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Trends in cancer incidence among people with human immunodeficiency virus in South Korea: a nationwide National Health Insurance Service data-based study

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ABSTRACT

Background: The application of antiretroviral therapy (ART) in people with human immunodeficiency virus (PWH) has led to a shift in cancer epidemiology.
Methods: PWH were selected from the National Health Insurance Service database from 2002 to 2018. Cancers were identified using the Korean Classification of Disease cancer codes from 2004 to 2019. For incidence analyses, only the first recorded cancer diagnosis per individual was considered. The trends in cancer epidemiology were analyzed according to the duration since HIV diagnosis, categorized as 0–3 years (duration 1), 4–7 years (duration 2), 8–11 years (duration 3), and 12–15 years (duration 4). Analyses were also stratified by the period before and after the implementation of expanded cancer screening programs in Korea: 2004–2011 (period 1) and 2012–2019 (period 2).
Results: Among 15,110 PWH, 774 developed cancers during follow-up. Of these, 241 were ADCs (234.26 per 100,000 person-years) and 533 were NADCs (523.08 per 100,000 person-years). The proportion of ADCs among all cancers was 37.1%, 21.1%, 20.0%, and 13.5% across increasing durations since HIV diagnosis.
Conclusions: In the ART era, NADCs represent an increasing disease burden in PWH, underscoring the importance of cancer screening following HIV diagnosis.
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1. Introduction

The Korea Centers for Disease Control and Prevention has monitored the status of human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) since 1985, when the

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first HIV diagnosis in Korea was reported [1]. As of 2019, South Korea had 13,857 people with HIV (PWH), including 1222 individuals newly diagnosed in 2019 [1]. The number of Korean PWH is steadily increasing, with approximately 1200 new HIV-positive individuals annually since 2016 [1]. Highly active antiretroviral therapy (ART) was introduced in Korea in 1997 [2–4], after which the survival rates among PWH improved substantially, consistent with trends in other resource-rich countries [2,4–6].

With the advent of ART, malignancies have become a major cause of death among PWH [7–10]. Historically, AIDS-defining cancers (ADCs), such as Kaposi's sarcoma (KS), non-Hodgkin lymphoma (NHL), and invasive cervical cancer, have been highly prevalent among PWH [11,12]. However, improved survival following ART has increased the relative importance of non-AIDS-defining cancers (NADCs) alongside ADCs [13–16]. ART application has also led to a shift in cancer epidemiology. Notably, a significant increase in NADCs and a decrease in ADCs have been reported in the United States and Europe [15–21]. However, research conducted in South Korea in this context remains limited, highlighting the need for further studies.

This study aimed to examine the epidemiological trends in cancer among Korean PWH in the ART era, including cancer incidence, characteristics, and mortality, using the National Health Insurance Service (NHIS) database over a 16-year period. The trends in cancer epidemiology were analyzed according to the duration since HIV diagnosis and the period before and after the implementation of expanded cancer screening programs in Korea, while acknowledging that changes in the age distribution of people with HIV may substantially influence these temporal patterns.

2. Material and methods

2.1. Data sources

Data from the NHIS database from 2002 to 2019 was used to evaluate recent trends and characteristics of malignancies among PWH in South Korea. The NHIS is a single insurer managed by the Korean government and provides information on healthcare utilization of 97% of the Korean population [22]. To minimize potential distortions in healthcare utilization and cancer diagnosis associated with the COVID-19 pandemic, we restricted the analysis to claims data through 2019.

2.2. Study design and population

In this nationwide, retrospective, descriptive cancer epidemiological study, PWH were selected from the NHIS database from 2002 to 2018 based on the Korea Classification of Disease (KCD) codes B20, B21, B22, B23, and B24. Among patients with a coded diagnosis of HIV infection, those without rare and intractable disease (RID) code V103 were excluded. In Korea, PWH are registered in the national registry for rare and intractable diseases and receive government reimbursement for medical expenses; therefore, the RID code is reliable for PWH. Although NHIS data were available from 2002 onward, the RID code for HIV infection (V103) has been in place since 2004. Therefore, claims data from 2002 to 2003 were treated as the wash-out period, and incident HIV cases were identified from 2004 onward. Accordingly, although we extracted data from 2002 to 2018, our analytic cohort effectively comprised PWH observed between 2004 and 2018. Individuals with the RID code V103 who had diagnostic codes B20–B24 prior to RID registration were excluded, as HIV has been registered in the RID system since January 2004. Patients aged >90 years at HIV diagnosis and those who visited the outpatient clinic only once were also excluded.

