Cancer Incidence and Survival among Adolescents and Young Adults in Korea



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Abstract

Background: In Korea, cancer is the third leading cause of death among adolescents and young adults (AYAs). However, cancer incidence and survival trends among AYAs (15–29 years) have never been studied in Korea. Therefore, this study aimed to investigate the incidence and relative survival rates and their trends among AYAs in Korea.

Materials and Methods: Cancer incidence data from 1999–2010 were obtained from the Korea Central Cancer Registry (KCCR). Each cancer was classified into subgroups according to the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) AYA site recode. Percent distributions, age-specific incidence rates, age-standardized incidence rates per million, and annual percent changes (APCs) were calculated for AYAs according to sex. Five-year relative survival rates were estimated for cases diagnosed between 1993 and 2010 and followed up to 2011.

Results: The age-standardized incidence rates of all cancers combined were 196.4 and 367.8 per million for males and females, respectively (male-to-female (M/F) ratio: 0.5). The age-standardized incidence rates increased from 208.7 per million in 1999 to 396.4 per million in 2010, and the APC was 6.3% (P<0.001). The five most common cancers among AYAs were thyroid carcinoma, non-Hodgkin lymphoma, stomach carcinoma, breast carcinoma, and acute myeloid leukemia. In males, the 5-year relative survival rate improved, from 46.5% in 1993–1995 to 75.9% in 2006–2010. In females, the 5-year relative survival rate also improved, from 66.7% in 1993–1995 to 89.1% in 2006–2010.

Conclusions: Our study showed increases in cancer incidence and improvements in the 5-year relative survival rate among Korean AYAs. This study also provides additional data regarding temporal and geographic trends in cancer that may enhance future efforts to identify factors affecting cancer incidence and responses to treatment among AYAs.

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Introduction

Cancers in adolescents and young adults (AYAs; 15–29 years) have distinctive characteristics compared with cancers in children and older cohorts.

The incidence pattern of specific cancer types differ between AYAs and younger and older patients. In addition, the genetic and histologic patterns of cancers among AYAs differ from those of older patients [1]. Because cancer is uncommon among AYAs, this patient population has not drawn public attention compared with the pediatric and adult populations. However, an increase in cancer incidence among AYAs has been reported in Europe [2–4] and the United States [5].

Over 200,000 new cancer patients are diagnosed annually in Korea [6], and approximately 3,200 (1.6%) AYAs were diagnosed with cancer in Korea in 2010. According to the U.S. National Cancer Institute Surveillance Epidemiology and End Results (SEER), 2% of all invasive cancers are diagnosed in individuals aged 15–29 years [5]. Although only a small proportion of all

malignancies are diagnosed in AYAs, high-grade and later-stage tumors of certain cancers are more likely to be diagnosed in this patient population [1]. Furthermore, cancer diagnosis in AYAs can greatly influence future quality of life and life expectancy [7]. In fact, in Korea, cancer is the leading cause of death among AYAs, after suicide and traffic accidents [8]. However, to the best of our knowledge, cancer incidence and survival among AYAs in Korea have never been studied. Therefore, this study aimed to investigate cancer incidence and survival among AYAs in Korea. We examined the trends in cancer incidence rates from 1999 to 2010 and the trends in relative survival rates from 1993 to 2010 among Korean AYAs.

Materials and Methods

Data Sources

In 1980, the Korean Ministry of Health and Welfare started the Korea Central Cancer Registry (KCCR), a nationwide,

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hospital-based cancer registry [9]. Until 1998, the registry collected cancer cases from more than 180 hospitals in Korea annually, and these data represent 80–90% of all cancer incidence in Korea [10]. Since 1999, the KCCR has covered the entire population under the population-based cancer registry program [6]. The Korea National Cancer Incidence Database (KNCIDB) KCCR data from 1999 to 2002 and from 2003 to 2007 have been published in Cancer Incidence in Five Continents, which reflects the completeness and validity of the incidence data [11].

Incidence data were collected for Korean AYAs aged 15–29 years who were newly diagnosed with cancer between 1999 and 2010. The incidence data were collected from the KNCIDB of the KCCR and included age, sex, diagnosis date, primary tumor site, morphology, the diagnostic method, and stage at diagnosis.

Survival data for individuals aged 15–29 years who were newly diagnosed with cancer from 1993–2010 were obtained from the KNCIDB, and the patients' vital status was followed until December 31, 2011. The survival analysis was based on the KNCIDB data and mortality data obtained from Statistics Korea.

Case Definition

In accordance with the guidelines of the National Cancer Institute SEER Program [5] and the Canadian Cancer Society [12] in this study, AYAs were defined as adolescents and young adults aged 15–29 years.

Cancer sites were coded by primary site and morphology using the International Classification of Diseases for Oncology (third edition) [13]. Cancers were classified according to the SEER AYA scheme, which is based on a modified version of the International Classification of Childhood Cancer [5]. In particular, the SEER AYA scheme is based on an updated classification proposed by Barr et al. and is composed of ten major groups and second- and third-level subgroups according to the site of origin [14].

Incidence

Age-specific incidence rates per million were analyzed in each diagnostic subgroup according to the age at diagnosis (15–19 years, 20–24 years, and 25–29 years), and age-standardized rates (ASRs) according to sex were calculated using the world standard population defined by the World Health Organization [15]. Trends in annual ASRs were calculated using the annual percent change (APC), which was estimated using the following formula: $100 \times (e^{\beta}-1)$, where β is the slope calculated from a linear regression of log age-standardized incidence rates in a calendar year [16]. The male-to-female (M/F) ratio was the ratio of the ASR among males to the ASR among females. Comparisons of age-standardized incidence rates in males and females were calculated by the direct method [17].

Survival

Relative survival rates were estimated according to the time period: 1993–1995, 1996–2000, 2001–2005 and 2006–2010. Relative survival rates according to the diagnostic group were calculated by dividing observed survival by expected survival among comparable groups in the general population [18] using the Ederer II method [19]. These survival rates were estimated using "complete analysis", which included "right-censored" patients. Due to this inclusion of the early survival experience of more recently recruited patients, the analysis provided more up-todate and precise survival rates were also calculated. Additionally, the effects of sex, diagnostic group, and time period on survival were assessed using a relative excess risk model. All analyses were performed using SAS version 9.2.

Results

Incidence

From 1999 to 2010, 39,639 cancer cases (2.3%) of all cancer patients) were newly diagnosed in AYAs. Of these cases, 14,016 (35.4%) and 25,623 (64.6%) cases were diagnosed in males and females, respectively. According to the age at diagnosis, 6,396 (16.1%) cases were diagnosed at 15–19 years of age, 10,433 (26.3%) cases were diagnosed at 20–24 years, and 22,810 (26.3%) cases were diagnosed at 25–29 years.

The number of cases per age group (15-19 years, 20-24 years) and 25-29 years) by sex, age-specific incidence rates, and age-standardized incidence rates among both males and females and M/F ratios according to the diagnostic group are shown in Table 1.

Between 1999 and 2010, the overall age-standardized incidence rate of cancers among AYAs in Korea was 279.9 per million. Cancer incidence was higher in females (367.8 per million) than in males (196.4 per million), and for all cancers combined, the male/ female ratio was 0.5 (P<0.05). The higher rate among females was largely due to a much higher incidence rate of thyroid carcinomas (24.7 per million among males vs. 154.2 per million among females). Because the incidence rate of thyroid carcinoma was unusually high, the age-standardized incidence rates of all cancers combined were recalculated, excluding thyroid carcinoma (group 8.1). Removing thyroid carcinomas, the overall ASR of cancers was 192.2 per million (171.7 per million for males and 213.6 per million for females) (Table 1).

The incidence increased with age, from 150.9 in males and 160.4 in females per million at 15–19 years of age to 170.7 in males and 305.6 in females per million, respectively, at 20–24 years of age. The incidence further increased at 25–59 years of age, to 273.4 in males and 663.3 in females per million, respectively (Table 1). The incidence rates were correlated with age group for most subtypes, with the notable exceptions of leukemia and osseous/chondromatous neoplasms, which were more common among younger AYAs (Table 1).

Table 2 shows the secular trends in cancer incidence among AYAs from 1999 to 2010 according to the diagnostic group. The incidence rate of all cancers among AYAs significantly increased, from 208.7 per million in 1999 to 396.4 per million in 2010 (APC = 6.3%; *P*<0.05). Over the studied time period, there was also a steady increase in the incidence of cancer among AYAs for both males (APC = 3.9%) and females (APC = 7.8%) (Figure 1).

