

Cancers among adolescents and young adults at one institution in Japan

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Abstract. Adolescents and young adults (AYAs) with cancer often live long lives following treatment and face many life events. No detailed studies of cancers in AYAs have described the epidemiology, treatment outcome, and social status in Japan. The present study defined AYAs as those aged 15-29 years old based on the US National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program. Data was collected from the hospital-based cancer registry and electronic medical charts at Niigata University Medical and Dental Hospital from 2007 to 2015. The present study analyzed the types of cancer, treatment methods and outcomes, fertility preservation, marital status, raising children, school admission, and employment status. A total of 362 (1.9%) cancer cases in AYAs (males 119, females 243) were identified. Carcinoma was the most common type of cancer in both sexes. Females had a high incidence of carcinoma of the genitourinary tract (28.0%). Fertility-sparing surgery (16.0%) was the most common method of fertility preservation. The 5-year survival was better in females (88.4%) than in males (79.9%). The percentage of married AYAs increased following cancer treatment. The proportion of unemployment increased following cancer treatment in all age groups and was greatest (12.6%) in those aged 20-24 years old. Compared with SEER data from the United States, the incidence of carcinoma was high among AYAs, particularly genitourinary tract carcinomas in females, while the incidence of melanoma and skin carcinomas was low. Therefore, AYAs with cancer requires social and economic support.

Introduction

Cancers of adolescents and young adults (AYAs) have distinct biological features compared to both pediatric and adult cancers (1). AYAs face many life events, such as school admission, employment, marriage, childbirth, and raising children. Cancers in AYAs greatly influence their lives after cancer treatment. Therefore, AYAs with cancer need specific support during and after cancer treatment (2). However, cancer in AYAs accounts for only a few cancers and there are various types (3). Consequently, insufficient attention has been paid to cancers in AYAs. Unmet service needs are present in cancers in AYAs, particularly financial, mental health, and support group services (4).

There is no universal definition of AYAs. The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program in the United States (3) and other countries (5) initially defined AYAs as those aged between 15 and 29 years old. Recently, however, the program defined widened that range to 15-39 years (6).

In Japan, two reports of cancers in AYAs, defined as from 15 to 39 years old, were published using data from the Monitoring Cancer Incidence in Japan Project for 2009-2011 (7) and 2011-2014 (8). No detailed studies have described the epidemiology, treatment outcomes, and social status of cancers in AYAs in Japan.

The distribution of cancer types in adults that are 30-39 years old is similar to that in those 40 years and older (7-9), and life events such as schooling, employment, and marriage are mainly experienced at 15-29 years of age. Therefore, we defined AYAs as being from 15-29 years old and analyzed the incidence, cancer types, treatment methods, and outcomes of cancer in this group. We also analyzed the family and social status of AYA patients in our institution.

Materials and methods

Definition of AYAs and cancer classification. We defined AYAs as being 15-29 years old and categorized AYAs according to sex by age groups in 5-year increments (15-19, 20-24, and 25-29 years). Cancer types were classified according to the SEER AYA Site Recode Classification/WHO 2008 Definition (10). We included cases of carcinoma *in situ* and

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benign tumors in the central nervous system and intracranial neoplasms.

Patients and data collection. This study was approved by the Ethics Review Committee of the School of Medicine of Niigata University (receipt no. 2611). In this retrospective study, we collected data from a hospital-based cancer registry and from electronic medical charts at Niigata University Medical and Dental Hospital from 2007 to 2015.

We analyzed the types of cancer, treatment methods and outcomes, fertility preservation, marital status, whether the patient had children, school admission, and employment status. The treatment methods were classified as surgery, radiation, chemotherapy, endocrine treatment, other treatment, and no treatment. Fertility preservation was classified as sperm banking, fertility-sparing surgery, chemotherapy withdrawal, egg freezing, others, and unknown. Marital status was classified as married, not married, divorced, widowed, and unknown. Marital status, parenting status, and employment were surveyed at the date of diagnosis and last date confirmed. Employment was classified as full-time work, full-time school, part-time work, part-time school, housewife, unemployed, and unknown.

