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Original Article

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Incidence and Survival of Childhood Cancer in Korea

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Purpose

An epidemiologic study of childhood cancer would provide useful information on cancer etiology and development of management guidelines.

Materials and Methods

Data from the Korea National Cancer Incidence Database were used to examine the incidence and survival of cancer in patients aged 0-14 years. Patients were grouped according to the International Classification of Childhood Cancer, 3rd edition. Age-specific and age-standardized incidences per million and estimated annual percentage change (APC) were calculated by sex and age. Five-year relative survival was calculated for four periods from 1993 to 2011.

Results

The study comprised 15,113 patients with malignant neoplasms. Age-standardized incidence rates for all cancers were 134.9 per million children in 1999-2011 and 144.0 and 124.9 per million for males and females, respectively (M/F ratio, 1.2; $p < 0.05$). The highest incidences were observed for 'leukemias, myeloproliferative diseases, and myelodysplastic diseases' (group I) (46.4), 'central nervous system neoplasms' (group III) (18.3), and 'lymphomas and reticuloendothelial neoplasms' (group II) (13.4). Age-standardized incidence increased from 117.9 in 1999 to 155.3 in 2011, with an APC of 2.4% (95% confidence interval, 2.1 to 2.7). There was a significant increase of APC in 'neuroblastoma and other peripheral nervous cell tumors' (group IV) (5.6%) and 'other malignant epithelial neoplasms and malignant melanomas' (group XI) (5.6%). The 5-year relative survival rate for all childhood cancers improved significantly from 56.2% (1993-1995) to 78.2% (2007-2011) (males, 56.7% to 77.7%; females, 55.5% to 78.8%).

Conclusion

This study provides reliable information on incidence and survival trends for childhood cancer in Korea.

Key words
Neoplasms, Child, Incidence, Survival, Korea

Introduction

The incidence of cancer in children younger than 15 years of age varies among countries worldwide. Despite dramatic improvements in therapeutics and early detection, cancer remains the second most common cause of childhood death in developed countries [1]. In some developed countries, such as Australia, Ireland, Switzerland, and the United States, childhood cancer incidence rates of 140-160 per mil-

lion children have been reported [2-4]. According to a GLOBOCAN estimation of cancer rates in 2012, leukemia was the most common childhood malignancy worldwide, followed by malignancies of the brain and nervous system, non-Hodgkin lymphomas, renal tumors, and Hodgkin lymphomas. However, the rank and outcome of the most common cancer types varied among countries.

Cancer is also the second leading cause of childhood death in Korea. However, an epidemiologic study of cancer in children aged 0-14 years has never been conducted. We conducted the first nationwide study describing the incidence and survival of all childhood cancers in Korea.

Materials and Methods

1. Data sources

This study was approved by the Institutional Review Board (NCC 2015-0069). Data on childhood cancer incidence and survival in Korea were obtained from the Korea National Cancer Incidence database in the Korea Central Cancer Registry (KCCR).

The KCCR was initiated by the Korean Ministry of Health and Welfare in 1980 and collected cancer cases from more than 180 hospitals in Korea annually until 1998. These data represent 80%-90% of cancer incidence in Korea and have been collected on the entire Korean population since 1999 through a population-based cancer registry program [5].

The KCCR collects data on variables including age, sex, first diagnosis date, primary tumor site, morphology, method of diagnosis, and stage at diagnosis. KCCR statistics from 1999-2002 and 2003-2007 have been published in *Cancer Incidence in Five Continents* volumes IX and X (http://ci5.iarc.fr/Default.aspx), in which the completeness and validity of the incidence data were assessed.

The incidence rates of cancer in children aged 0-14 years who were diagnosed in 1999-2011 were calculated. For estimation of cancer survival, data on childhood cancer in 1993-2011 were obtained from the KCCR, and patients' vital status was followed up until December 31, 2012.

2. Case definition

To enable comparison with several previous studies of childhood cancer, the age group in this study was 0-14 years old [6-8]. Diagnoses were grouped into 12 main diagnostic groups and 47 subgroups according to the International Classification of Childhood Cancer, 3rd edition (ICCC-3) [9], which is based on the International Classification of Disease for Oncology, 3rd edition (ICD-O-3). The ICCC scheme, which is based on cancer topography and morphology, was specifically established for classification of tumors in children.

3. Statistical methods

1) Incidence

Frequencies, percent distribution, crude incidence rates and annual percent change (APC) were computed by sex and age group (< 1 year, 1-4 years, 5-9 years, and 10-14 years). Age-standardized incidence rates (ASRs) in males and females were estimated by the direct method using world standard population defined by the World Health Organization for age groups 0-14 years. The male/female ratio of the ASRs was also calculated. Cancer incidence trends were based on the 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 ASRs in a calendar year (http://seer.cancer.gov/csr/1975_2010/).

2) Survival

The 5-year survival rate for each diagnostic group was analyzed based on relative survival for the following time periods: 1993-1995, 1996-2000, 2001-2005, 2006-2010, and 2007-2011. These time periods were chosen to enable direct comparison with earlier studies [10,11]. The relative survival rates for each diagnostic group were calculated by dividing the observed survival by expected survival among comparable groups in the general population according to the Ederer II method. The survival rates were calculated by "complete analysis," which included "right-censored" patients. This analysis provided more up-to-date and precise survival rates in long-term survival, due to inclusion of the early survival experience of more recently recruited patients [12].

Trends in 5-year relative survival rates by time period were assessed using a relative excess risk model [13]. Statistical analyses were performed using SAS ver. 9.2 (SAS Institute Inc., Cary, NC).

Results

1. Incidence

A total of 15,113 cancer patients aged 0-14 years were diagnosed in 1999-2011, and the average annual incidence