Most cancer sites showed a trend of increasing incidence, with the exception of unspecified malignant neoplasms (group 10) among AYAs (APC = -10.9%). For miscellaneous specified neoplasms, NOS (group 9), a rapid increase in the incidence rate was observed for both sexes (APC = 9.8%), but the number of cases was small. For carcinomas (group 10), a large increase in the incidence rate was also observed among AYAs (APC = 9.4%). In particular, among carcinomas, the incidence of thyroid carcinoma showed the most rapid increase (APC = 17.9%; P<0.05). The annual percent change in all cancer combined, excluding thyroid carcinoma, was 1.8% (P<0.05) among AYAs (Table 2), with 1.9%(P<0.05) for males and 1.8% (P<0.05) for females (data not shown). Although the incidence of kidney carcinoma also exhibited a notable increase (APC = 9.1%), the number of cases was small.

The incidence of lymphomas (group 2) exhibited a large increase among AYAs (APC = 5.3%, P<0.05). In particular, Hodgkin lymphoma rapidly increased in incidence (APC = 9.1%, P<0.05) (Table 2).

Table 1. Number of cases, age-specific incidence rates, and age-standardized incidence rates from 1999 to 2010 according to sex and age.

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5.2 Rhabdomyosarcoma 58 2.7 26 1.1 25	25 1.0 109	1.7	36 1.8	16	0.7	19 0	0.8 71	1.2	1.4	1.4*
5.3 Other soft tissue sarcoma 118 5.5 159 7.0 228	228 9.1 505	7.1	103 5.2	148	6.9	195 8	8.1 446	5 6.7	6.9	1.1*
6. Germ Cell and Trophoblastic 340 15.8 417 18.3 473 Neoplasms	473 18.8 1,230	17.6	341 17.4	300	14.0	295 1	12.3 936	6 14.7	16.1	1.2†

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Diagnostic group (SEER)	Males								Females								Total	M/F
	15-19 years	years	20-24 years	/ears	25-29)	years	15-29)	years	15-19 years	ears	20-24)	years	25-29 years	ears	15-29 years	ears		Ratio*
	Cases	g	Cases	ម	Cases	ម	Cases	ASR	Cases	ម	Cases	£	Cases	ß	Cases s	ASR	ASR	
6.1 Germ cell and trophoblastic neoplasms of gonads	84	3.9	231	10.1	364	14.5	679	9.3	283	14.4	243	11.4	195	8.1	721	11.4	10.3	0.8†
6.2 Germ cell and trophoblastic neoplasms of nongonadal sites	256	11.9	186	8.2	109	4.3	551	8.3	58	3.0	57	2.7	100	4.2	215	3.2	5.9	2.5†
7. Melanoma and Skin Carcinomas	21	1.0	40	1.8	107	4.3	168	2.3	19	1.0	42	2.0	86	4.1	159	2.3	2.3	1.0
7.1 Melanoma	12	0.6	20	0.9	50	2.0	82	1.1	11	0.6	26	1.2	46	1.9	83	1.2	1.2	0.9
7.2 Skin carcinomas	6	0.4	20	0.9	57	2.3	86	1.2	8	0.4	16	0.7	52	2.2	76	1.1	11	1.1
8. Carcinomas	516	24.0	1,272	55.8	3,653	145.2	5,441	73.0	1,257	64.1	4,451	207.9	12,959	539.4	18,667	262.2	165.0	0. 3 [†]
8.1 Thyroid carcinoma	184	8.5	446	19.6	1,211	48.1	1,841	24.7	872	44.4	2,882	134.6	7,141	297.3	10,895	154.2	87.7	0.2†
8.2 Other carcinoma of head and neck	81	3.8	133	5.8	213	8.5	427	5.9	72	3.7	133	6.2	199	8.3	404	6.0	5.9	1.0
8.2.1 Nasopharyngeal carcinoma	40	1.9	43	1.9	47	1.9	130	1.9	17	0.9	19	0.9	28	1.2	64	1.0	1.4	1.9*
8.2.2 Other sites in lip, oral cavity, and pharynx	36	1.7	81	3.6	143	5.7	260	3.6	47	2.4	104	4.9	152	6.3	303	4.4	4.0	0.8
8.2.3 Nasal cavity, middle ear, sinuses, larynx, and other ill-defined sites in head/neck	Ω.	0.2	6	0.4	23	6.0	37	0.5	ω	0.4	10	0.5	19	0.8	37	0.5	0.5	1.0
8.3 Carcinoma of trachea, bronchus, and lung	25	1.2	20	2.2	104	4.1	179	2.4	16	0.8	52	2.4	121	5.0	189	2.7	2.6	0.9†
8.4 Carcinoma of breast			2	0.1	m	0.1	5	0.1	15	0.8	265	12.4	1,672	69.6	1,952	26.5	13.0	0.003†
8.5 Carcinoma of genitourinary tract	30	1.4	93	4.1	290	11.5	413	5.5	154	7.8	524	24.5	1,986	82.7	2,664	37.1	20.9	0.1*
8.5.1 Carcinoma of kidney	17	0.8	52	2.3	173	6.9	242	3.2	18	0.9	34	1.6	108	4.5	160	2.3	2.8	1.4⁺
8.5.2 Carcinoma of bladder	12	0.6	30	1.3	103	4.1	145	1.9	2	0.1	16	0.7	31	1.3	49	0.7	1.3	2.8†
8.5.3 Carcinoma of gonads			m	0.1	2	0.1	S	0.1	123	6.3	242	11.3	420	17.5	785	11.5	5.6	0.01*
8.5.4 Carcinoma of cervix and uterus		ı						ı	8	0.4	229	10.7	1,399	58.2	1,636	22.2	10.8	
8.5.5 Carcinoma of other and ill-defined sites in genitourinary tract	-	0.0	ω	0.4	12	0.5	21	0.3	m	0.2	m	0.1	28	1.2	34	0.5	0.4	0.6†
8.6 Carcinoma of gastrointestinal tract	161	7.5	500	21.9	1,715	68.2	2,376	31.5	113	5.8	553	25.8	1,740	72.4	2,406	33.5	32.5	0.9*
8.6.1 Carcinoma of colon and rectum	67	3.1	176	7.7	530	21.1	773	10.3	46	2.3	165	7.7	402	16.7	613	8.7	9.5	1.2†
8.6.2 Carcinoma of stomach	41	1.9	179	7.9	764	30.4	984	12.9	33	1.7	298	13.9	1,116	46.5	1,447	19.9	16.3	0.6†
8.6.3 Carcinoma of liver and intrahepatic bile ducts	51	2.4	121	5.3	373	14.8	545	7.3	18	0.9	66	3.1	151	6.3	235	3.3	5.4	2.2 [†]
8.6.4 Carcinoma of pancreas	-	0.0	16	0.7	21	0.8	38	0.5	12	0.6	14	0.7	32	1.3	58	0.9	0.7	0.6†
8.6.5 Carcinoma of other and ill-defined sites in gastrointestinal tract	-	0.0	ø	0.4	27	1.1	36	0.5	4	0.2	10	0.5	39	1.6	53	0.7	0.6	0.6†

Diagnostic group (SEER)	Males								Females								Total	M/F
	15-19 years	rears	20-24 years	rears	25–29 years	ears	15–29 years	ears	15-19 years	ears	20–24 years	ears	25-29 years	ars	15-29 years	ears		Ratio*
	Cases	ម	Cases	ម	Cases	ម	Cases	ASR	Cases	ម	Cases	ម	Cases	చ	Cases s	ASR	ASR	
8.7 Carcinoma of other and ill-defined sites	35	1.6	48	2.1	117	4.7	200	2.7	15	0.8	42	2.0	100	4.2	157	2.2	2.5	1.2*
8.7.1 Adrenocortical carcinoma	-	0.0	5	0.2	9	0.2	12	0.2	m	0.2	7	0.3	8	0.3	18	0.3	0.2	0.6†
8.7.2 Carcinoma of other and ill-defined sites, NOS	34	1.6	43	9.1	111	4.4	188	2.6	12	0.6	35	1.6	92	3.8	139	2.0	2.3	1.3*
9. Miscellaneous Specified Neoplasms, NOS	120	5.6	117	5.1	181	7.2	418	6.0	100	5.1	141	6.6	254	10.6	495	7.3	6.6	0.8†
9.1 Other pediatric and embryonal tumors, NOS	30	1.4	20	6.0	24	1.0	74	1.1	20	1.0	17	0.8	22	6.0	59	6.0	1.0	1.2 [†]
9.2 Other specified and embryonal tumors, NOS	06	4.2	97	4.3	157	6.2	344	4.9	80	4.1	124	5.8	232	9.7	436	6.4	5.6	0.8*
10. Unspecified Malignant Neoplasms	67	3.1	125	5.5	259	10.3	451	6.2	88	4.5	203	9.5	428	17.8	719	10.4	8.2	0.6†
*M/F Ratio = Male ASR/Female ASR. *P-values <0.05.																		