Statistical analyses. Survival curves were drawn using the Kaplan-Meier method. The log-rank test was used to compare survival in each group. Fisher's exact test was used to compare the two groups. For multiple comparisons, the Bonferroni correction was used. $P < 0.05$ was considered to be significant in two groups comparison, $P < 0.017$ in three group comparisons (e.g., age group), $P < 0.0033$ in six group comparisons (e.g., cancer types). All calculations were performed using SPSS Statistics, version 22.0 software (IBM Corp., Armonk, NY, USA).

Results

Types of cancer and distribution. We identified 399 cancer cases in AYAs (2.1%) from the 18,663 cases in the hospital-based cancer registry from 2007 to 2015 (Fig. 1A). Of these, patients were excluded if non-cancer was the final diagnosis after surgery or pathological analyses ($n=32$; e.g., severe dysplasia in the uterine cervix), they were not Japanese ($n=2$), or they were younger than 15 years old at the date of diagnosis ($n=3$). Ultimately, we identified 362 (1.9%) cancer cases in AYAs (Fig. 1B). Table I shows the age- and sex-specific distributions according to the SEER AYA Site Recode Classification. There were more cases of females (243 cases) than males (119 cases) (Fig. 2).

Fig. 2 shows the distribution of cancer types in AYAs by sex. In males, carcinomas (29.4%) were the most common type, followed by germ cell and trophoblastic neoplasms (15.1%), leukemias (11.8%), and CNS and other intracranial and intraspinal neoplasms (all behaviors) (11.8%) (Fig. 2A). In females, carcinomas (58.0%) were the most common, followed by CNS and other intracranial and intraspinal neoplasms (all behaviors) (14.0%) and soft tissue sarcomas (6.2%) (Fig. 2B). The carcinomas were subclassified in this analysis. In males, carcinoma of other and ill-defined sites (11.8%) were the most common, followed by carcinoma of gastrointestinal tract (10.1%) and other carcinoma of head and neck (4.2%) (Fig. 2A). In females, carcinoma of genitourinary tract (28.0%) was the

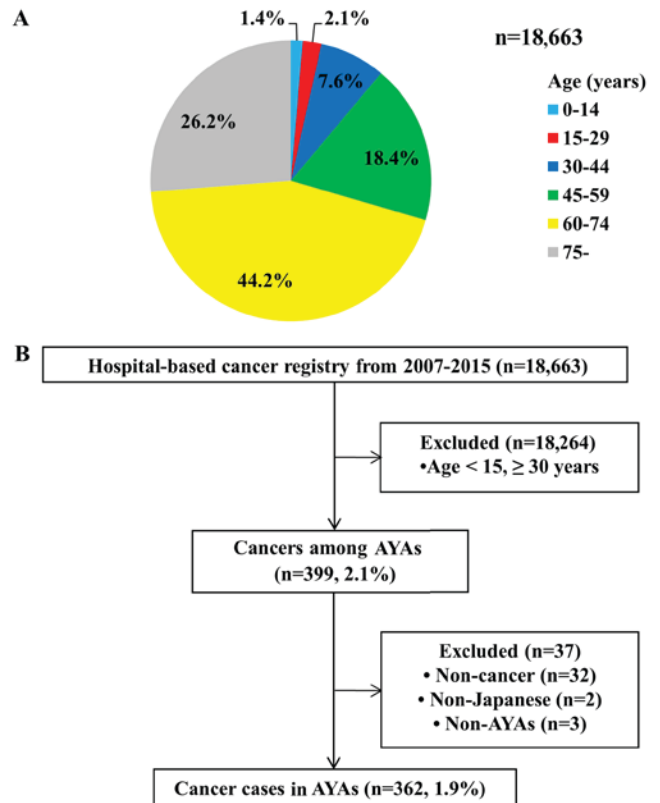


Figure 1. Proportion of cancers among AYAs: Study design and flow diagram. (A) Percentage of cancer cases in each age group. (B) Process used to identify cancer cases in AYAs from the cancer registry. Cancer cases included benign tumors in the central nervous system, intracranial neoplasms, and *in situ* cancers of any organ. AYAs, adolescents and young adults.

most common, followed by carcinoma of other and ill-defined sites (16.5%) and thyroid carcinoma (5.3%) (Fig. 2B). Most of the genitourinary tract cancer was cervical cancer ($n=61$, 25.1%). The proportion of carcinomas was significantly higher in females than in males (carcinomas vs. all other types, $P < 0.001$), but females had a lower proportion of germ cell and trophoblastic neoplasms and leukemias than did males (germ cell and trophoblastic neoplasms vs. all other types, leukemias vs. all other types, $P < 0.05$).