By the end of 2018, 79,247 patients with a coded diagnosis of HIV infection (KCD codes B20–B24) were identified, of whom 63,022 patients without the RID code V103 were excluded. An additional 1110 patients with codes B20–B24 before 2004 were excluded, even if they had the RID code V103. Five patients aged >90 years at HIV diagnosis were also excluded.

Cancers were confirmed using KCD cancer codes (C-codes) between 2004 and 2019. Patients diagnosed with malignancies before the HIV diagnosis were excluded. Individuals with a history of cancer prior to HIV diagnosis remained in the cohort but were considered at risk only for new cancer diagnoses occurring after HIV diagnosis. Cancer incidence was analyzed over time after the HIV diagnosis. Cancer trends were analyzed by classifying them into ADCs and NADCs based on the 1993 CDC classification criteria [11]. KS, NHL, and invasive cervical cancer were defined as ADCs, whereas all other cancers were defined as NADCs [11]. In patients diagnosed with multiple cancers, the initial analysis was based on the first diagnosis of cancer, and when multiple cancers were diagnosed simultaneously, the analysis was performed based on the code registered as a major disease.

The time since HIV or AIDS diagnosis was categorized into four groups: 0–3 years (duration 1), 4–7 years (duration 2), 8–11 years (duration 3), and 12–15 years (duration 4). Because incident HIV cases were identified from 2004 and follow-up extended through 2019, the maximum possible duration of follow-up was approximately 15 years; therefore, no individuals had a duration exceeding 15 years within the study period.

The year of cancer diagnosis was classified into two observational periods (2004–2011 and 2012–2019) based on the calendar year of cancer diagnosis, rather than the year of HIV diagnosis. Person-time was accrued from the date of HIV diagnosis until cancer diagnosis, death, or the end of follow-up (December 31, 2019). This period classification was used for descriptive temporal comparison only and was not intended to imply a causal relationship between the expansion of the national cancer screening program and changes in cancer incidence [23,24].

Exposure to ART was defined as the prescription of ≥1 antiretroviral medication for >30 days.

2.3. Statistical analysis

Descriptive statistics were used to analyze the baseline characteristics. Categorical variables were presented as numbers and percentages, whereas continuous variables were described using means and standard deviations. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

2.4. Ethics statement

This study was approved by the Institutional Review Board of Incheon St. Mary's Hospital with a waiver of informed consent.

3. Results

3.1. Baseline characteristics

This study enrolled 15,110 PWH between 2002 and 2018 (Figure 1), including 13,462 (89.09%) males and 1648 (10.91%) females. The mean age at HIV diagnosis was 39.71 years overall, 39.24 years for men, and 43.53 years for women.

3.2. Epidemiology of malignancy in PWH

Malignancies were identified in 1041 patients (6.88%) among PWH between 2004 and 2019. Of these, 267 individuals had a cancer diagnosis prior to HIV diagnosis; these cases were excluded