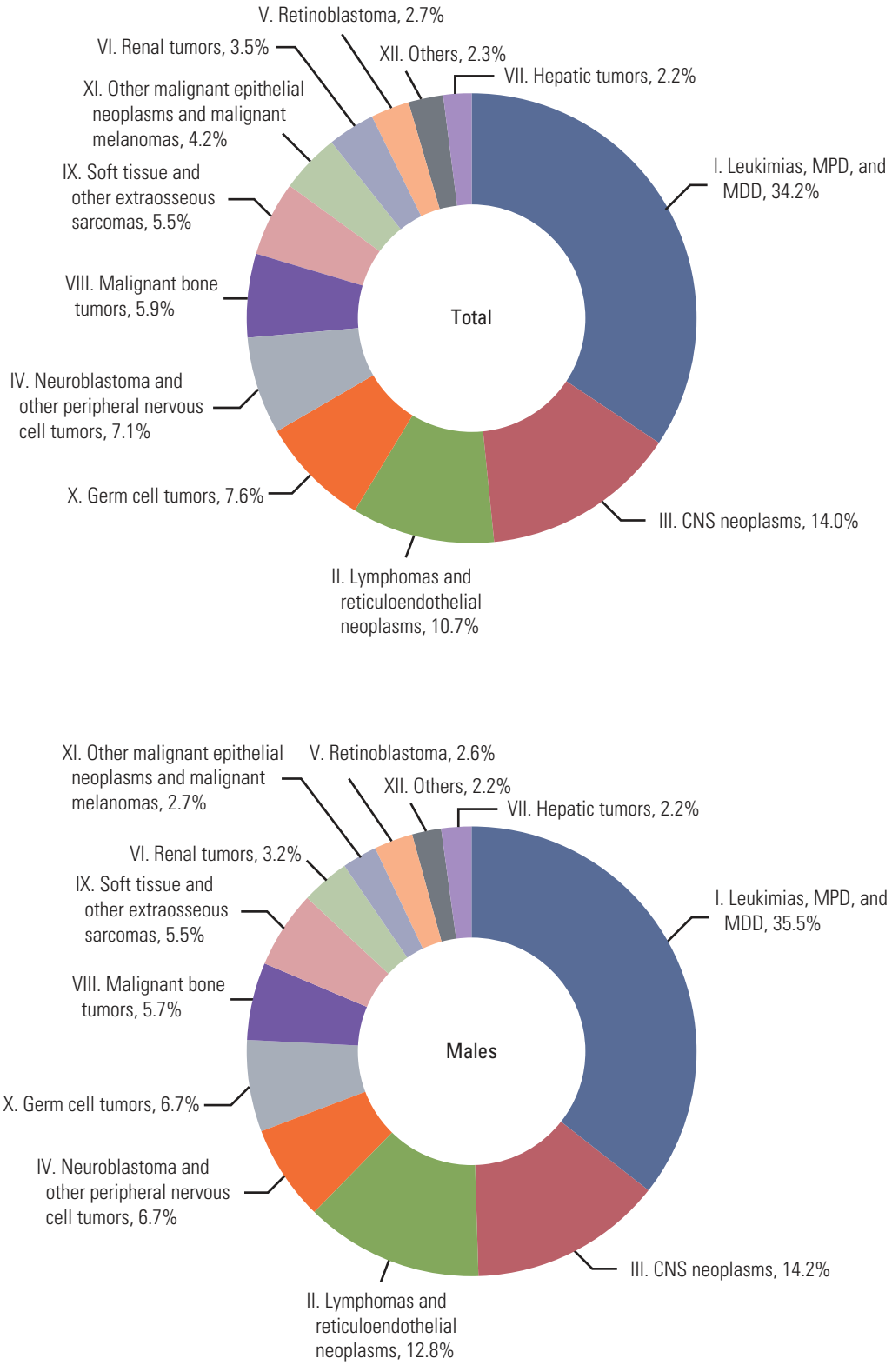

Fig. 1. Cancer incidence by diagnostic groups in children (0-14 years of age) in Korea, 1999-2011. MPD, myeloproliferative diseases; MDD, myelodysplastic diseases; CNS, central nervous system. *(Continued to the next page)*

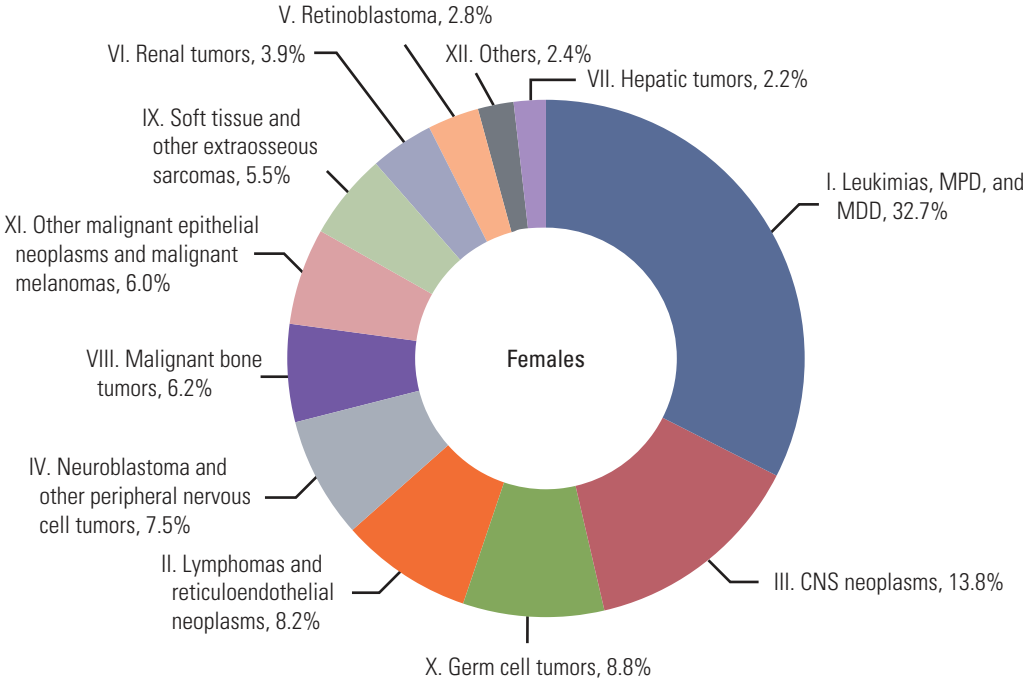

Fig. 1. *(Continued from the previous page)*

was 1,163 cases; 8,435 patients (55.8%) were males, and 6,678 (44.2%) were females. The age distribution was as follows: < 1 year, 1,740 (11.5%); 1-4 years, 4,694 (31.1%); 5-9 years, 3,814 (25.2%); and 10-14 years, 4,865 (32.2%). The most common cancer was 'leukemias, myeloproliferative diseases, and myelodysplastic diseases' (group I), which accounted for 34.2% of all cancers in both sexes (males, 35.5%; females, 32.7%); 'lymphoid leukemia' (group I.a) represented almost one third of this group. 'Leukemias, myeloproliferative diseases, and myelodysplastic diseases' (group I), 'central nervous system (CNS) neoplasms' (group III), and 'lymphomas and reticuloendothelial neoplasms' (group II) accounted for more than half of all childhood cancer cases (Fig. 1).

Between 1999 and 2011, the age-standardized incidence rate of all cancers was 144.0 and 124.9 per million for males and females, respectively. Higher cancer incidence was observed in males (male/female ratio, 1.2; $p < 0.05$). The higher rate among males was due to a substantially higher incidence of 'lymphomas and reticuloendothelial neoplasms' (group II) (male, 16.9 per million; female, 9.6 per million). The highest incidence rate was observed in children < 1 year old (277.3 per million), followed by those aged 1-4 years (164.9 per million), 10-14 years (111.7 per million), and 5-9 years (92.8 per million) (Table 1). The higher rate among children < 1 year old was largely due to a substantially higher incidence rate of 'leukemias, myeloproliferative diseases, and myelodysplastic diseases' (group I) (63.7 per million), 'neuroblastoma and other peripheral nervous cell tumors' (group IV) (55.6 per million) and CNS neoplasms (group III) (26.1 per million).