[‡]Thyroid section awas excluded from the calculation of the incidence rate of all cancers combined because of its unusually high incidence rate. CR, crude incidence rate; CNS, central nervous system; PNET, primitive neuroectodermal tumor; NOS, not otherwise specified. doi:10.1371/journal.pone.0096088.t001

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r soft tissue sarcoma 6.3 5.0 Cell and Trophoblastic Neoplasms 13.5 14.0 I cell and trophoblastic neoplasms of 9.1 8.6 I cell and trophoblastic neoplasms of 4.4 5.5 adai	1.2 1.6	0.6 2.5	5 1.3	2.4	1.5	0.7	1.0	1.3	-1.6
Cell and Trophoblastic Neoplasms 13.5 14.0 n cell and trophoblastic neoplasms of 9.1 8.6 n cell and trophoblastic neoplasms of 4.4 5.5	7.7 5.9	7.2 5.	5.7 5.9	6.8	8.3	7.7	9.4	7.3	3.2*
n cell and trophoblastic neoplasms of 9.1 8.6 n cell and trophoblastic neoplasms of 4.4 5.5 adal	14.8 14.3	14.5 14	14.7 17.0	16.4	19.1	17.8	18.3	20.2	3.6*
4.4 5.5	0.6 6.6	9.0 10	10.2 10.3	10.3	11.2	12.0	11.4	12.9	3.3*
	4.9 5.3	5.6 4.4	4 6.7	6.1	8.0	5.9	7.0	7.3	4.2*
and Skin Carcinomas 1.7 2.1	2.6 1.8	1.0 1.5	5 3.7	2.5	2.3	2.7	3.2	2.5	4.8
7.1 Melanoma 1.1 1.2 1.2	1.2 0.9	0.5 0.9	9 2.0	0.9	0.9	1.4	1.9	1.1	2.6

Table 2. Cont.													
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	APC
7.2 Skin carcinomas	9.0	0.8	1.5	0.9	0.6	0.5	1.7	1.6	1.4	1.3	1.4	1.5	7.2*
8 Carcinomas	105.3	102.0	116.4	123.2	141.5	155.2	163.7	173.1	191.8	225.1	244.4	270.7	9.4*
8.1 Thyroid carcinoma	33.9	33.8	42.1	47.4	62.6	78.2	82.1	93.6	112.0	144.9	162.2	188.9	17.9*
8.2 Other carcinoma of head and neck	4.9	5.1	5.0	5.9	6.7	5.9	6.1	5.3	6.8	6.7	8.1	5.2	2.5
8.2.1 Nasopharyngeal carcinoma	1.1	1.8	1.2	1.2	1.9	1.6	1.3	1.1	1.4	1.7	1.8	1.4	1.2
8.2.2 Other sites in lip, oral cavity and pharynx	3.2	3.0	3.3	4.2	3.9	3.8	4.4	3.9	5.0	4.4	5.5	3.6	3.4*
8.2.3 Nasal cav,mid ear,sinuses,larynx,oth ill-def head/neck	0.6	0.4	0.4	0.5	0.9	0.6	0.4	0.3	0.5	0.7	0.7	0.3	-0.6
8.3 Carcinoma of trachea,bronchus, and lung	2.4	1.5	2.9	2.2	2.5	3.0	3.1	3.0	1.9	2.2	2.9	3.4	2.6
8.4 Carcinoma of breast	8.5	11.4	12.3	13.6	12.2	12.6	15.1	13.8	13.9	14.1	13.8	15.3	3.5*
8.5 Carcinoma of genitourinary tract	18.4	14.7	17.2	18.7	21.5	21.1	20.9	23.8	22.2	24.5	24.0	25.7	4.2*
8.5.1 Carcinoma of kidney	2.2	0.9	2.3	2.1	2.1	2.8	2.5	4.2	2.4	4.3	4.4	3.3	9.1*
8.5.2 Carcinoma of bladder	1.4	0.8	1.4	1.1	1.7	1.5	1.8	1.1	1.6	1.2	0.9	1.4	0.7
8.5.3 Carcinoma of gonads	5.9	5.9	4.9	5.5	6.8	5.2	5.8	5.2	6.4	4.9	4.4	6.1	-0.8
8.5.4 Carcinoma of cervix and uterus	8.6	6.7	8.4	9.5	10.3	11.1	10.3	13.0	11.3	13.9	13.7	14.6	6.2*
8.5.5 Carc of other and ill-def sites, geniourinary tract	0.2	0.3	0.2	0.5	0.5	0.4	0.5	0.3	0.5	0.2	0.5	0.3	2.8
8.6 Carcinoma of gastrointestinal tract	34.2	32.3	34.2	33.1	34.3	31.6	34.0	31.2	31.7	31.1	31.1	30.4	-1.0*
8.6.1 Carcinoma of colon and rectum	9.1	8.1	8.4	7.7	9.1	8.3	9.2	9.4	9.8	12.9	11.8	11.3	3.7*
8.6.2 Carcinoma of stomach	18.8	17.3	18.4	18.7	17.4	15.8	17.3	15.4	15.3	13.2	13.7	13.2	-3.3*
8.6.3 Carcinoma of liver and intrahepatic bile ducts	5.2	5.5	6.8	5.8	6.3	5.4	6.0	5.2	5.3	3.6	4.3	4.5	-3.2*
8.6.4 Carcinoma of pancreas	0.4	0.8	0.3	0.6	0.6	1.0	0.8	0.8	0.8	0.6	0.4	1.1	4.8
8.6.5 Carc other and ill-def sites, gastrointestinal tract	0.7	0.6	0.4	0.2	0.8	1.0	0.6	0.4	0.6	0.8	1.0	0.3	0.1
8.7 Carcinoma of other and ill-def sites	3.0	3.3	2.7	2.3	1.8	2.8	2.4	2.5	3.1	1.7	2.4	2.0	-3.0
8.7.1 Adrenocortical carcinoma	0.2	0.2	0.1	0.2	0.2	0.1	0.1	0.4	0.5	0.1	0.4	,	6.7
8.7.2 Carcinoma of other and ill-defined sites, NOS	2.8	3.0	2.6	2.1	1.6	2.7	2.3	2.1	2.6	1.6	1.9	2.0	-3.4*
9 Miscellaneous specified neoplasms, NOS	3.1	4.4	4.3	4.3	7.5	6.4	7.5	8.2	8.2	9.7	8.1	9.1	9.8*
9.1 Other pediatric and embryonal tumors, NOS	0.7	1.3	0.7	0.8	1.4	0.6	1.3	0.9	0.9	1.5	0.7	1.4	3.0
9.2 Other specified and embryonal tumors, NOS	2.5	3.1	3.6	3.5	6.0	5.8	6.3	7.4	7.3	8.3	7.4	7.7	11.3
10 Unspecified Malignant Neoplasms	15.1	13.1	12.7	8.8	8.8	7.1	5.6	5.3	5.0	5.1	4.6	4.7	-10.9*
*P-values <0.05. [†] Thyroid carcinoma was excluded from the calculation of the incidence rate AYAs, adolescents and young adults (aged 15–29 years); CNS, central nervou doi:10.1371/journal.pone.0096088.t002	on of the incide ars); CNS, centra	nce rate of al al nervous sys	l cancers com tem; PNET, p	ibined becaus rimitive neuro	e of its unusu ectodermal tu	of all cancers combined because of its unusually high incidence rate. s system; PNET, primitive neuroectodermal tumor; NOS, not otherwise specified.	lence rate. t otherwise s	pecified.					

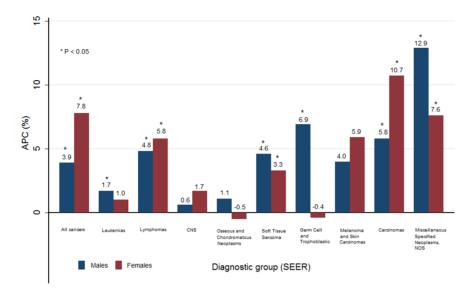


Figure 1. Annual percent change (APC) from 1999–2010 according to the diagnostic group (SEER). doi:10.1371/journal.pone.0096088.g001

Cancer incidence trends within diagnostic groups were observed to differ by gender. Among males, the incidence of most cancer sites was increased. Miscellaneous specified neoplasms, NOS, showed the largest increase in incidence (APC = 12.9%, P < 0.05), followed by germ cell and trophoblastic neoplasms (APC = 6.9%, P < 0.05). Among females, the incidence of most cancer sites was also increased. Carcinomas (APC = 10.7%, P < 0.05) and miscellaneous specified neoplasms, NOS (APC = 7.6%, P < 0.05), showed the greatest increases. However, osseous/chondromatous neoplasms (APC = -0.5%) and germ cell and trophoblastic neoplasms (APC = -0.4%) slightly decreased in incidence (Figure 1). Additionally, a notable increase in the incidence of carcinomas among females was observed in the cervix (APC = 6.2%, P < 0.05) and breast (APC = 3.5%, P < 0.05) (data not shown).

