.

We observed distinct incidence rates per 10,000 PYs for various cancers in SLE patients over an extended period, including breast cancer (IR 8.67, 95% CI 6.36–10.98), cervical cancer (IR 3.85, 95% CI 2.31–5.39), and endometrial cancer (IR 1.93, 95% CI 0.84–3.02). Cervical cancer emerged as one of the most common malignancies in SLE patients, corroborating findings from a Danish cohort study, which also reported an increased risk of cervical, vaginal, and vulvar cancers among SLE patients [23],

Table 4 The association between immunosuppressive agents and cancer in SLE patients ($n = 3,047$)

Variables	Case	(%)	Control	(%)	Univariable OR (95% CI)	Multivariable OR[a] (95% CI)
Type of insurance						
National health insurance	260	(93.9)	2,639	(95.3)	Ref	Ref
Medical aid	17	(6.1)	131	(4.7)	1.33 (0.78– 2.26)	1.33 (0.50, 3.55)
Income level						
1–4 quartile	152	(54.9)	1,516	(54.7)	Ref	Ref
5–8 quartile	60	(21.7)	632	(22.8)	0.94 (0.69–1.29)	0.92 (0.67–1.26)
9–12 quartile	28	(10.1)	294	(10.6)	0.95 (0.62– 1.45)	0.91 (0.59–1.39)
13–16 quartile	14	(5.0)	132	(4.8)	1.06 (0.60–1.88)	1.02 (0.57–1.81)
17–20 quartile	23	(8.3)	196	(7.1)	1.18 (0.74–1.89)	0.84 (0.36–2.00)
Immunosuppressive agents						
Never exposed	140	(50.5)	1,490	(53.8)	Ref	Ref
Ever exposed	137	(49.5)	1,280	(46.2)	1.14 (0.89–1.47)	1.03 (0.79–1.35)
Azathioprine						
Never exposed	219	(79.1)	2,199	(79.4)	Ref	Ref
Ever exposed	58	(20.9)	571	(20.6)	1.02 (0.75–1.39)	0.97 (0.71–1.32)
Cyclophosphamide						
Never exposed	248	(89.5)	2,559	(92.4)	Ref	Ref
Ever exposed	29	(10.5)	211	(7.6)	1.43 (0.94–2.17)	1.26 (0.82–1.93)
Cyclosporine						
Never exposed	256	(92.4)	2,565	(92.6)	Ref	Ref
Ever exposed	21	(7.6)	205	(7.4)	1.03 (0.64–1.64)	0.93 (0.57–1.49)
Leflunomide						
Never exposed	274	(98.9)	2,684	(96.9)	Ref	Ref
Ever exposed	3	(1.1)	86	(3.1)	0.34 (0.11–1.09)	0.34 (0.11–1.08)
Methotrexate						
Never exposed	242	(87.4)	2,442	(88.2)	Ref	Ref
Ever exposed	35	(12.6)	328	(11.8)	1.08 (0.74–1.57)	1.11 (0.75–1.61)
Mizoribine						
Never exposed	264	(95.3)	2,598	(93.8)	Ref	Ref
Ever exposed	13	(4.7)	172	(6.2)	0.74 (0.42–1.33)	0.73 (0.41–1.30)
Mycophenolate						
Never exposed	228	(82.3)	2,374	(85.7)	Ref	Ref
Ever exposed	49	(17.7)	396	(14.3)	1.31 (0.93–1.84)	1.09 (0.75–1.58)
Tacrolimus						
Never exposed	261	(94.2)	2,575	(93.0)	Ref	Ref
Ever exposed	16	(5.8)	195	(7.0)	0.80 (0.47–1.37)	0.68 (0.39–1.17)

SLE systemic lupus erythematosus, *OR* odds ratio, CI

[a] Adjusted for insurance type, income level, comorbidities (hypertension, hyperlipidemia, chronic kidney disease, and avascular necrosis), Charlson comorbidity index, and medication (nonsteroidal anti-inflammatory drug, hydroxychloroquine, and glucocorticoids)

This heightened risk of cervical cancer is likely linked to HPV infection [24], as SLE patients are three times more likely to contract HPV infections compared with the general population [25, 26]. Immunosuppressive therapies used to treat SLE may contribute to the greater prevalence of HPV in SLE patients, underscoring the need for regular gynecological screenings to ensure early detection and timely intervention [27]. Additionally, SLE patients have been reported to have a higher risk of thyroid cancer compared with age- and sex-matched non-SLE individuals [28]. Previous meta-analysis revealed a pooled relative risk of 1.78 (95% CI 1.35–2.33) for thyroid cancer in SLE patients [29], suggesting that hormonal influences and genetic predispositions may contribute to this elevated risk [30]. The association between SLE and thyroid autoimmunity further supports the likelihood of increased thyroid cancer risk in SLE patients [31, 32]. Therefore, a heightened awareness of thyroid nodules or

abnormal thyroid activity is essential for early detection and management.