Incidence trends showed a significant increase between 1999 and 2011 (APC: 2.4% per year in both sexes; 2.3% per year in males; 2.6% per year in females) (Fig. 2). The incidence of most cancer types showed an increasing trend, with the exception of 'other and unspecified malignant neoplasms' (group XII) (APC, –7.4%; 95% confidence interval [CI], –12.2 to –2.3). There was a significant increase of APC in 'neuroblastoma and other peripheral nervous cell tumors' (group IV, 5.6%) and 'other malignant epithelial neoplasms and malignant melanomas' (group XI, 5.6%). However, in assessment by diagnostic group, the incidence of different cancer types varied between males and females. Among males, the highest increase in incidence was observed for 'other malignant epithelial neoplasms and malignant melanomas' (group XI) (APC, 6.1%; 95% CI, 1.1 to 11.3), followed by 'lymphomas and reticuloendothelial neoplasms' (group II) (APC, 4.8%; 95% CI, 2.4 to 7.2) and 'neuroblastoma and other peripheral nervous cell tumors' (group IV) (APC, 4.3%; 95% CI, 1.5 to 7.2). Among females, the highest increase in incidence was observed for 'neuroblastoma and other peripheral nervous cell tumors' (group IV) (APC, 7%; 95% CI, 4.9 to 9.3), followed by 'other malignant epithelial neo-

Table 1. Number of cases, crude incidence rates, and age-standardized rates (ASR) per million of childhood cancers in Korea for the period 1999-2011

Diagnostic group (ICCC-3)	Total											Male	Female	M/F ratio[a]
	0 yr		1-4 yr		5-9 yr		10-14 yr		0-14 yr			ASR	ASR	
	Cases	CR	Cases	CR	Cases	CR	Cases	CR	Cases	CR	ASR			
All cancers	1,740	277.3	4,694	164.9	3,814	92.8	4,865	111.7	15,113	126.6	134.9	144.0	124.9	1.2*
I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases	400	63.7	1,861	65.4	1,491	36.3	1,424	32.7	5,176	43.4	46.4	50.9	41.4	1.2*
a. Lymphoid leukemias	145	23.1	1,319	46.3	929	22.6	734	16.9	3,127	26.2	28.3	31.0	25.4	1.2*
b. Acute myeloid leukemias	116	18.5	330	11.6	349	8.5	454	10.4	1,249	10.5	10.8	11.7	9.8	1.2*
c. Chronic myeloproliferative diseases	21	3.3	29	1.0	62	1.5	93	2.1	205	1.7	1.7	2.1	1.3	1.6
d. Myelodysplastic syndrome and other myeloproliferative diseases	54	8.6	67	2.4	57	1.4	47	1.1	225	1.9	2.2	2.8	1.5	1.9*
e. Unspecified and other specified leukemias	64	10.2	116	4.1	94	2.3	96	2.2	370	3.1	3.4	3.3	3.5	0.9
II. Lymphomas and reticuloendothelial neoplasms	81	12.9	369	13.0	498	12.1	673	15.5	1,621	13.6	13.4	16.9	9.6	1.8*
a. Hodgkin disease	-	-	12	0.4	38	0.9	105	2.4	155	1.3	1.1	1.4	0.8	1.8*
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	15	2.4	118	4.1	255	6.2	370	8.5	758	6.3	5.9	7.2	4.5	1.6*
c. Burkitt lymphoma	1	0.2	78	2.7	104	2.5	95	2.2	278	2.3	2.3	3.6	0.9	4.0*
d. Miscellaneous lymphoreticular neoplasms	55	8.8	125	4.4	57	1.4	45	1.0	282	2.4	2.8	3.0	2.5	1.2*
e. Unspecified lymphomas	10	1.6	36	1.3	44	1.1	58	1.3	148	1.2	1.2	1.6	0.8	1.9*
III. CNS and miscellaneous intracranial and intraspinal neoplasms	164	26.1	566	19.9	736	17.9	655	15.0	2,121	17.8	18.3	19.7	16.8	1.2*
a. Ependymomas and choroid plexus tumors	22	3.5	103	3.6	61	1.5	31	0.7	217	1.8	2.1	2.1	2.0	1.0
b. Astrocytomas	24	3.8	88	3.1	142	3.5	184	4.2	438	3.7	3.6	3.7	3.5	1.1
c. Intracranial and intraspinal embryonal tumors	57	9.1	230	8.1	266	6.5	191	4.4	744	6.2	6.6	7.5	5.5	1.4*
d. Other gliomas	11	1.8	48	1.7	110	2.7	97	2.2	266	2.2	2.2	2.1	2.2	1.0
e. Other specified intracranial and intraspinal neoplasms	7	1.1	12	0.4	11	0.3	13	0.3	43	0.4	0.4	0.4	0.4	1.2
f. Unspecified intracranial and intraspinal neoplasms	43	6.9	85	3.0	146	3.6	139	3.2	413	3.5	3.5	3.8	3.2	1.2*
IV. Neuroblastoma and other peripheral nervous cell tumors	349	55.6	565	19.8	121	2.9	34	0.8	1,069	9.0	11.6	11.8	11.4	1.0
a. Neuroblastoma and ganglioneuroblastoma	349	55.6	562	19.7	117	2.8	28	0.6	1,056	8.8	11.5	11.7	11.4	1.0
b. Other peripheral nervous cell tumors	-	-	3	0.1	4	0.1	6	0.1	13	0.1	0.1	0.1	0.1	2.0*
V. Retinoblastoma	141	22.5	255	9.0	15	0.4	-	-	411	3.4	4.6	4.8	4.4	1.1*
VI. Renal tumors	126	20.1	282	9.9	90	2.2	27	0.6	525	4.4	5.5	5.4	5.7	0.9
a. Nephroblastoma and other nonepithelial renal tumors	121	19.3	261	9.2	79	1.9	11	0.3	472	4.0	5.0	4.8	5.2	0.9
b. Renal carcinomas	-	-	5	0.2	9	0.2	15	0.3	29	0.2	0.2	0.2	0.2	1.1
c. Unspecified malignant renal tumors	5	0.8	16	0.6	2	0.0	1	0.0	24	0.2	0.3	0.3	0.2	1.5*