Survival

A total of 52,077 cancer cases diagnosed from 1993 to 2010 were used for the survival analysis. Table 3 shows the 5-year relative survival rates and numbers of cases in the four time periods (1993–1995, 1996–2000, 2001–2005 and 2006–2010). For all cancers combined, the 5-year relative survival rate of AYAs significantly improved, from 58.9% in 1993–1995 to 84.8% in 2006–2010 (P<0.05). AYAs with leukemia and lymphoma showed the most marked improvement in survival from 25.8% (95% CI: 22.9–28.7) and 55.4% (95% CI: 50.6–59.9) in 1993–1995 to 58.8% (95% CI: 55.5–61.8) and 83.6% (95% CI: 80.9–85.9) in 2006–2010, respectively. Conversely, decreases in survival were observed from 1993–1995 to 2006–2010 for other glioma (group 3.2), carcinoma of gonads (group 8.5.3), and carcinoma of pancreas (group 8.6.4) (Table 3).

Survival rates for thyroid carcinoma (group 8.1) and skin carcinoma (group 7.2) were very high across all time periods. The five-year relative survival rate for thyroid carcinoma among males increased slightly, from 95.3% in 1993–1995 to 99.7% in 2006–2010, whereas the rate was unchanged among females from 1993–1995 (99.9%) to 2006–2010 (100.0%). The survival rates for germ cell and trophoblastic neoplasms (group 6), skin carcinoma (group 7.2), and carcinoma of the genitourinary tract (group 8.5)

consistently exceeded 80-90% in all time periods. Conversely, the lowest survival rates were observed for rhabdomyosarcoma (group 5.2); carcinoma of the trachea, bronchus, and lung (group 8.3); and carcinoma of liver and intrahepatic bile ducts (group 8.6.3) (Table 3).

The survival rates for all cancers combined significantly increased from 1993 to 2010 in both males and females. In particular, the 5-year relative survival rate increased from 46.5% to 75.9% in males (P<0.05) and from 66.7% to 89.1% in females (P<0.05). However, the 5-year relative survival rate for all cancers combined was slightly lower in males than in females, regardless of whether thyroid carcinoma was excluded (Table 4).

Leukemia (group 1) showed the greatest increase in survival in both males (32.5%) and females (33.7%). In particular, chronic myeloid leukemia had the largest and second-largest increases in survival in males (48.6%); from 40.5% to 89.1%) and females (50.5%); from 42.7% to 93.2%), respectively.

Figure 2 depicts the 5-year relative survival rates of all cancer patients in each of the four time periods according to age (15-19 years, 20-24 years and 25-29 years) and sex. Both gender, the 5year relative survival rates increased in all age groups. For males aged 15-19 years, the 5-year relative survival rates in 1993-1995, 1996-2000, 2001-2005, and 2006-2010 for all cancers combined were 45.3% (95.% CI: 41.2-49.2), 55.4% (95% CI: 52.5-58.1), 65.3% (95% CI: 62.5-67.9), and 72.2% (95% CI: 69.2-75.0), respectively. The survival rates of males aged 20-24 years were 43.9% (95% CI: 40.2-47.5), 55.0% (95% CI: 52.2-57.7), 65.0% (95% CI: 62.5-67.3), and 77.0% (95% CI: 74.3-79.5) in 1993-1995, 1996-2000, 2001-2005, and 2006-2010, respectively. The survival rates of males aged 25-29 years were 48.8% (95% CI: 45.9-51.7), 55.0% (95% CI: 52.9-57.0), 66.5% (95% CI: 64.6-68.3), and 77.2% (95% CI: 75.3–79.0) in 1993–1995, 1996–2000, 2001-2005, and 2006-2010, respectively. For females aged 15-19 years, the 5-year relative survival rates for all cancers combined were 62.0% (95% CI: 58.0-65.8), 72.0% (95% CI: 69.4-74.5), 78.8% (95% CI: 76.3-81.0), and 82.2% (95% CI: 79.7-84.5) in 1993-1995, 1996-2000, 2001-2005, and 2006-2010, respectively. The survival rates of females aged 20-24 years were 67.4% (95% CI: 64.6-70.1), 74.4% (95% CI: 72.4-76.3), 83.7% (95% CI:

	Both sexes	S							Change⁺	ط
	1993-1995	5	1996-2000		2001-2005	10	2006-2010	0		
	Cases	RSR	Cases	RSR	Cases	RSR	Cases	RSR		
All Cancers	6,387	58.9	12,453	66.4	14,310	76.5	18,927	84.8	25.9	*
All Cancers (excluding thyroid carcinoma) ‡	5,525	52.6	10,474	60.2	10,555	68.2	10,884	74.4	21.8	*
1. Leukemias	866	25.8	1,440	35.9	1,397	47.7	1,435	58.8	33.0	*
1.1 Acute lymphoid leukemia	237	19.9	433	29	379	33.9	425	48.6	28.7	*
1.2 Acute myeloid leukemia	375	26.0	602	37.5	624	47.2	588	52.7	26.7	*
1.3 Chronic myeloid leukemia	141	41.4	251	51.2	252	76	262	90.5	49.1	*
1.4 Other and unspecified leukemia	113	17.8	154	24.1	142	36	160	58.8	41.0	*
2. Lymphomas	439	55.4	937	65	1,133	75.8	1,315	83.6	28.2	*
2.1 Non-Hodgkin lymphoma	372	51.3	290	60.6	906	72.5	1,037	82.0	30.7	*
2.2 Hodgkin lymphoma	67	78.0	147	88.8	227	88.8	278	89.4	11.4	*
3. CNS and Other Intracranial and Intraspinal Neoplasms	371	53.4	689	54.5	730	60	750	65.6	12.2	*
3.1. Astrocytoma	179	43.2	305	45.1	275	45.2	291	54.3	11.1	*
3.2 Other glioma	65	72.7	83	61.7	141	66.1	177	71.2	-1.5	
3.3 Ependymoma	14	86.1	49	79.9	57	88.0	62	87.0	0.9	
3.4 Medulloblastoma and other PNET	18	44.6	84	49	92	47.9	84	52.3	7.7	
3.5 Other specified intracranial and intraspinal neoplasms	13	61.9	27	74.4	20	80.2	18	72.6	10.7	
3.6 Unspecified intracranial and intraspinal neoplasms	82	55.2	141	61.2	145	76.1	118	80.6	25.4	*
4. Osseous and Chondromatous Neoplasms	262	48.3	516	66.1	479	68.7	447	74.8	26.5	*
4.1 Osteosarcoma	160	43.3	305	65.5	281	65.3	231	72.2	28.9	*
4.2 Chondrosarcoma	28	64.6	75	87.0	69	87.2	77	94.9	30.3	*
4.3 Ewing tumor	30	40.2	66	39.5	67	52.4	72	51.0	10.8	
4.4 Other specified and unspecified bone tumors	44	61.7	70	71.7	62	80.9	67	85.5	23.8	*
5. Soft Tissue Sarcomas	243	58.7	481	58.8	554	67.5	617	73.4	14.7	*
5.1 Fibromatous neoplasms	51	78.8	103	78	135	93.6	193	95.1	16.3	*
5.2 Rhabdomyosarcoma	32	28.3	73	37.1	66	34.9	55	37.5	9.2	
5.3 Other soft tissue sarcoma	160	58.4	305	57.6	353	63.6	369	67.8	9.4	*
6. Germ Cell and Trophoblastic Neoplasms	278	81.6	745	87	842	89.9	936	91.7	10.1	*
6.1 Germ cell and trophoblastic neoplasms of gonads	174	89.4	465	92.3	558	94.3	613	96.2	6.8	*
6.2 Germ cell and trophoblastic neoplasms of nongonadal sites	104	68.6	280	78.1	284	81.2	323	83.2	14.6	
7. Melanoma and Skin Carcinomas	56	64.6	111	59.7	122	77.3	138	86.3	21.7	*
7.1 Melanoma	25	32.2	64	43.9	63	60.5	59	65.0	32.8	*
7.2 Skin carcinomas	31	90.8	47	81.2	59	95.2	79	0.66	8.2	*
8 Carcinomae	2 206	ļ	100 0				102.01			