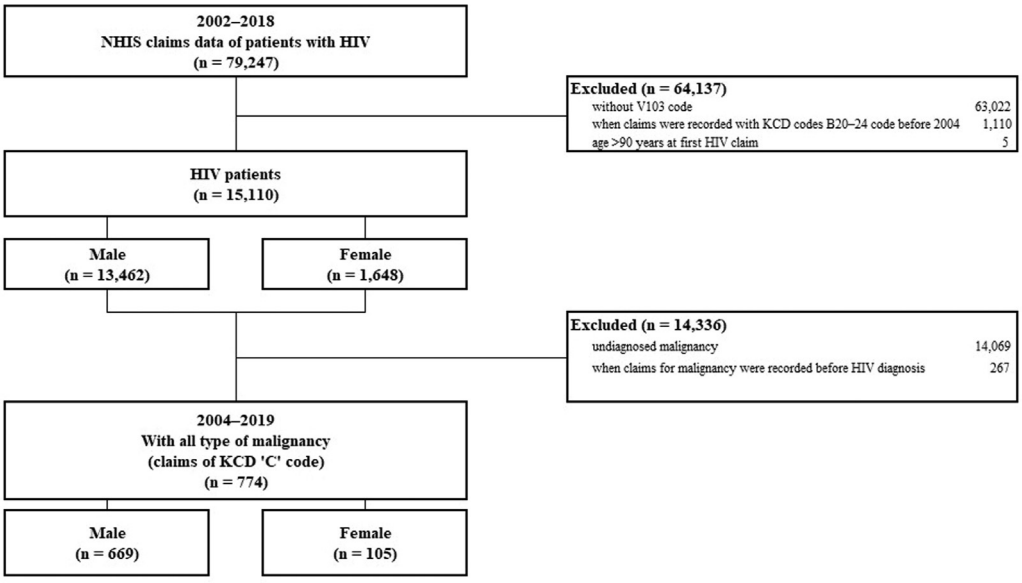


Figure 1. Flowchart of population selection.

from the incidence analysis, and only cancers occurring after HIV diagnosis were considered incident events. Finally, 774 individuals diagnosed with cancer of the enrolled 15,110 PWH were analyzed retrospectively, including 669 (4.96%) males and 105 (6.37%) females (Figure 1).

During the study period, 964 cancer episodes were diagnosed in 774 of the 15,110 PWH, including 612,135, 26, and 1 with a single, two, three, and four primary cancers, respectively. In cases of multiple cancers, only the first or primary diagnosis of cancer was included in the analysis. In 32 participants, multiple cancers were diagnosed at the same time; therefore, the analysis was performed based on the cancer registered as a major disease. Accordingly, 774 of the 964 cases were included in the analysis.

Among the 774 patients with cancer, 241 (234.26 per 100,000 person-years) were diagnosed with ADCs and 533 (523.08 per 100,000 person-years) with NADCs. During follow-up, 48% of PWH diagnosed with cancer died; this represents a crude mortality proportion rather than a time-to-event survival estimate. In both female and male PWH, NHL was the single most common cancer among all cancers, including NADCs and ADCs. The mean patient age at cancer diagnosis was 52.87 years. The mean ages for women and men at cancer diagnosis were 52.85 and 52.97 years, respectively. At cancer diagnosis, 383 (49.48%) patients were receiving ART, 19 (2.46%) discontinued ART, and 372 (48%) were naïve to ART.

Of the 241 ADCs, most cases were NHL (n = 200,193.86 per 100,000 person-years), followed by KS (n = 32, 30.85 per 100,000 person-years) and invasive cervical cancer (n = 9, 8.67 per 100,000 person-years). KS was diagnosed only in men. At ADC diagnosis, the mean age was 46.39 years, and 127 (52.69%) patients were receiving ART treatment with 316.76 days of mean ART duration. During follow-up, 48%, 53%, and 44% of patients diagnosed with NHL, KS, and cervical cancer died, respectively; these figures represent crude mortality proportions rather than time-to-event survival estimates.

Of the 533 NADCs, lung cancer (n = 88, 84.89 per 100,000 person-years) was the most commonly observed, followed by stomach (n = 80, 77.22 per 100,000 person-years) and colorectal (n = 77, 74.31 per 100,000 person-years) cancers. Lung (n = 82, 90.25 per 100,000 person-years), stomach (n = 72, 79.29 per 100,000 person-years), and colorectal (n = 72, 79.30 per 100,000 person-years) cancers were the most common NADCs in men. Thyroid (n = 15,118.56 per 100,000 person-years), breast (n = 15,118.38 per 100,000 person-years), stomach (n = 8, 62.94 per 100,000 person-years), and liver/pancreas/biliary (n = 8, 62.86 per 100,000 person-years) cancers were the most common NADCs in women. At NADC diagnosis, the mean age was 55.79 years, and 256 (48.03%) patients were receiving ART with 720.15 days of mean ART duration. During follow-up, 73%, 46%, and 43% of patients diagnosed with lung, stomach, and colorectal cancers died, respectively; these values reflect crude mortality proportions (Tables 1 and 2).