Table 1. Continued

Diagnostic group (ICCC-3)	Total											Male	Female	M/F ratio[a]
	0 yr		1-4 yr		5-9 yr		10-14 yr		0-14 yr			ASR	ASR	
	Cases	CR	Cases	CR	Cases	CR	Cases	CR	Cases	CR	ASR			
VII. Hepatic tumors	99	15.8	144	5.1	45	1.1	45	1.0	333	2.8	3.4	3.6	3.3	1.1*
a. Hepatoblastoma	90	14.3	114	4.0	23	0.6	7	0.2	234	2.0	2.6	2.8	2.3	1.2*
b. Hepatic carcinomas	3	0.5	17	0.6	20	0.5	37	0.8	77	0.6	0.6	0.6	0.6	1.0
c. Unspecified malignant hepatic tumors	6	1.0	13	0.5	2	0.0	1	0.0	22	0.2	0.2	0.2	0.3	0.6
VIII. Malignant bone tumors	13	2.1	71	2.5	219	5.3	595	13.7	898	7.5	6.6	6.7	6.5	1.0
a. Osteosarcomas	-	-	20	0.7	144	3.5	443	10.2	607	5.1	4.3	4.4	4.2	1.1*
b. Chondrosarcomas	-	-	-	-	1	0.0	24	0.6	25	0.2	0.2	0.2	0.2	1.1
c. Ewing tumors and related sarcomas of bone	9	1.4	30	1.1	49	1.2	81	1.9	169	1.4	1.4	1.3	1.4	0.9
d. Other specified malignant bone tumors	1	0.2	6	0.2	9	0.2	18	0.4	34	0.3	0.3	0.2	0.3	0.7
e. Unspecified malignant bone tumors	3	0.5	15	0.5	16	0.4	29	0.7	63	0.5	0.5	0.5	0.5	1.1
IX. Soft tissue and other extraosseous sarcomas	96	15.3	221	7.8	192	4.7	320	7.3	829	6.9	7.2	7.9	6.5	1.2*
a. Rhabdomyosarcomas	42	6.7	151	5.3	101	2.5	85	2.0	379	3.2	3.5	3.9	3.1	1.2*
b. Fibrosarcomas, peripheral nerve sheath tumors and other fibrous neoplasms	23	3.7	13	0.5	15	0.4	38	0.9	89	0.7	0.8	0.9	0.7	1.4*
c. Kaposi sarcoma	-	-	-	-	-	-	-	-	-	-	-	-	-	-
d. Other specified soft tissue sarcomas	24	3.8	41	1.4	59	1.4	160	3.7	284	2.4	2.3	2.3	2.2	1.1
e. Unspecified soft tissue sarcomas	7	1.1	16	0.6	17	0.4	37	0.8	77	0.6	0.6	0.7	0.6	1.2*
X. Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	178	28.4	200	7.0	227	5.5	547	12.6	1,152	9.6	9.8	9.7	9.9	1.0
a. Intracranial and intraspinal germ cell tumors	11	1.8	9	0.3	111	2.7	273	6.3	404	3.4	2.9	3.9	1.9	2.0*
b. Malignant extracranial and extragonadal germ cell tumors	103	16.4	43	1.5	7	0.2	17	0.4	170	1.4	1.9	1.4	2.5	0.5
c. Malignant gonadal germ cell tumors	59	9.4	142	5.0	104	2.5	220	5.1	525	4.4	4.6	4.3	4.9	0.9
d. Gonadal carcinomas	1	0.2	2	0.1	1	0.0	21	0.5	25	0.2	0.2	0.1	0.3	0.2
e. Other and unspecified malignant gonadal tumors	4	0.6	4	0.1	4	0.1	16	0.4	28	0.2	0.2	0.2	0.3	0.8
XI. Other malignant epithelial neoplasms and malignant melanomas	5	0.8	27	0.9	121	2.9	479	11.0	632	5.3	4.5	3.1	6.1	0.5
a. Adrenocortical carcinomas	2	0.3	8	0.3	5	0.1	1	0.0	16	0.1	0.2	0.0	0.3	0.1
b. Thyroid carcinomas	-	-	1	0.0	45	1.1	242	5.6	288	2.4	2.0	0.8	3.3	0.2
c. Nasopharyngeal carcinomas	-	-	-	-	5	0.1	35	0.8	40	0.3	0.3	0.4	0.1	4.1*
d. Malignant melanomas	2	0.3	9	0.3	11	0.3	17	0.4	39	0.3	0.3	0.2	0.4	0.6
e. Skin carcinomas	-	-	4	0.1	11	0.3	16	0.4	31	0.3	0.2	0.2	0.2	0.9
f. Other and unspecified carcinomas	1	0.2	5	0.2	44	1.1	168	3.9	218	1.8	1.5	1.4	1.7	0.8
XII. Other and unspecified malignant neoplasms	88	14.0	133	4.7	59	1.4	66	1.5	346	2.9	3.4	3.6	3.2	1.1*
a. Other specified malignant tumors	3	0.5	25	0.9	8	0.2	9	0.2	45	0.4	0.4	0.3	0.5	0.6
b. Other unspecified malignant tumors	85	13.5	108	3.8	51	1.2	57	1.3	301	2.5	3.0	3.3	2.7	1.2*

ICCC-3, International Classification of Childhood Cancer, 3rd edition; CR, crude incidence rate (per million), ASR, age standardized incidence rate (per million).
*$p < 0.05$. [a]M/F ratio=male ASR/female ASR.

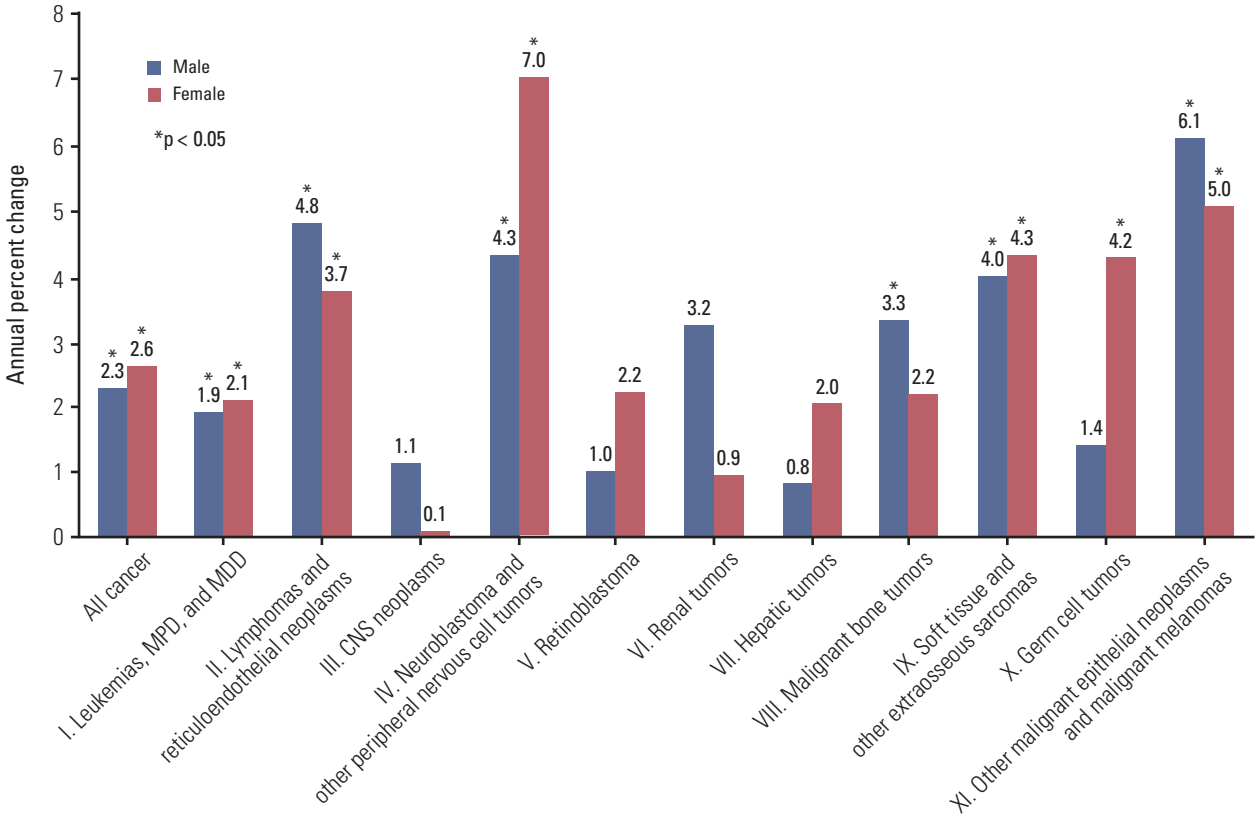

Fig. 2. Annual percent change of cancer incidence by diagnostic groups in children (0-14 years of age) in Korea, 1999-2011. MPD, myeloproliferative diseases; MDD, myelodysplastic diseases; CNS, central nervous system. *p < 0.05.

plasms and malignant melanomas' (group XI) (APC, 5%; 95% CI, –0.1 to 10.5) and 'soft tissue and other extraosseous sarcomas' (group IX) (APC, 4.3%; 95% CI, 1.1 to 7.6) (Fig. 2).