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X	1993-1995 Cases 862 140		1996-2000						-6	r
	ses				2001-2005		2006-2010			
	2 0	RSR	Cases	RSR	Cases	RSR	Cases	RSR		
	0	99.3	1,979	9.66	3,755	6.99	8,043	6.99	0.6	*
		69.6	289	77.8	339	83.1	333	85.5	15.9	*
		70.4	104	65.7	79	80.0	75	85.1	14.7	*
ad/neck		79.8	159	87.7	233	85.6	235	88.6	8.8	
		41.0	26	65.6	27	70.6	23	60.5	19.5	
8.3 Carcinoma of trachea, bronchus, and lung		24.8	136	36.2	144	47.4	132	43.1	18.3	*
8.4 Carcinoma of breast 310	0	68.0	691	77.2	825	82.0	841	86.5	18.5	*
8.5 Carcinoma of genitourinary tract 602	2	85.3	1,191	85.5	1,194	88.9	1,371	86.5	1.2	
8.5.1 Carcinoma of kidney 35		68.9	94	76.9	142	87.6	209	87.0	18.1	*
8.5.2 Carcinoma of bladder 39		85.1	77	94.0	90	93.6	73	95.9	10.8	
8.5.3 Carcinoma of gonads 234	+	86.6	396	84.5	326	88.2	291	82.7	-3.9	
8.5.4 Carcinoma of cervix and uterus 285	10	86.6	605	86.7	611	89.1	781	87.0	0.4	
8.5.5 Carcinoma of other and ill-defined sites, genitourinary tract		78.3	19	79.2	25	84.2	17	88.1	9.8	
8.6 Carcinoma of gastrointestinal tract 1,123	23	38.0	2,127	42.3	1,974	50.2	1,766	59.2	21.2	*
8.6.1 Carcinoma of colon and rectum 246	10	47.0	527	52.8	500	63.2	603	73.9	26.9	*
8.6.2 Carcinoma of stomach 723	~	36.3	1,239	41.4	1,091	49.0	831	58.2	21.9	*
8.6.3 Carcinoma of liver and 90 intrahepatic bile ducts		23.5	277	23.6	308	33.6	256	31.6	8.1	*
8.6.4 Carcinoma of pancreas		56.9	35	57.3	39	59.1	42	43.8	-13.1	
8.6.5 Carcinoma of other and ill-defined sites in 34 gastrointestinal tract		29.6	49	45.1	36	39.0	34	59.1	29.5	*
8.7 Carcinoma of other and ill-defined sites		41.3	194	39.3	135	44.6	115	54.0	12.7	*
8.7.1 Adrenocortical carcinoma N/S	10									
8.7.2 Carcinoma of other and ill- defined sites, NOS		40.0	181	39.4	128	46.2	66	56.2	16.2	*
9. Miscellaneous Specified Neoplasms, NOS	-	54.0	213	72.5	348	79.2	453	79.7	25.7	*
9.1 Other pediatric and embryonal 33 tumors, NOS		30.5	43	46.7	51	57.0	51	63.1	32.6	*
9.2 Other specified and embryonal tumors, NOS 88		62.8	170	79.1	297	83.0	402	81.7	18.9	*
10. Unspecified Malignant Neoplasms	Q	62.0	714	70.8	339	79.0	235	77.8	15.8	*
*P-values <0.05 for trend. ¹ Change (%) in the 5-year RSR from 1993-1995 to 2006-2010. ⁴ Thyroid carcinoma was excluded from the calculation of the incidence rate of all cancers combined because of its unusually high incidence rate. N/S: not shown because <20 cases were reported in each period. AYAs, adolescents and young adults (aged 15–29 years); CNS, central nervous system; PNET, primitive neuroectodermal tumor; NOS, not otherwise specified. doi:10.1371/journal.pone.0096088.t003	te of all cano ous system;	cers combined PNET, primitiv	because of its e neuroectoder	unusually high ir mal tumor; NOS,	icidence rate. not otherwise s	pecified.				

Table 3. Cont.

Table 4. Five-year RSRs for Korean AYAs according to the time period of cancer diagnosis and sex.