Our study reveals a substantial proportion of SLE patients were diagnosed with cancer at localized (50.8%) and regional (28.3%) stages, suggesting opportunities for early detection. Compared with the general population of Korea, it was demonstrated that approximately 80% of patients were diagnosed at an early stage [33]. Early cancer detection in SLE patients can be attributed to various factors. For example, enhanced medical surveillance and regular monitoring protocols that SLE patients typically undergo could play a crucial role in the early detection of cancer cases. Additionally, increased awareness among both patients and healthcare professionals regarding potential associations between SLE and cancer could prompt a proactive approach to cancer screening. However, our study was limited by the relatively small sample size, making it difficult to conduct a comprehensive comparison of stage distribution among site-specific cancer types. Nevertheless, our findings underscore the necessity for further research with larger cohorts to elucidate patterns of cancer staging among SLE patients facilitating a more thorough understanding of cancer progression and aiding in the development of tailored screening and management strategies for this vulnerable population.

Immunosuppressive agents are essential for managing severe lupus activity, particularly when major organs are involved. Drugs such as azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, and cyclophosphamide have proven effective in controlling disease progression [34]. However, certain immunosuppressive agents could potentially be associated with an increased cancer risk [35, 36]. Despite this concern, evidence for the association between cancer and immunosuppressive agents remains inconsistent. Some studies have reported an elevated risk of cancer with these therapies, while others have found no significant correlation. For example, one cohort study found no increase in overall cancer risk for SLE patients undergoing immunosuppressive therapy [37]. Similarly, our study found no statistically significant association between immunosuppressive therapy and cancer among SLE patients. Nevertheless, it is important to consider that factors such as drug accumulation over time, overall dosage, and the specific types of immunosuppressive agents used may increase the risk of developing certain types of cancer [38]. Therefore, examining subgroups of SLE patients based on these variables could offer more detailed insights.

Our study has several limitations. Firstly, integrating databases from three national institutions may introduce variability in data format, recording methods, and other institutional factors, which could potentially lead to statistical bias because of the anonymized nature of patient information obtained from each institution [39]. Despite these challenges, using a large-scale dataset allowed us to perform a comprehensive analysis of the cancer profile in SLE patients. Secondly, we focused on estimating the cancer incidence in Korean SLE patients without a direct comparison with a non-SLE control group. While this was not the primary aim, such a comparison could have provided additional context for our findings. Thirdly, our analysis of immunosuppressive agents mainly focused on the timing of exposure and did not account for cumulative doses, potential drug interactions, or the effects of concurrent or sequential use of multiple agents and biologics. Although we analyzed the timing of exposure in relation to cancer risk, other factors, such as changes in medication regimens or disease activity over time, were not evaluated. Additionally, the increased use of mycophenolate mofetil as a maintenance therapy in recent years has significantly reduced the number of patients undergoing long-term cyclophosphamide therapy. This shift in practice likely contributed to a reduction in cumulative cyclophosphamide doses and may have influenced the observed cancer risk outcomes. The declining number of long-term cyclophosphamide users may also have impacted the statistical power of our study, limiting its ability to detect small but meaningful associations. These limitations highlight the need for future research to comprehensively evaluate the cumulative impact of drug exposure, interaction effects, and evolving treatment practices on cancer risk. Lastly, although we adjusted for measured risk factors including comorbidities and immunosuppressive medications, by the nature of administrative claims database, information on some relevant risk factors including smoking, alcohol drinking, and family history of cancer were not available. There our results should be interpreted cautiously.

Our study also has several strengths. Firstly, we included a substantial proportion of all SLE patients in Korea, providing a statistically significant sample size for analysis. Additionally, despite the relatively small sample size of cancer cases attributed to the rarity of the disease, we were able to obtain comprehensive results through a population-based database. Moreover, the longitudinal follow-up of SLE patients over an extended period enabled us to assess cancer risk trends over time, offering valuable insights into the long-term effects of SLE on cancer incidence.

Conclusion

Korean SLE patients exhibit increased susceptibility to thyroid cancer and cancers of the breast, cervix, uterus, and ovaries. Over half of these cancers were diagnosed at a localized stage, with a substantial proportion at the

regional stage. The use of immunosuppressive agents was not associated with a significant increase in overall cancer risk. These findings highlight the importance of regular cancer screening and further research into long-term outcomes and contributing factors.

Abbreviations

SLE	Systemic lupus erythematosus
HPV	Human papillomavirus
NHIS	National Health Insurance Service
HIRA	Health insurance review and assessment service
KCCR	Korea Central Cancer Registry
ICD-O-3	International Classification of Diseases for Oncology, 3rd Edition
IR	Incidence rate,
PYs	Person-years
SEER	Surveillance, Epidemiology, and End Results
SD	Standard deviation
CIs	Confidence intervals
OR	Odds ratio
NHL	Non-Hodgkin lymphoma
HL	Hodgkin lymphoma

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13075-025-03482-2.

Supplementary Material 1.

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None.

Authors' contributions
SKC and YKS contributed to the study design, data analyses, interpretation of results, and writing of the manuscript. JYH contributed to the data analyses, interpretation of results, and writing of the manuscript. YJ and SHY contributed to the data analyses and interpretation of results. SYJ and EJJ contributed to the data analyses and interpretation of results. All authors read and approved the final manuscript.

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Data availability
The data underlying this article are available in the article.

Declarations

Ethics approval and consent to participate
The databases extracted from NHID could not be identified directly or through identifiers linked to the subjects. Therefore, our study was exempted by the Institutional Review Board (IRB) of Hanyang University Hospital (IRB file NO. HYUH 2020–05-041).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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