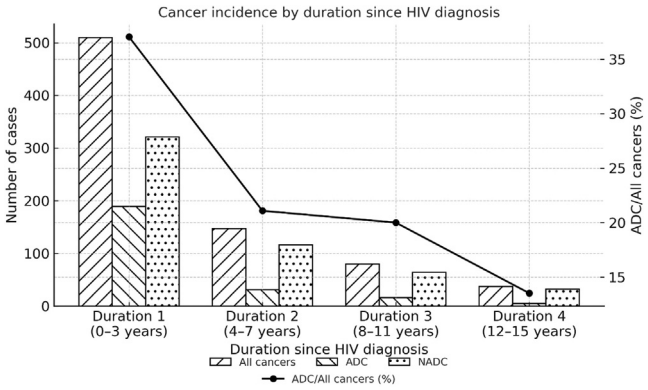


Figure 2. Distribution of cancer cases by duration since HIV diagnosis. Bar graphs show the number of all cancers, ADCs, and NADCs diagnosed within each duration category. The line graph represents the proportion of ADCs among all cancers (%) for each duration. Person-time denominators for each duration category were not available; therefore, this figure presents descriptive case counts and proportions rather than incidence rates. Patterns in the bars are used to distinguish cancer categories for black-and-white printing.

3.3. Trends of malignancy in PWH from 2004 to 2019

Both ADCs and NADCs were most frequently diagnosed within the first year after HIV diagnosis (<1 year), with 130 ADC and 193 NADC cases identified during this period. Across all duration categories, the number of NADC cases exceeded that of ADC cases. The proportion of ADCs among all cancers was 37.06%, 21.09%, 20.00%, and 13.51% for durations 1, 2, 3, and 4, respectively (Figure 2).

Table 1
Epidemiological characteristics of cancers diagnosed in people with HIV, by cancer type

	N (PY100,000)/Mean age			n/N (%)
	Total	Male	Female	Mortality[a]
Age at cancer diagnosis	774 (766.11)/52.9	669 (754.34)/52.9	105 (855)/53.0	375/774 (48)
AIDS-defining cancers	241 (234.26)/46.4	211 (233.79)/45.9	30 (237.65)/49.7	128/267 (48)
Kaposi's sarcoma	32 (30.85)/45.3	32 (35.21)/45.3	-	20/38 (53)
Cervical cancer	9 (8.67)/46.9	-	9 (70.82)/46.9	4/9 (44)
Non-Hodgkin lymphoma	200 (193.86)/46.5	179 (197.97)/46.0	21 (165.81)/50.9	108/224 (48)
Non-AIDS-defining cancers	533 (523.08)/55.8	458 (511.75)/56.0	75 (604.82)/54.3	278/559 (50)
Brain and CNS	25 (24.08)/50.1	23 (25.28)/50.1	2 (15.69)/49.5	18/28 (64)
Bladder	11 (10.59)/61.7	11 (12.09)/61.7	-	4/13 (31)
Breast	16 (15.41)/48.0	1 (1.10)/72.0	15 (118.38)/46.4	4/17 (24)
Colorectal	77 (74.31)/54.7	72 (79.30)/54.5	5 (39.28)/57.8	38/89 (43)
Esophagus	7 (6.74)/52.4	7 (7.69)/52.4	-	1/7 (14)
Hodgkin lymphoma	17 (16.37)/50.2	15 (16.48)/49.1	2 (15.69)/58.0	7/20 (35)
Kidney	2 (1.93)/41.0	2 (2.20)/41.0	-	1/2 (50)
Leukemia	5 (4.81)/55.8	4 (4.39)/52.3	1 (7.85)/70.0	9/10 (90)
Liver/Pancreas/Biliary	73 (70.40)/56.9	65 (71.52)/55.4	8 (62.86)/68.5	59/76 (78)
Lung	88 (84.89)/60.1	82 (90.25)/60.6	6 (47.18)/52.5	107/147 (73)
Melanoma	1 (0.96)/20.0	-	1 (7.85)/20.0	1/2 (50)
Multiple myeloma	8 (7.70)/50.5	7 (7.69)/79.4	1 (7.85)/58.0	4/8 (50)
Musculoskeletal	4 (3.85)/55.3	3 (3.29)/53.0	1 (7.84)/62.0	5/8 (63)
Oropharynx	22 (21.19)/53.8	20 (21.98)/53.5	2 (15.69)/57.0	9/26 (35)
Soft tissue	15 (14.44)/57.2	11 (12.08)/53.2	4 (31.42)/68.3	10/20 (50)
Stomach	80 (77.22)/59.4	72 (79.29)/59.8	8 (62.94)/56.0	39/84 (46)
Thyroid	36 (34.72)/50.7	21 (23.09)/52.2	15 (118.56)/48.5	1/37 (3)
Urogenital	28 (26.98)/58.9	25 (27.49)/59.0	3 (23.54)/57.7	10/29 (34)
Other	16 (15.41)/48.8	15 (16.48)/47.9	1 (7.84)/62.0	45/66 (68)
Other hematologic	2 (1.93)/59.5	2 (2.20)/59.5	-	2/2 (100)