j991-1995 j996-2000 2001-2005 2006-2010 Amode Cases RSR \sim RSR \sim RSR RSR Amode 2,478 46.5 4,801 55.1 5.1-6 5.3 6,149 7.5 26.3 2,478 46.5 4,801 55.1 5.1-6 5.3 4,92 7.9 29.4 2,478 46.5 4,801 52.1 5.1-6 7.9 26.3	Males			Females						
Gase RSr Case RSr Case RSr Case RSr RSr RSr 2478 465 4801 55.1 5.16 5.3 6.14 75.9 29.4 2366 44.2 451 791 330 826 6.14 75.9 20.4 140 223 237 213 237 213 233 214 26.5 140 223 50.7 51.6 51.8 41.5 24.6 230 40.5 53.7 51.6 51.8 51.4 41.5 242 50.7 53.6 53.7 51.4 51.3 24.6 231 40.5 53.7 51.4 51.3 51.4 51.5 232 54.7 53.7 53.7 53.7 53.7 53.7 232 53.7 53.7 53.7 53.7 53.7 53.7 53.7 241 53 53.7 54.7 53.7	1996–2000			1993-1995	1996–2000	0 2001-2005		2006–2010	Change [†]	م
2478 46.5 4,010 55.1 5,16 6,14 7,5 2,4 2,366 44.2 5,14 5,24 4,92 7,93 2,63 492 25.4 791 330 8,45 6,33 4,92 7,5 2,63 140 253 307 303 303 303 303 304 4,65 140 253 307 303 303 303 303 304 466 171 999 793 532 443 543 543 543 543 544 543 314 445 250 490 553 543 543 543 543 543 543 251 490 553 523 441 54 543 543 543 252 490 554 543 544 543 543 543 254 543 543 544 54 543 543 <th>RSR Cases RSR Cases</th> <th>Cases</th> <th>~</th> <th>Cases RSR</th> <th>Cases R:</th> <th>RSR Cases RS</th> <th>RSR</th> <th>Cases RSR</th> <th></th> <th></th>	RSR Cases RSR Cases	Cases	~	Cases RSR	Cases R:	RSR Cases RS	RSR	Cases RSR		
2,366 4,1 4,51 5,24 4,50 6,23 4,92 7,5 2,53 492 25,4 791 33.0 87 40 77 82 53.3 140 223 307 304 318 445 313 817 816 140 265 307 354 318 445 313 816 171 99 755 89 37.2 819 415 314 262 50.7 555 80 37.2 816 116 816 2755 59 755 57 72 72 819 415 270 450 552 72 72 819 415 416 260 563 575 58 663 673 610 72 416 270 561 57 58 563 673 610 72 72 260 57 58	46.5 4,801 55.1	6,149	29.4	3,909 66.7	7,652 73	73.6 9,144 82	82.6 1	12,778 89.1	22.4	*
492 25.4 791 33.0 826 4.6 841 57.9 32.5 140 223 273 273 273 303 317 403 312 246 87 405 152 515 516 133 740 173 269 87 405 152 516 53 80 37 80 31 246 230 473 560 555 80 57 83 514 415 230 473 560 555 80 57 84 10 319 232 755 78 61 72 72 118 232 755 74 57 72 61 73 118 240 35 52 72 72 72 61 74 15 230 35 52 44 51 52 61 73 74 <td< th=""><th>44.2 4,516 52.4 4,696</th><th>4,924</th><th>26.3</th><th>3,159 58.9</th><th>5,958 60</th><th>66.0 5,859 72</th><th>72.9 5</th><th>5,960 77.6</th><th>18.7</th><th>*</th></td<>	44.2 4,516 52.4 4,696	4,924	26.3	3,159 58.9	5,958 60	66.0 5,859 72	72.9 5	5,960 77.6	18.7	*
140 223 274 36 302 313 445 313 511 246 87 405 122 516 83 445 313 511 246 87 405 122 516 83 140 173 891 415 71 99 72 567 527 587 891 415 416 262 507 588 603 517 516 417 416 <td< td=""><td>25.4 791 33.0</td><td>841</td><td>32.5</td><td>374 26.3</td><td>649 39</td><td>39.4 571 49</td><td>49.8 5</td><td>594 60.0</td><td>33.7</td><td>*</td></td<>	25.4 791 33.0	841	32.5	374 26.3	649 39	39.4 571 49	49.8 5	594 60.0	33.7	*
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230 473 800 557 722 702 601 792 319 32 755 78 863 115 846 147 873 118 32 755 78 863 155 846 147 873 118 220 49.9 368 169 393 52.2 817 59.4 83.0 83.1 41 761 53 86.9 86.0 39.4 66.9 99.2 94.0 66.9 92 intraspinal N5 708 84.4 51 374 46 41.5 37 intraspinal N5 703 65.0 65.1 703 74.7 26.9 intraspinal S4 317 65.0 57.7 72 73.3 24.2 sepinal 54 48.6 176 74.7 26.3 24.4 intraspinal 163 48.8 174 26.7 28.4 <td>50.7 558 60.9</td> <td>748</td> <td>30.2</td> <td>177 62.3</td> <td>379 7</td> <td>71.1 496 79</td> <td>79.6 5</td> <td>567 87.0</td> <td>24.7</td> <td>*</td>	50.7 558 60.9	748	30.2	177 62.3	379 7	71.1 496 79	79.6 5	567 87.0	24.7	*
32 755 78 863 115 846 147 873 118 220 49.9 393 52.2 417 59.4 423 63.0 13.1 220 49.9 368 169 393 52.2 417 59.4 43.3 11.6 104 36.8 169 393 55.9 68 70.8 10.5 64.9 94.0 65.9 94.0 65.9 95.0 65.9 95.0 94.0 65.6 95.7	47.3 480 56.7	601	31.9	142 57.9	310 66	66.6 384 75	75.7 4	436 85.9	28.0	*
220 49.9 39.3 52.2 41 59.4 423 63.0 13.1 104 36.8 169 39.8 169 39.8 155 48.4 11.6 41 76.1 53 56.9 68 70.8 102 66.9 92.2 5 100.6 32 84.4 51 37.4 46 41.5 3.7 intraspinal NS 37.8 43.3 54.4 54.3 54.3 54.4 54.3 54.4 54.3 54.4 54.3 54.4 54.3 54.4 54.3 54.4 <td>75.5 78 86.3</td> <td>147</td> <td>11.8</td> <td>35 80.2</td> <td>69 91</td> <td>91.5 112 93</td> <td>93.0 1</td> <td>131 91.3</td> <td>11.1</td> <td>*</td>	75.5 78 86.3	147	11.8	35 80.2	69 91	91.5 112 93	93.0 1	131 91.3	11.1	*
	49.9 393 52.2	423	13.1	151 58.4	296 51	57.6 313 60	60.8 3	327 68.9	10.5	*
41 761 53 56.9 68 708 102 66 92 7 8 100.6 32 84.8 28 80.0 39 94.0 66 7 8 37.8 43 444 51 37.4 46 41.5 3.7 intraspinal N/S 37.8 43 44 51 37.4 46 41.5 3.7 intraspinal N/S 37.8 44.4 51 37.7 72 78.3 24.2 aspinal 54 54.1 80 61.5 102 77.7 72 74.7 28.3 intraspinal 163 48.8 317 65.0 77.7 72 74.7 28.3 intraspinal 163 48.8 317 65.0 290 66.1 290 24.3 24.3 intraspinal 163 48.3 174 65.0 74.7 28.3 24.3 28.3	36.8 169 39.8	155		75 52.2	136 51	51.6 119 48	48.0 1	136 60.8	8.6	
5 100.6 32 84.8 28 86.0 39 94.0 66 intraspinal N/S 37.8 43 51 37.4 46 41.5 3.7 intraspinal N/S 77.7 72 78.3 24.3 3.7 sspinal 54 54.1 80 61.5 102 77.7 72 78.3 24.2 sspinal 54 54.1 80 61.5 102 77.7 72 78.3 24.2 signal 48.8 317 65.0 290 66.1 296 74.7 25.9 106 427 195 644 93.5 24.4 28.7 28.4 117 71.1 43 38.6 44.9 46.6 49.7 28.7 126 64.4 38.6 44.9 82.6 49.7 28.4 29.7 126 52.4 34 84.9 66.3 34.2 28.7 28.4	76.1 53 56.9	102		24 66.9	30 70	70.2 73 61	61.8 7	75 77.0	10.1	
IT 8 37.8 43 44.4 51 37.4 46 41.5 3.7 intraspinal N/S N/S 54.1 80 61.5 102 77.7 72 78.3 24.2 sspinal 54 54.1 80 61.5 102 77.7 72 78.3 24.2 sspinal 54 317 65.0 290 66.1 296 74.7 25.9 106 42.7 195 64.4 174 60.5 160 71.4 28.7 17 71.1 43 86.5 44.9 93.5 44.9 28.7 25.4 17 71.1 43 86.5 44.9 93.5 24.4 28.7 15 47.0 36.7 37.4 38.8 44.9 46 29.7 27.4 255 60.4 36.5 74.7 28.6 46.9 29.7 29.7 260 52.4 38 24.9 38.6 54.9 36.7 29.7 29.7 27 28.7<	100.6 32 84.8	39		9 78.0	17 70	70.7 29 89	89.8 2	23 74.6	-3.4	
Intraspinal N/S sepinal 54 80 61.5 102 77.7 72 78.3 24.2 sepinal 54 80 61.5 102 77.7 72 78.3 24.2 sepinal 54 81 81 65.0 290 66.1 296 74.7 25.9 106 42.7 195 64.4 174 60.5 160 71.4 28.7 17 71.1 43 86.5 44 93.5 44.9 93.5 24.4 15 47,0 43 37.4 38 44.9 46 49.7 27.4 15 60.4 36 75.4 38 84.9 46.9 29.7 24.4 15 60.4 36 75.4 38.7 64.9 7.4 29.7 27.4 16 74.0 75.8 84.9 95.6 44.9 95.6 24.9 29.7 25 60.4 57.7 28.7 28.7 28.7 28.4 29.7 29.7 <	37.8 43 44.4	46 41		10 50.1	41 53	53.8 41 61.1	.1 38	8 63.8	13.7	
Sepinal 54 54.1 80 61.5 102 77.7 72 78.3 24.2 163 48.8 317 65.0 290 66.1 296 74.7 25.9 106 42.7 195 64.4 174 60.5 160 71.4 28.7 17 71.1 43 86.5 44 93.5 44.9 35.5 22.4 17 71.1 43 86.5 44.9 93.5 44.9 28.7 28.4 15 47.0 43 37.4 38 44.9 46 49.7 21.4 255 60.4 36 75.4 38.7 64.9 93.5 24.4 263 52.7 244 57.7 287 46.7 297 27.4 2126 52.7 244 57.7 287 68.9 16.6 17.6 27.4 23 23.4 24.7 24.7 24.7 24.7 2	N/S			N/S					ı	
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106 42.7 195 64.4 174 60.5 160 71.4 28.7 17 71.1 43 86.5 44 93.5 44 93.5 24.4 15 47.0 43 37.4 38 44.9 46 49.7 27.4 25 60.4 36 75.4 38 84.9 46 49.7 27.4 25 60.4 36 75.4 38 82.6 46 89.4 29.0 126 52.7 244 57.7 287 63.3 342 68.8 16.1 23 78.8 61 75.8 64 90.9 103 93.4 146 29 25.2 140 56.7 182 60.1 103 93.4 146 28 52.2 140 56.7 182 61.1 80.9 106 33 52.2 140 56.7 182 61.1 20.4 1	48.8 317 65.0	296	25.9	99 47.6	199 68	68.0 189 72	72.6 1	151 75.4	27.8	*
17 71.1 43 86.5 44 93.5 44 93.5 224 15 47.0 43 37.4 38 44.9 46 93.5 224 25 60.4 36 75.4 34 82.6 46 89.4 29.0 27 25 60.4 36 75.4 34 82.6 46 89.4 29.0 27 126 52.7 244 57.7 287 63.3 342 68.8 16.1 23 78.8 61 75.8 64 90.9 103 93.4 146 20 25.2 43 35.0 41 34.2 35.3 34.1 8.9 83 52.2 140 56.7 182 60.1 20.4 20.6 10.6 83 52.2 140 56.7 182 60.1 204 62.8 10.6	42.7 195 64.4	160	28.7	54 44.6	110 67	67.4 107 73	73.0 71	1 74.6	30.0	*
15 47.0 43 37.4 38 44.9 46 49.7 2.7 25 60.4 36 75.4 34 82.6 46 89.4 29.0 25 60.4 36 75.4 34 82.6 46 89.4 29.0 126 52.7 244 57.7 287 63.3 342 68.8 16.1 23 78.8 61 75.8 64 90.9 103 93.4 146 20 25.2 43 35.0 41 34.2 35.3 34.1 8.9 83 52.2 140 56.7 182 60.1 204 62.8 10.6 83 52.2 140 56.7 182 60.1 204 62.8 10.6	71.1 43 86.5	44		11 54.7	32 87	87.7 25 76	76.2 3	33 96.4	41.7	
25 60.4 36 75.4 34 82.6 46 89.4 29.0 126 52.7 244 57.7 287 63.3 34.2 68.8 16.1 23 78.8 61 75.8 64 90.9 103 93.4 146 20 25.2 43 35.0 41 34.2 35 34.1 8.9 83 52.2 140 56.7 182 60.1 204 628 106	47.0 43 37.4	46		15 33.4	23 43	43.6 29 62	62.2 2	26 53.3	19.9	
126 52.7 244 57.7 287 63.3 342 68.8 16.1 23 78.8 61 75.8 64 90.9 103 93.4 14.6 20 25.2 43 35.0 41 34.2 35.3 34.1 8.9 83 52.2 140 56.7 182 60.1 204 62.8 10.6	60.4 36 75.4	46	29.0	19 63.3	34 67	67.8 28 78	78.7 21	1 77.1	13.8	
23 78.8 61 75.8 64 90.9 103 93.4 14.6 20 25.2 43 35.0 41 34.2 35 34.1 8.9 83 52.2 140 56.7 182 60.1 204 62.8 10.6	52.7 244 57.7	342	16.1	117 65.1	237 6(60.1 267 72	72.1 2	275 78.6	13.5	*
20 25.2 43 35.0 41 34.2 35.1 8.9 83 52.2 140 56.7 182 60.1 204 62.8 10.6	78.8 61 75.8	103	14.6	28 78.8	42 81	81.1 71 96	96.0 9	90 96.7	17.9	*
83 52.2 140 56.7 182 60.1 204 62.8 10.6	25.2 43 35.0	35		12 33.4	30 40	40.1 25 36	36.1 2	20 44.9	11.5	
	52.2 140 56.7	204	10.6	77 65.1	165 58	58.3 171 67	67.4 1	165 73.4	8.3	
72.9 323 79.3 457 85.8 574 88.8 15.9	98 72.9 323 79.3 457	85.8 574 88	.8 15.9 *	180 86.4	422 92.	9 385	94.7 3	362 96.3	9.9	*