2. Survival

The survival analysis comprised 20,523 children diagnosed with cancer in 1993-2011 (males, 11,644; females, 8,879). Table 2 shows the 5-year relative survival rates and the number of cases in each of the five time periods (1993-1995, 1996-2000, 2001-2005, 2006-2010, and 2007-2011). In analysis by 12 main diagnostic group, 'leukemias, myeloproliferative diseases, and myelodysplastic diseases' (group I) and 'neuroblastoma and other peripheral nervous cell tumors' (group IV) showed the most marked improvements in survival, from 47.4% and 43.2% in 1993-1995 to 75.4% and 73.9% in 2007-2011, respectively. Survival rates for 'retinoblastoma' (group V) and 'other malignant epithelial neoplasms and malignant melanomas' (group XI) consistently exceeded 80%-90% for all periods measured. The lowest improvement in survival rate was observed for 'CNS neoplasms' (group III).

For all childhood cancers, the 5-year relative survival rate increased significantly, from 56.2% in 1993-1995 to 78.2% in 2007-2011 ($p < 0.05$), with significant improvements in both males (from 56.7% in 1993-1995 to 77.7% in 2007-2011; $p < 0.05$) and females (from 55.5% in 1993-1995 to 78.8% in 2007-2011) ($p < 0.05$) and for all age groups tested (Fig. 3). The improvement in the 5-year relative survival rate was slightly higher for females (23.3%) compared with males (21.0%). Among males, 5-year relative survival improved from 60.6% in 1993-1995 to 76.4% in 2007-2011 in children aged < 1 year, from 54.9% to 82.9% in children aged 1-4 years, from 52.0% to 77.0% in children aged 5-9 years, and from 54.0% to 75.4% in children aged 10-14 years. Among females, 5-year relative survival improved from 48.6% in 1993-1995 to 73.5% in 2007-2011 in children aged < 1 year, from 53.1% to 77.6% in children aged 1-4 years, from 55.0% to 76.6% in children aged 5-9 years, and from 56.1% to 80.3% in children aged 10-14 years (Fig. 3).

Table 2. Five-year relative survival rates for childhood cancer in Korea in 1993-2011 according to ICCC-3 diagnostic groups

Diagnostic group (ICCC-3)	Total										Change*
	1993-1995		1996-2000		2001-2005		2006-2010		2007-2011		
	Cases	RSR[a)]	Cases	RSR[a)]	Cases	RSR[a)]	Cases	RSR[a)]	Cases	RSR[a)]	
All cancers	2,921	56.2	5,441	64.1	5,563	72.3	5,496	77.2	5,481	78.2	22.0*
I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases	1,076	47.4	1,944	58.4	1,999	68.2	1,875	74.9	1,883	75.4	28.0*
a. Lymphoid leukemias	665	57.3	1192	67.7	1215	77	1,164	80.6	1,156	81	23.7*
b. Acute myeloid leukemias	250	26.5	504	41.8	494	50.9	424	58.9	435	59.7	33.2*
c. Chronic myeloproliferative diseases	38	34.3	81	47	66	66.7	84	88.5	88	86.1	51.8
d. Myelodysplastic syndrome and other myeloproliferative diseases	6	100.4	24	66.8	99	62.8	85	75.3	98	75.6	–24.8
e. Unspecified and other specified leukemias	117	37.7	143	44.1	125	56.9	118	66.4	106	69.1	31.4*
II. Lymphomas and reticuloendothelial neoplasms	252	64.1	495	71.9	606	82.9	624	83.5	642	86.6	22.5*
a. Hodgkin disease	26	84.8	37	94.7	60	95.1	62	93.4	61	95.1	10.3
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	107	58.1	246	69.6	286	78.4	310	74.9	300	78.8	20.7*
c. Burkitt lymphoma	18	72.4	71	77.6	100	86.1	121	86	120	87.4	15.0
d. Miscellaneous lymphoreticular neoplasms	28	46.6	59	69.7	89	91.2	107	98.3	140	99.4	52.8*
e. Unspecified lymphomas	73	70	82	64.8	71	76.2	24	91.8	21	90.6	20.6
III. CNS and miscellaneous intracranial and intraspinal neoplasms	443	48.7	775	46.7	798	54.7	759	57.3	734	59	10.3*
a. Ependymomas and choroid plexus tumors	27	55.7	83	58	80	66.3	81	66.6	78	70.2	14.5
b. Astrocytomas	104	54.9	179	48.7	159	56.7	151	53.6	157	51.1	–3.8
c. Intracranial and intraspinal embryonal tumors	128	49.4	251	55.1	302	57.4	275	60.9	278	60.4	11.0
d. Other gliomas	41	68.5	73	46.7	88	45.5	134	43.9	119	49.7	–18.8*
e. Other specified intracranial and intraspinal neoplasms	6	33.5	19	26.4	12	50.1	17	53	15	66.1	32.6
f. Unspecified intracranial and intraspinal neoplasms	137	36.6	170	28.9	157	47.2	101	64.3	87	69.9	33.3*
IV. Neuroblastoma and other peripheral nervous cell tumors	151	43.2	373	54.9	354	70.3	364	71.5	360	73.9	30.7*
a. Neuroblastoma and ganglioneuroblastoma	145	43.6	361	54.2	351	70	359	71.7	354	73.9	30.3*
b. Other peripheral nervous cell tumors	6	33.4	12	75.2	3	100.1	5	57.2	6	71.5	38.1
V. Retinoblastoma	103	90.7	173	88.8	185	95.4	136	97.3	137	95.5	4.8*
VI. Renal tumors	112	78.1	225	78.5	192	86.1	193	91.8	184	94.1	16.0*
a. Nephroblastoma and other nonepithelial renal tumors	88	83.4	193	80.6	180	86.9	178	92.2	170	93.6	10.2*
b. Renal carcinomas	5	40.1	9	66.8	8	75.1	10	100.1	11	100.1	60.0*
c. Unspecified malignant renal tumors	19	63.5	23	65.5	4	75.1	5	60.1	3	100.1	36.6
VII. Hepatic tumors	60	48.5	145	59.5	117	66.8	110	71.2	117	69.5	21.0*
a. Hepatoblastoma	26	65.8	79	72.5	87	76.1	86	77.7	93	76.1	10.3
b. Hepatic carcinomas	19	36.9	42	35.8	24	33.4	20	43.4	20	38.9	2.0
c. Unspecified malignant hepatic tumors	15	33.5	24	58.6	6	66.8	4	75.1	4	75.1	41.6