Data are presented as number of cases (n), incidence rate per 100,000 person-years (PY), and mean age at cancer diagnosis (years). Mortality is reported as crude all-cause mortality observed during follow-up (n, %). Incidence rates were calculated using total person-time accrued after HIV diagnosis. Sex-stratified values are presented where applicable.
Abbreviation: PY = person-years
[a] For mortality, if a patient had multiple cancers at the time of death, each cancer was counted separately in both the numerator and the denominator.

Table 2
ART-related characteristics at cancer diagnosis among people with HIV

	N	Diagnosis age Mean ± SD		ART status at cancer diagnosis N (%)			ART duration (day) Median (IQR)
		At cancer	At HIV	On ART	Discontinued	Naïve	
Total	774	52.9 ± 13.5	49.9 ± 13.2	383 (49)	19 (2)	372 (48)	0 (0–753)
AIDS-defining cancers	241	46.4 ± 12.3	44.4 ± 12.5	127 (53)	4 (2)	110 (46)	0 (0–261)
Kaposi's sarcoma	32	45.3 ± 11.9	44.0 ± 12.7	19 (59)	-	13 (41)	0 (0–89)
Cervical cancer	9	46.9 ± 14.9	43.4 ± 15.7	6 (67)	-	3 (33)	931 (0–1887)
Non-Hodgkin lymphoma	200	46.5 ± 12.3	44.5 ± 12.3	102 (51)	4 (2)	94 (47)	0 (0–252)
Non-AIDS-defining cancers	533	55.8 ± 13.0	52.3 ± 12.8	256 (48)	15 (3)	262 (49)	0 (0–1048)
Brain and CNS	25	50.1 ± 11.5	49.6 ± 11.4	5 (20)	1 (4)	19 (76)	0 (0–0)
Bladder	11	61.7 ± 11.0	57.9 ± 9.7	8 (73)	-	3 (27)	1054 (0–2000)
Breast	16	48.0 ± 9.7	45.1 ± 10.1	4 (25)	-	12 (75)	0 (0–3.5)
Colorectal	77	54.7 ± 13.8	50.8 ± 13.9	46 (60)	2 (3)	29 (38)	295 (0–1597)
Esophagus	7	52.4 ± 11.0	46.6 ± 5.1	2 (29)	-	5 (71)	0 (0–2929)
Hodgkin lymphoma	17	50.2 ± 11.0	45.9 ± 11.7	16 (94)	1 (6)	-	753 (38–1309)
Kidney	2	41.0 ± 1.4	38.0 ± 1.4	1 (50)	-	1 (50)	399 (0–798)
Leukemia	5	55.8 ± 11.5	54.8 ± 12.5	-	-	5 (100)	0 (0–0)
Liver/pancreas/biliary	73	56.9 ± 13.3	53.1 ± 13.6	31 (42)	3 (4)	39 (53)	0 (0–730)
Lung	88	60.1 ± 11.9	56.7 ± 11.5	44 (50)	2 (2)	42 (48)	0 (0–1057)
Melanoma	1	20.0 ±	20.0 ±	1 (100)	-	-	110 (110–110)