Diagnostic group (SEER)	Males										Females								
	1993-1995	995	1996–2000	5000	2001-2005	2005	2006-2010	10	Change [†]	٩	1993-1995		1996–2000	2001-2005	2005	2006-2010	_	Change [†]	٩
	Cases	RSR	Cases	RSR	Cases	RSR	Cases	RSR			Cases RSR	R Cases	s RSR	Cases	RSR	Cases	RSR		
6.1 Germ cell and trophoblastic neoplasms of gonads	47	90.06	157	85.8	255	90.5	331	95.4	5.4	*	127 89.2	308	95.7	303	97.5	282	97.0 7.	7.8	*
6.2 Germ cell and trophoblastic neoplasms of nongonadal sites	51	57.2	166	73.2	202	79.9	243	79.9	22.7		53 79.5	114	85.3	82	84.3	80	93.6 1	14.1	
7. Melanoma and Skin Carcinomas	24	71.3	66	57.9	66	73.0	67	83.9	12.6	*	32 59.6	6 45	62.4	1 56	82.3	71	89.1 2	29.5	*
7.1 Melanoma	11	45.8	38	45.0	33	51.7	26	45.0	-0.8		14 21.5	5 26	42.4	30	70.1	33	76.5 5	55.0	*
7.2 Skin carcinomas	13	93.0	28	75.4	33	94.3	41	97.9	4.9		18 89.2	19	89.7	26	96.4	38	100.2 1	11.0	
8. Carcinomas	872	52.3	1,787	57.0	1,935	68.2	2,561	80.5	28.2	*	2,333 73.1	1 4,820	0 77.9	6,431	86.6	10,040	92.4 1	19.3	*
8.1 Thyroid carcinoma	112	95.3	285	97.3	470	100.2	1,225	99.7	4.4	*	750 99.9	1,694	6.66	3,285	99.8	6,818	100.0 0.1	-	
8.2 Other carcinoma of head and neck	76	62.3	147	71.1	177	79.4	170	86.8	24.5	*	64 78.4	142	84.7	162	87.2	163	84.5 6.1	-	
8.2.1 Nasopharyngeal carcinoma	28	71.9	70	60.3	56	80.6	48	91.6	19.7	*	12 66.9	34	76.7	23	78.4	27	77.6 1	10.7	
8.2.2 Other sites in lip, oral cavity, and pharynx	32	72.4	65	86.6	108	79.9	112	86.6	14.2	•	41 85.6	94	88.5	125	90.5	123	90.3 4.7	7	
8.2.3 Nasal cavity, middle ear, sinuses, larynx, and other ill-defined sites in head/neck	N/S									-	N/S								
8.3 Carcinoma of trachea, bronchus, and lung	41	24.6	68	37.0	65	52.5	64	39.6	15.0	,	32 25.1	68	35.4	79	43.1	68	46.7 2	21.6	*
8.4 Carcinoma of breast	N/S										309 67.9	686	77.3	822	81.9	838	86.6 1	18.7	*
8.5 Carcinoma of genitourinary tract	52	83.3	116	91.0	158	91.5	197	92.2	8.9		550 85.5	1,075	85.0	1,036	88.5	1,174	85.5 0		
8.5.1 Carcinoma of kidney	14	79.2	43	86.5	85	89.8	129	91.9	12.7		21 62.1	51	68.8	57	84.4	80	78.8 1	16.7	*
8.5.2 Carcinoma of bladder	30	87.3	61	95.6	61	95.4	60	95.0	7.7		N/S								
8.5.3 Carcinoma of gonads	N/S										231 86.8	392	84.4	324	88.1	290	82.6 -4	-4.2	
8.5.4 Carcinoma of cervix and uterus	N/S										285 86.6	605	86.7	611	89.1	781	87.0 0.	0.4	
8.5.5 Carcinoma of other and ill-defined sites in genitourinary tract	N/S									_	N/S								
8.6 Carcinoma of gastrointestinal tract	536	43.1	1,064	43.0	984	49.4	842	56.5	13.4	*	587 33.3	1,063	41.5	066	51.0	924	61.7 2	28.4	*
8.6.1 Carcinoma of colon and rectum	140	51.1	299	50.1	287	62.6	330	73.6	22.5	*	106 41.6	5 228	56.3	213	64.0	273	74.6 3	33.0	*
8.6.2 Carcinoma of stomach	307	44.0	530	48.0	445	51.9	310	56.5	12.5	*	416 30.6	200	36.5	646	47.0	521	59.3 2	28.7	*
8.6.3 Carcinoma of liver and intrahepatic bile ducts	62	26.0	193	19.3	226	28.4	170	31.4	5.4	*	28 17.9	84	33.4	82	47.7	86	31.4 1	13.5	
8.6.4 Carcinoma of pancreas	N/S										21 66.9) 18	83.5	24	71.0	28	69.3 2.4	4	
8.6.5 Carcinoma other and ill-defined sites in gastrointestinal tract	18	28.0	25	44.3	11	45.6	18	45.3	17.3		16 31.3	24	46.0	25	36.1	16	75.2 4	43.9	*
8.7 Carcinoma of other and ill-defined sites	54	31.7	102	44.3	78	51.5	60	48.1	16.4	*	41 53.8	3 92	33.8	57	35.2	55	60.2 6.4	4	
8.7.1 Adrenocortical carcinoma	N/S										N/S								
8.7.2 Carcinoma of other and ill-defined sites, NOS	51	33.6	94	44.9	76	51.5	53	48.7	15.1	*	37 48.8	8 87	33.4	52	38.5	46	66.1 1	17.3	

Diagnostic group (SEER)	Males										Females	s							
	1993-1995	95	1996-2000	000	2001-	-2005	2001-2005 2006-2010		Change [†] <i>P</i>	٩	1993-1	. 566	1996-2(000	1993-1995 1996-2000 2001-2005	05	2006-2010	0 Change [†]	nge⁺ <i>P</i>
	Cases	RSR	Cases	RSR	Cases RSR	RSR	Cases	RSR			Cases RSR	l I	Cases	RSR	Cases RSR Cases RSR	l	Cases R	RSR	
9. Miscellaneous Specified Neoplasms, NOS	51	49.4	80	52.8	154	71.0	221	81.0	31.6	*	70	57.3 1	133	84.4 194		85.7	232 7	78.6 21.3	
9.1 Other pediatric and embryonal tumors, NOS	21	33.6	24	33.5	32	53.3	27	62.6	29.0	*	12 25	25.1 1	19	63.3 19		63.3	24 6	63.4 38.3	
9.2 Other specified and embryonal tumors, NOS	30	60.4	56	61.0	122	75.6	194	83.4	23.0	*	58 64	64.0 1	114	87.9 1	175 8	88.2	208 8	80.3 16.3	
10. Unspecified Malignant Neoplasms	170	40.9	242	56.1	97	64.2	76	70.7	29.4	*	376 7	71.5 4	472	78.4 242		84.9	159 8	81.3 9.8	*

primitive neuroectodermal tumor; NOS, not otherwise specified ^tThyroid carcinoma was excluded from the incidence rate of all cancers combined because of its unusually high incidence rate. PNET, central nervous system; not shown because <20 cases were reported in each period. vears); CNS, escents and young adults (aged 15–29 1/journal.pone.0096088.t004 adolescents and AYAs, a doi:10. N/S:

82.2-85.1), and 88.9% (95% CI: 87.4-90.2) in 1993-1995, 1996-2000, 2001-2005, and 2006-2010, respectively. The survival rates of females aged 25-29 years were 67.7% (95% CI: 65.7-69.6), 73.6% (95% CI: 72.2-74.9), 82.9% (95% CI: 81.9-83.9), and 90.4% (95% CI: 89.5-91.2) in 1993-1995, 1996-2000, 2001-2005, and 2006-2010, respectively.