Table 2. Continued

Diagnostic group (ICCC-3)	Total										Change*
	1993-1995		1996-2000		2001-2005		2006-2010		2007-2011		
	Cases	RSR[a)]	Cases	RSR[a)]	Cases	RSR[a)]	Cases	RSR[a)]	Cases	RSR[a)]	
VIII. Malignant bone tumors	184	57.2	292	65.8	322	68.1	353	75.3	339	77.4	20.2*
a. Osteosarcomas	132	55.4	205	64.9	222	68.5	249	78.6	241	81.5	26.1*
b. Chondrosarcomas	4	75.2	9	66.8	8	75.1	12	91.8	12	91	15.8
c. Ewing tumors and related sarcomas of bone	16	50.1	49	67.4	58	53.5	59	56.1	57	58.5	8.4
d. Other specified malignant bone tumors	4	75.2	6	66.8	13	100.1	13	66.4	10	55.2	–20.0
e. Unspecified malignant bone tumors	28	64.4	23	69.7	21	81	20	90.1	19	89.6	25.2
IX. Soft tissue and other extraosseous sarcomas	146	57	243	68.5	292	72.7	277	78.2	281	77.2	20.2*
a. Rhabdomyosarcomas	70	48.7	129	62.2	139	64.9	115	75.6	115	78.8	30.1*
b. Fibrosarcomas, peripheral nerve sheath tumors, and other fibrous neoplasms	15	66.9	20	85.2	37	75.9	32	84.2	31	79.4	12.5
c. Kaposi sarcoma	-	-	2	50.1	-	-	-	-	-	-	-
d. Other specified soft tissue sarcomas	49	69.6	64	73.6	92	78.3	102	82.5	106	79.3	9.7
e. Unspecified soft tissue sarcomas	12	41.8	28	75.2	24	91.8	28	65.8	29	60.8	19.0
X. Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	196	79.4	433	88.3	408	92.8	454	93.8	452	94.6	15.2*
a. Intracranial and intraspinal germ cell tumors	44	68.3	104	75.2	138	84.2	174	89	160	89.9	21.6*
b. Malignant extracranial and extragonadal germ cell tumors	31	55.2	73	85.4	49	96.4	62	95.4	70	97.4	42.2*
c. Malignant gonadal germ cell tumors	97	90.1	228	95	201	97.7	200	98	206	98.5	8.4*
d. Gonadal carcinomas	8	75.2	12	83.5	8	87.7	9	77.8	10	69.4	–5.8
e. Other and unspecified malignant gonadal tumors	16	94.2	16	93.9	12	100.2	9	100.1	6	100.1	5.9
XI. Other malignant epithelial neoplasms and malignant melanomas	91	87	214	83.8	177	84.8	284	94.8	290	93.8	6.8*
a. Adrenocortical carcinomas	2	50.1	4	50.2	6	66.8	8	71.7	6	77.9	27.8
b. Thyroid carcinomas	37	100.2	90	96.8	77	100.1	134	100.1	148	100.1	–0.1
c. Nasopharyngeal carcinomas	10	100.3	8	75.1	8	62.6	21	88.5	21	85.4	–14.9
d. Malignant melanomas	7	85.9	10	70.2	7	71.5	22	86.5	23	91.1	5.2
e. Skin carcinomas	2	100.2	12	91.8	6	100.1	10	100.1	12	100.1	–0.1
f. Other and unspecified carcinomas	33	69.9	90	73.4	73	72.7	89	92	80	86.2	16.3
XII. Other and unspecified malignant neoplasms	107	52.6	129	73.1	113	79	67	83.9	62	80.4	27.8*
a. Other specified malignant tumors	6	16.7	15	53.4	17	82.5	11	72.8	13	77	60.3*
b. Other unspecified malignant tumors	101	54.7	114	75.7	96	78.4	56	86.3	49	82.1	27.4*

ICCC-3, International Classification of Childhood Cancer, 3rd edition; CNS, central nervous system. *$p < 0.05$ for trend. [a)]Relative survival rate (%).

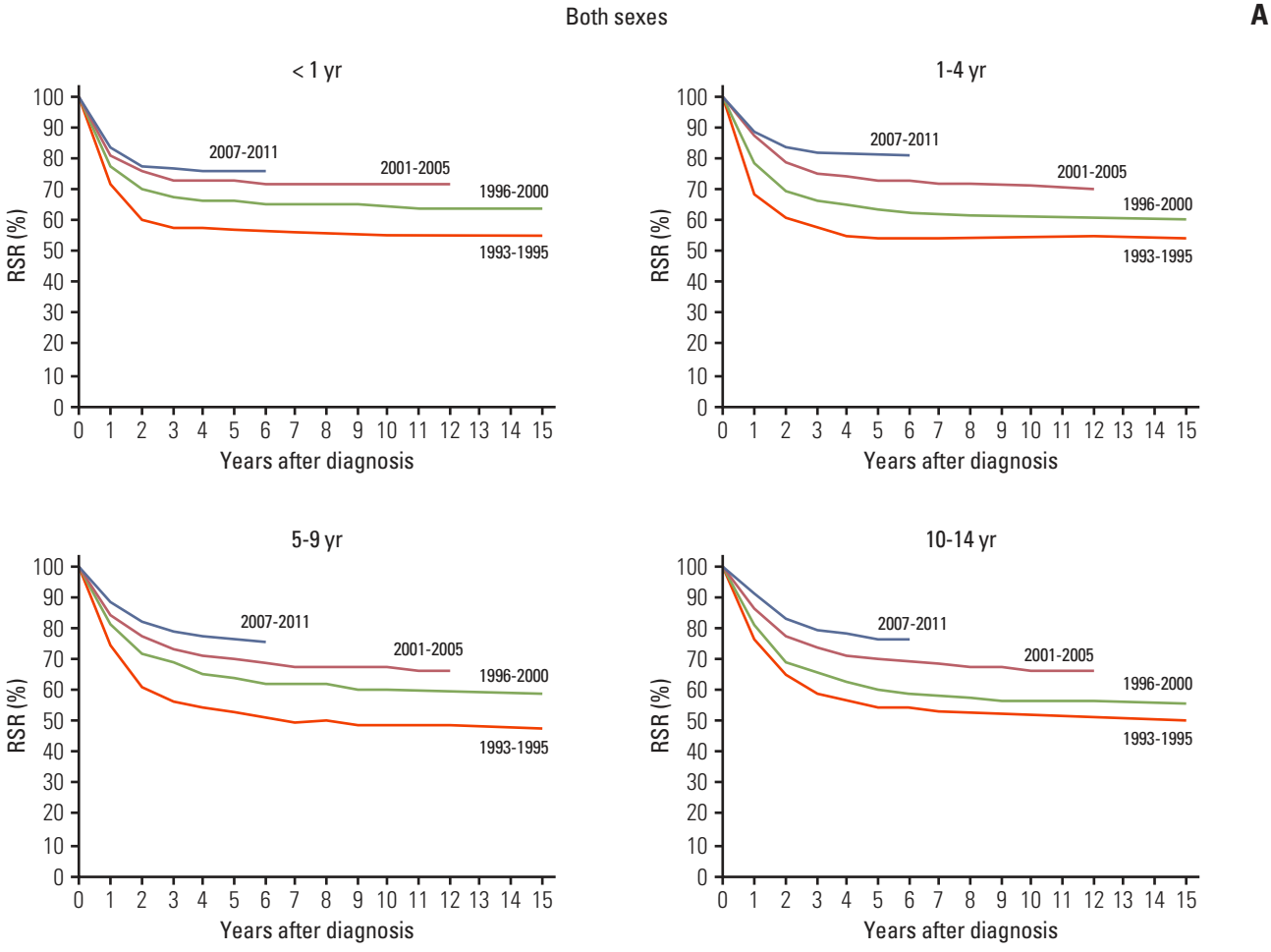

Fig. 3. Trends in relative survival rate (RSR) of childhood cancer in Korea according to age and the time period, 1993-2011. (A) Both sexes. *(Continued to the next page)*