Multiple myeloma	8	50.5 ± 14.4	49.0 ± 13.2	1 (13)	2 (25)	5 (63)	0 (0–0)
Musculoskeletal	4	55.3 ± 21.9	55.0 ± 21.8	2 (50)	-	2 (50)	0 (0–131.5)
Oropharynx	22	53.8 ± 10.6	49.5 ± 10.8	16 (73)	-	6 (27)	242 (0–2129)
Soft tissue	15	57.2 ± 17.5	52.6 ± 15.9	10 (67)	-	5 (33)	588 (0–1048)
Stomach	80	59.4 ± 12.0	56.0 ± 11.6	33 (41)	-	47 (59)	0 (0–1398)
Thyroid	36	50.7 ± 10.8	46.8 ± 10.5	12 (33)	2 (6)	22 (61)	0 (0–289.5)
Urogenital	28	58.9 ± 13.8	54.9 ± 13.5	14 (50)	1 (4)	13 (46)	46 (0–1814)
Other	16	48.8 ± 9.9	46.9 ± 10.9	9 (56)	1 (6)	6 (38)	20.5 (0–916.5)
Other hematologic	2	59.5 ± 12.0	59.0 ± 11.3	1 (50)	-	1 (50)	7 (0–14)

Data are presented as number of cases (n), mean ± standard deviation (SD) for age at cancer and HIV diagnosis, and n (%) for ART status at cancer diagnosis. ART duration is reported as median (interquartile range, IQR) in days.
Abbreviations: ART = antiretroviral therapy; IQR = interquartile range.

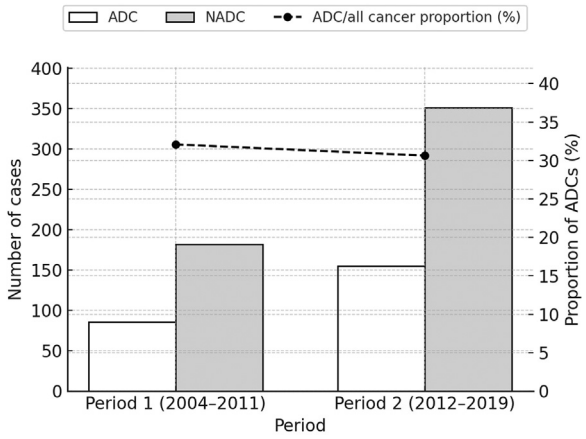


Figure 3. Distribution of ADC and NADC cases by calendar period (2004–2011 vs 2012–2019). Period 1 (2004–2011) and Period 2 (2012–2019) are compared. Bars represent the number of ADC and NADC cases, and the dashed line indicates the proportion of ADCs among all cancers. Period-specific person-time denominators were not available; therefore, this figure presents descriptive case counts and proportions rather than incidence rates. The period classification was used for descriptive comparison only and does not imply a causal relationship with the expansion of the national cancer screening program.

When classified by calendar period, 86 ADCs and 182 NADCs were diagnosed in period 1 (2004–2011), and 155 ADCs and 351 NADCs in period 2 (2012–2019). The proportion of ADCs among all cancers was 32.09% in period 1 and 30.63% in period 2 (Figure 3).

Figures 2 and 3 present descriptive distributions of cases by duration and calendar period.