Discussion

This is the first study to investigate cancer incidence, survival and their trends among AYAs using the population-based national cancer registry in Korea. The major findings of this study were that cancer in AYAs showed a trend of increasing incidence, with an increase of 6.3% per year ($P \le 0.05$), from 1999 to 2010 and that age- and gender-related cancer incidence patterns differed according to the primary site. Moreover, five-year relative survival rates for most cancers improved from 1993-1995 (58.9%) to 2006-2010 (84.8%) among AYAs.

When comparing our study with studies from other countries, cancer incidence rates among AYAs in our study were lower than incidence rates in the U.S. [5], France [21], Portugal [22], and Netherlands [3] and among males in Canada [12], even though the time period and age group differs. In other studies, cancer incidence in AYA males was generally similar to or higher than cancer incidence in AYA females. Conversely, we reported much lower incidence rates in males than in females. The reason for this difference in the incidence rate by gender was that thyroid carcinoma has the highest incidence and rapidly increased in incidence among AYA females in Korea.

Consistent with other studies, we found a rising incidence of cancer among AYAs during the study period.

The data on AYAs in Korea reported here exhibited several important differences from site-specific cancer incidence rates among AYAs in other regions of the world. Since the 2000s, an annual increase in incidence of 0.6-2.0% has been reported in several countries [16,23-25]. However, our results showed an annual increase in incidence of 6.3%, which is a more rapid increase than observed in other studies. The increased cancer incidence rate may be partially explained by changes in cancer classification, as exemplified by changes in the classification of hematologic malignancies in a study by Park et al. [26]

The increased incidence of carcinomas was primarily due to an increase in the incidence rates of thyroid carcinoma (APC = 17.9%). An increased incidence rate of thyroid carcinoma has also been noted among AYAs in Western countries [23,27,28]. However, the incidence of thyroid carcinoma among AYAs is more than three- to tenfold higher in Korea than in Canada [12], England [23], the United States [5], the Netherlands [3] and Portugal [22]. The reasons for the high incidence of thyroid carcinoma in Korean AYAs compared with other nationalities are unknown. Although the rapid increase and high incidence rate of thyroid cancer among older individuals worldwide might be attributable to the development of improved technologies for early detection [29], the exact cause of the increased incidence of most cancers in AYAs is unknown. Because of the difficulty in recommending thyroid cancer screening for AYAs solely based on incidence rates, further research to identify associated risk factors, such as family history, socioeconomic status, and environmental exposure, is needed.

In this study, a notable trend of increasing incidence was also observed for cervical carcinoma (APC = 6.2%) among female AYAs in Korea. Although the incidence of cervical carcinoma in Korean females of all ages is decreasing (APC = -4.3%) [6], the

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incidence of cervical carcinoma has been increasing among Korean females under 30 years of age [30]. A steady increase in cervical carcinoma in young women (20-29 years) has also been observed in England [31]. The increased incidence of cervical carcinoma among AYAs has been attributed to increases in human papillomavirus (HPV) infection [32,33]. More specifically, an increase in sexual behavior among younger age groups has led to an increased rate of HPV infection [34,35], and the prevalence rate of HPV has been reported to increase with decreasing age [32]. Therefore, since 2007, the Korean Society of Gynecologic Oncology and Colposcopy (KSGOC) has recommended the HPV vaccine for females aged 15-17 for the prevention of cervical carcinoma. In fact, certain recent studies have reported a decrease in the incidence of cervical carcinoma due to the use of the HPV vaccine at an earlier age [36,37]. Therefore, the incidence of cervical carcinoma is expected to gradually decline among AYAs in Korea due to the HPV vaccine.

In terms of survival, our data are consistent with that reported for other geographic regions. Although the time period in our study differed, the overall cancer survival rate among AYAs in Korea was similar to the rate and significantly improvement reported in the U.S. and Germany. Improvements in relative survival rates among AYAs can be partially explained by advances in cancer detection, more intensive treatments, and increased expertise in adolescent oncology [38]. Additionally, access to effective protocols and the development of health infrastructures may have also contributed to improvements in survival rates [39].

However several important differences should be highlighted in lymphoma and leukemia. In the present study, the most significant improvements in survival were observed in leukemia and lymphoma patients, but the survival rates for leukemia and lymphoma were noticeably lower than in the U.S. and Germany [40,41]. This reason for this difference in the survival rate by ethnic was that the incidence cases of subgroup of leukemia and lymphoma was different between U.S. AYAs [41] and Korea AYAs. More, ethnic disparities in tumor biology and clinical factors may influence cancer treatment and survival [42].

Compared with the survival of patients aged 1 to 10 years, overall survival and disease-specific survival are clinically significantly poorer among AYA patients with acute lymphoblastic leukemia [43]. The survival rates for leukemia among the Korean AYAs in our study have remained worse than among Korean children based on data from the KCCR [44].

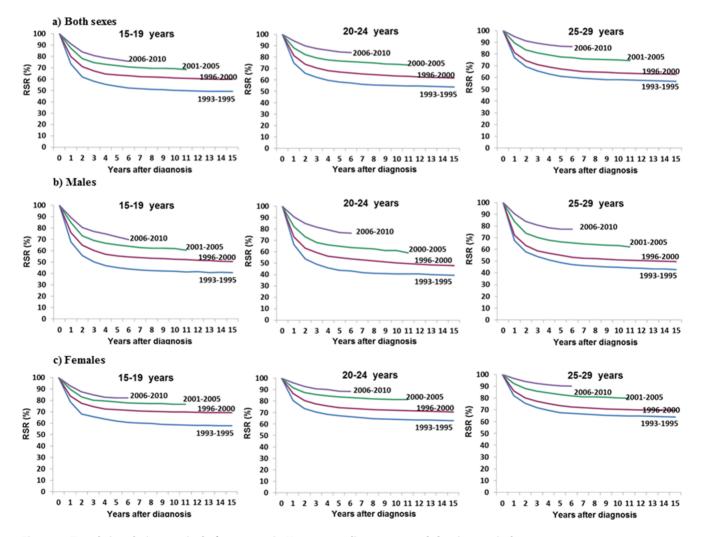


Figure 2. Trends in relative survival after cancer in Korea according to age and the time period. doi:10.1371/journal.pone.0096088.g002

Among AYAs, breast cancer accounts for approximately 7% and 4.9% of all cancers diagnosed in the United States [5] and Korea, respectively. In the United States, the 5-year survival rate for breast cancer is lower among AYAs (80.2%) than among patients in other age groups (30–39 years, 83.4%; 40–49 years, 88.9%), and particularly older patients [41]. Our study showed similar results. The relative survival rate for breast cancer among Korean females aged 15–29 years was 86.8% in 2006–2010, whereas the relative survival rate among Korean females aged \geq 40 years was 91.0% based on a direct estimate from the KNCIDB.

One limitation of our study is that the follow-up period began relatively soon after the diagnosis of cancer, in contrast to the protocols in other studies [3–5]. Another limitation of this study is that we could not estimate the survival rates after adjusting for cancer stage and treatment because our registry database did not include information on cancer stage and treatment.

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In conclusion, our study provides representative cancer statistics regarding temporal trends in the AYA population in Korea. In particular, the results showed an increasing trend in cancer incidence and an improving survival trend among AYAs in Korea. These results may support cancer control and prevention plans focusing on AYAs.

In the future, further research will help to identify factors affecting cancer incidence and responses to treatment among AYAs. In particular, research on the etiological factors related to the rapid increase in thyroid carcinoma in AYAs is needed.

Author Contributions

Conceived and designed the experiments: Y-JW . Analyzed the data: E-KM . Wrote the paper: E-KM Y-JW. Interpreted the results: HJP E-KM Y-JW. Contributed to the discussion and reviewed manuscript: HJP HYS BKP C-MO K-WJ E-KM Y-JW.

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