Discussion

Epidemiologic studies of childhood cancer can provide useful information. By understanding the age distribution of cancer, we can identify the likely period of initiation of various tumors, which can provide insights regarding their etiology. For example, childhood cancer incidence rate is the highest in infancy when embryonal neoplasms such as neuroblastoma predominate, indicating that many childhood cancers result from aberrations in early developmental processes [14]. Further, as children may be more vulnerable to environmental exposures because their organs are developing rapidly. The studies of childhood cancer etiology will provide useful information in terms of evaluating the risks and causal roles of environmental factors. In addition, survival data are useful in the development of surveillance programs for childhood cancer survivors, and survival trends can be used to evaluate progress in relation to treatment. However, there have been few nationwide epidemiological reports on childhood cancer providing reliable data over an extended period, particularly for Asian countries.

The KCCR is a national, population-based registry in South Korea. Annual incidence, survival, and prevalence rates of all cancers in Korea have been reported by the KCCR. In addition, a recent study provided epidemiological data on cancer in adolescents and young adults in Korea [11]. However, our study is the first to report cancer statistics for children younger than 15 years old in South Korea.

In comparison with other countries, our study found that the overall incidence of childhood cancer in South Korea was higher than that in other Asian countries such as China [15] and Thailand [16]. However, the incidence was lower than in countries in North America [2,7] and Europe [17]. The rea-

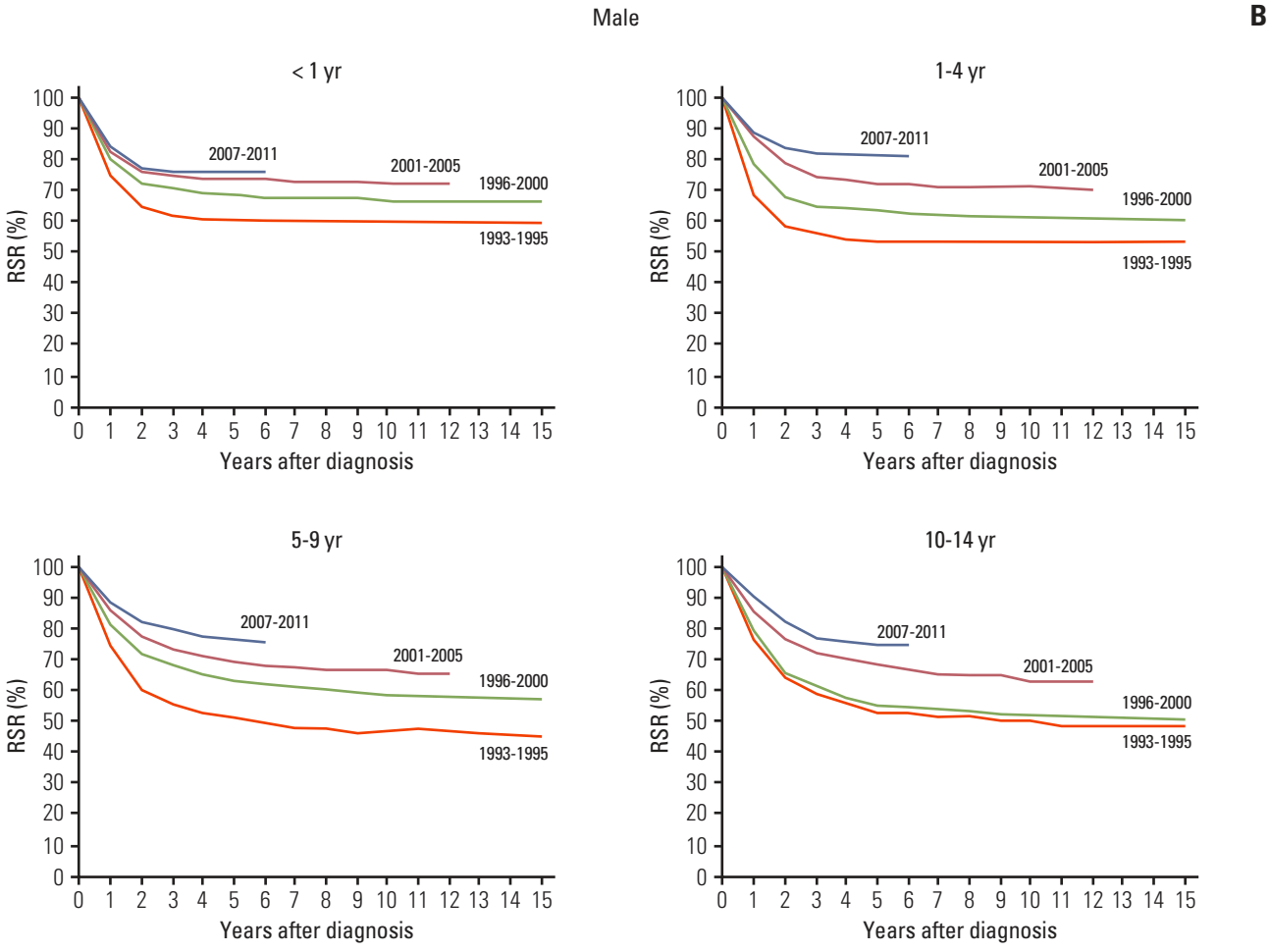

Fig. 3. *(Continued from the previous page)* (B) Male. *(Continued to the next page)*

son for this worldwide variability in childhood cancer incidence is unclear. In general, low- and middle-income countries have lower rates of childhood cancer than developed countries, which can be explained in part by under-diagnosis and under-reporting in these countries [18]. In the United States, childhood cancer incidence differs between racial and ethnic groups; in 2006-2010, the incidence rate was lowest in an American Indian/native Alaskan group (111.7 per million) and highest in a non-Hispanic White group (178.2 per million) [19]. These racial/ethnic differences may be attributable to differences in genetic predisposition as well as environmental exposure [20].

In our study, the proportions of childhood cancer subtypes differed between age groups. In infants (aged < 1 year), the most frequent cancer was neuroblastoma/ganglioneuroblastoma, followed by lymphoid leukemia. In children older than 1 year of age, lymphoid leukemia was the most common cancer.