4. Discussion

This study revealed that between 2004 and 2019, the crude incidence of NADCs (n = 533) was at least two-fold higher than that of ADCs (n = 241) among PWH in Korea. The proportion of ADCs among cancers tended to decrease with increasing number of years since HIV/AIDS diagnosis, implying that prolonged survival in people who survived HIV infection increases the likelihood of developing NADCs due to aging.

When classified by period, the more recent the period, the more the overall cancers, NADCs, and ADCs, whereas the proportion of ADCs in the total cancer decreased. In recent years, more active cancer surveillance programs have been implemented in Korea [23,24]. Consequently, a greater number of overall cancers, NADCs, and ADCs may have been detected in Korean PWH as well as in the general population. The division into two calendar periods was intended for descriptive comparison only and does not imply a direct causal effect of national cancer screening expansion on cancer incidence. The temporal increase in diagnosed cancers should therefore be interpreted cautiously, as it may reflect changes in detection practices and population structure rather than a true increase in underlying cancer risk. The decreasing proportion of ADCs suggests that the relative contribution of NADCs to the overall cancer burden in Korean PWH is increasing.

Previous studies in the United States and Europe on cancers in PWH have reported a decrease in ADCs and an increase in NADCs following the introduction of ART [15–21]. In contrast to Western cohorts, no such finding was observed in our study or in previous Korean national studies conducted in 2006, 2009, and 2022 [25–27]. However, a Korean domestic study in 2017 and another study in 2022 reported a gradually decreasing trend of ADCs, although the difference was not statistically significant [28,29]. Unlike earlier domestic studies, the most recent Korean study, published in 2023, showed a decrease in ADCs and a corresponding increase in NADCs [30].

The findings regarding specific cancer types in the present study indicated that NHL (an ADC) was the most frequently observed malignancy in PWH—a result consistent with previous studies conducted in Korea [25–30]. Among the 533 NADCs, lung cancer was the most common—a result aligning with previous Korean studies conducted in 2017 and 2023 [29,30]. However, in two Korean nationwide cohort studies from 2022, liver cancer was the most frequently observed NADC, whereas the distribution of other NADCs varied between the studies [26,28]. Consistent with our findings, previous studies conducted in Europe and the United States have reported either NHL or KS as the most common ADCs, depending on the region and time period [16,20,31]. However, NHL has generally been reported more frequently than KS [16,20,31]. Among the NADCs, lung, anal, and liver cancers are the most prevalent in Europe and the United States, although their prevalence varies across time and geographic regions [16,20,31].

The major difference was observed in the incidence of NHL and thyroid cancer between PWH and the general population. Compared to the general population, the incidence of NHL was markedly higher in our cohort [32], consistent with a previous Korean cohort reporting the standardized incidence ratio for NHL of 15.62 [26]. The distribution of the other cancer types largely mirrored that of the most commonly diagnosed cancers in the general population [32]. However, thyroid cancer, the most frequently diagnosed cancer in the general population, was uncommon among PWH [32]. This discrepancy is unlikely to suggest a protective effect of HIV against thyroid cancer but may reflect the low proportion of women among PWH in South Korea. As of 2023, women accounted for 6.3% of the cumulative reported HIV cases [33]. In the general Korean population, the incidence of thyroid cancer is higher in women than in men [32]. According to the *Cancer Statistics in Korea, 2019*, thyroid cancer was the most prevalent cancer overall, with a crude prevalence of 1467.6 and 330.2 per 100,000 in women and men, respectively, indicating a significantly higher incidence in women [32]. The lower incidence of thyroid cancer among PWH may be attributable to the predominance of male participants (89.09%) in this study.

In this analysis, a notable characteristic of cancer diagnoses was that most cancers were detected within the first year of HIV diagnosis. Both ADCs and NADCs had the highest incidence in the year of HIV or AIDS diagnosis, with a prevalence of <1 year. This suggests that HIV infection may have been diagnosed at a late stage, when significant immunosuppression had already developed, ultimately contributing to cancer. In South Korea, the proportion of late presenters, generally defined as individuals with a CD4+ T-cell count <200 cells/mm³ at HIV diagnosis, remains substantial (16.3%–39.4%), indicating a delayed diagnosis in a significant number of cases [34,35].