The incidence rate of lymphoid leukemias was 28.3 per million in our study; in other countries, this ranged from 28 per million [17] to 40.8 per million [4]. In our study, incidence peaked around 3 years of age in both sexes (males, 55.7 per million; females, 60.4 per million). Similar peaks were also observed in data from white populations in the UK and United States in the early 20th century [21] and in recent studies conducted in Argentina [6]. The incidence of certain types of cancer is disproportionately high in some areas compared with overall incidence. For example, in sub-Saharan Africa, Burkitt lymphoma accounts for 25%-50% of all new childhood cancers, which can be explained by endemic Epstein-Barr virus [22].

In South Korea, incidence of childhood cancer increased by 2.4% annually from 1999 to 2011. It is possible that improvements in diagnostic technologies are leading to

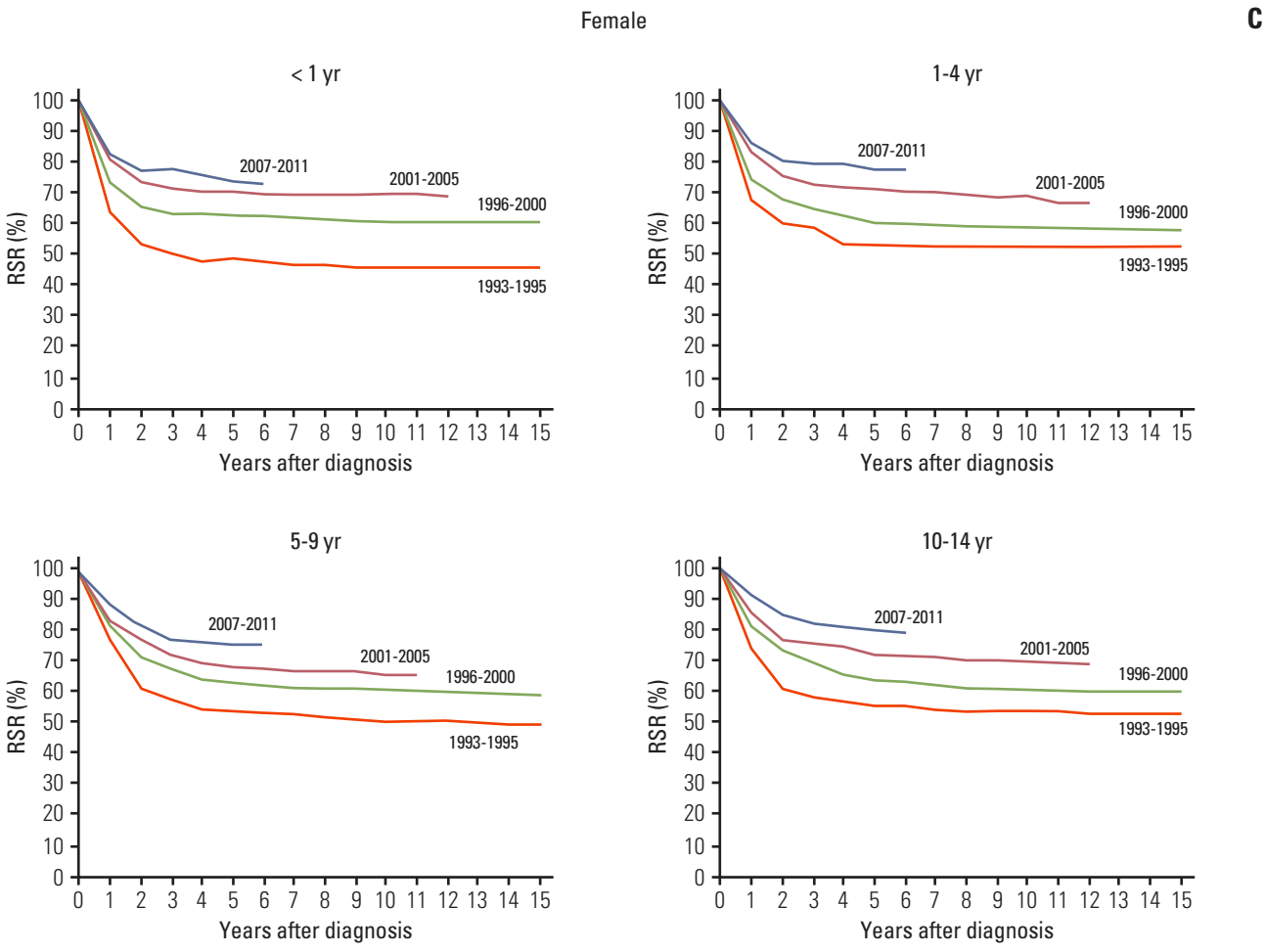

Fig. 3. *(Continued from the previous page)* (C) Female.

increased detection rates and thus increased incidence rates. Another possible reason for this increase is easy accessibility to hospital and treatment. Early studies in developed countries, based on data from the mid- to late-1970s, show increasing trends in incidence of childhood cancer [23,24]; however, more recent data from the United States (1992-2004) [2], Australia (1983-2006) [4], and Canada (1992-2006) [7] show a plateau in childhood cancer incidence.

In this study, the incidence of most cancer subtypes showed an increasing trend; however, the incidence of 'other and unspecified malignant neoplasms' decreased annually (APC, –7.4%). This can be explained in part by improvements in diagnostic methods and in the quality of characterization, leading to more specific diagnoses. In the study of cancer incidence in Korean adolescents and young adults (aged 15-29 years), cancer incidence also increased over time, and the rate of increment was steeper (APC, 6.3%) [11].

In this study, the overall 5-year cancer survival rate was 78.2% for 2007-2011. This rate is lower than that of developed countries such as Italy [25] and the United States [19], but higher compared with developing countries in Asia such as China [15] and Thailand [16] (although the time periods are slightly different between these studies). These disparities may be caused by multiple factors, with a country's economic status being one contributor. In countries with a high economic status, children are more likely to have access to health insurance and to receive a timely diagnosis and high quality treatment and supportive care, and parents are more likely to have a high level of disease knowledge and adherence to therapy, all of which contribute to improved childhood cancer survival rates [20].

The current survival rate in South Korea is similar to that of the United States from 1995 to 1999 [23] and of Britain from 1998 to 2005 [8]. In the United States, the 5-year survival rate

increased from 79.3% in 1995-1999 to 83.1% in 2004-2010 [19,23]. This implies that improvements in the survival rate are possible in South Korea, and efforts should be made to achieve this.

In this study, survival rates varied between cancer subtype, increasing steadily from 1993-2011 for lymphoid leukemias and neuroblastoma, but with little change since 2005 for CNS tumors, soft tissue sarcoma, or osteosarcoma. Efforts to improve survival should be continued, especially for cancers with low survival rates such as CNS tumors.

In this study, it was not possible to describe long-term trends for incidence and survival due to the relatively short existence of the official population-based cancer registry in Korea. Another limitation is that information on cancer stage or treatment was not included.

Conclusion

This study provides reliable information on incidence and survival trends for childhood cancers, providing a more comprehensive understanding of these cancers. The results from this study will be useful for professionals related with childhood cancer in the development of optimized healthcare services for childhood cancer patients and survivors.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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