In our study, individuals diagnosed with NADCs had a higher mean age at diagnosis (55.79 years) than those diagnosed with ADCs (46.39 years). This age difference is consistent with the findings of a Korean single-center cohort study that reported a median age of 53 years for NADCs and 47 years for ADCs at cancer diagnosis [29]. Similar trends were observed in European and United States studies, where patients diagnosed with NADCs were significantly older than those with ADCs [31,36]. These findings suggest that chronological aging likely plays a substantial role in the increasing burden of NADCs, whereas ADCs may be more closely related to HIV-associated immunologic factors.

As a retrospective descriptive study, we were unable to determine whether deaths were cancer-related or due to other causes; however, 48% of PWH diagnosed with cancer died during follow-up. Formal time-to-event survival analyses (e.g., Kaplan–Meier estimates) were not performed; therefore, these crude mortality

proportions should be interpreted cautiously. The observed mortality burden may be influenced by multiple factors, including delayed cancer detection, delayed HIV diagnosis, oncogenic viral co-infections, and lifestyle-related risk factors such as smoking [14,19,34,35,37,38].

Our study also has some limitations. First, we only used the NHIS data; therefore, we did not have access to clinical data or medical records, including the cause of mortality. For instance, no information on CD4+ lymphocyte counts at HIV diagnosis or malignancy was available. Second, our study did not investigate other significant cancer risk factors such as genetic background, comorbidities, family history, lifestyle habits such as smoking and drinking, and viral co-infection. Third, universal ART, defined as initiating ART regardless of CD4 count, were widely recommended by the WHO in 2015 [39]. In South Korea, this strategy was progressively adopted between 2014 and 2016 and has since become the standard of care [40]. The majority of the observation period in this study included the period before the introduction of universal treatment. Therefore, further research on trends in cancer incidence before and after the introduction of universal treatment is necessary. Fourth, although we reported incidence rates based on person-years of follow-up, age-standardized incidence rates and fully adjusted comparisons across calendar periods were not performed. Therefore, residual confounding by age, sex, and duration since HIV diagnosis may have influenced comparisons of temporal trends. Fifth, we did not calculate calendar period–specific incidence rates. Changes in cohort size and follow-up time across periods may therefore have influenced comparisons between period 1 and period 2.

Nevertheless, the major strength of our study is the inclusion of nationwide longitudinal data on Korean PWH, derived from the RID registry and NHIS. As the RID code for HIV is strictly managed and linked to government reimbursement of medical expenses, our study represents almost all Korean PWH. Moreover, this was a nationwide cancer epidemiological study with up to 16 years of follow-up.

5. Conclusions

In the ART era, from 2004 to 2019, the crude incidence of NADCs was higher than that of ADCs among Korean PWH. Furthermore, the decreased proportion of ADCs in the total cancers suggests that the disease burden of NADCs is becoming increasingly significant in PWH. However, NHL is the most common malignancy among PWH, underscoring the importance of ADCs. Both ADCs and NADCs peaked in the first year after HIV diagnosis, highlighting the importance of cancer screening at diagnosis, while the rise in cancer cases following expansion of the national screening program underscores the need for ongoing screening thereafter.

Author contributions

Youn Jeong Kim and Yeon Jeong Jeong contributed to the conceptualization of the study. Sang Il Kim and Yoon Hee Jun designed the methodology. Boyoung Park and Yunsu Choi was primarily responsible for data acquisition. Jun Yong Choi, Jung Ho Kim, Hyo Youl Kim, Jang Wook Sohn and Joon Young Song performed the formal analysis and contributed to visualization. Yeon Jeong Jeong was responsible for writing the original draft of the manuscript. Shin-Woo Kim, YeonJae Kim, and Hee Jung Choi critically reviewed and edited the manuscript. Youn Jeong Kim provided overall supervision. All authors read and approved the final manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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