Fig. 3 shows the distribution of cancer types in each age group. The number of cases increased with age group with 79 (21.8%), 99 (27.3%), and 184 (50.8%) in the 15-19, 20-24, and 25-29 years groups, respectively. Carcinomas were the most common in all age groups, and the percentage of carcinomas significantly increased with age group (19.0, 45.5, and 63.0%, respectively; carcinomas vs. all other types, $P < 0.017$). Three types of cancer decreased with age: germ cell and trophoblastic neoplasms (17.7, 8.1 and 2.7%, respectively), osseous and chondromatous neoplasms (15.2, 4.0 and 1.6%, respectively), and soft tissue sarcomas (12.7, 7.1 and 6.0%, respectively).

Treatments and outcomes. Of the 362 cases, we excluded 12 cases that were admitted to the hospital but not treated because of a second opinion or referral to other hospitals from the analyses of treatments, outcomes, and family/social status.

Surgery ($n=228$) was the most common treatment method, followed by chemotherapy ($n=136$), radiation ($n=90$), endocrine treatment ($n=51$), no treatment ($n=17$), and other

Table I. Cancer classification (age and sex specific distribution).

Site group	Total, n (%)	Male, n (%)	Female, n (%)	Age group, 15-19, n (%)	Age group, 20-24, n (%)	Age group 25-29, n (%)
Leukemias	25 (6.9)	14 (3.9)	11 (3.0)	8 (2.2)	9 (2.5)	8 (2.2)
Acute lymphoid leukemia	7 (1.9)	4 (1.1)	3 (0.8)	3 (0.8)	3 (0.8)	1 (0.3)
Acute myeloid leukemia	15 (4.1)	7 (1.9)	8 (2.2)	4 (1.1)	5 (1.4)	6 (1.7)
Chronic myeloid leukemia	3 (0.8)	3 (0.8)	0	1 (0.3)	1 (0.3)	1 (0.3)
Other and unspecified leukemia	0	0	0	0	0	0
Lymphomas	19 (5.2)	8 (2.2)	11 (3.0)	6 (1.7)	5 (1.4)	8 (2.2)
Non-Hodgkin lymphoma	15 (4.1)	7 (1.9)	8 (2.2)	4 (1.1)	4 (1.1)	7 (1.9)
Hodgkin lymphoma	4 (1.1)	1 (0.3)	3 (0.8)	2 (0.6)	1 (0.3)	1 (0.3)
CNS and other intracranial and intraspinal neoplasms (all behaviors)	48 (13.3)	14 (3.9)	34 (9.4)	10 (2.8)	18 (5.0)	20 (5.5)
Astrocytoma	11 (3.0)	2 (0.6)	9 (2.5)	1 (0.3)	3 (0.8)	7 (1.9)
Specified low-grade astrocytic tumors	3 (0.8)	0	3 (0.8)	0	1 (0.3)	2 (0.6)
Astrocytoma, NOS Glioblastoma and anaplastic astrocytoma	4 (1.1)	2 (0.6)	2 (0.6)	0	1 (0.3)	3 (0.8)
Astrocytoma, NOS	4 (1.1)	0	4 (1.1)	1 (0.3)	1 (0.3)	2 (0.6)
Other glioma	10 (2.8)	3 (0.8)	7 (1.9)	0	3 (0.8)	7 (1.9)
Ependymoma	4 (1.1)	1 (0.3)	3 (0.8)	2 (0.6)	1 (0.3)	1 (0.3)
Medulloblastoma and other PNET	2 (0.6)	1 (0.3)	1 (0.3)	0	1 (0.3)	1 (0.3)
Medulloblastoma	2 (0.6)	1 (0.3)	1 (0.3)	0	1 (0.3)	1 (0.3)
Supratentorial PNET	0	0	0	0	0	0
Other specified intracranial and intraspinal neoplasms	14 (3.9)	3 (0.8)	11 (3.0)	3 (0.8)	7 (1.9)	4 (1.1)
Unspecified intracranial and intraspinal neoplasms	7 (1.9)	4 (1.1)	3 (0.8)	4 (1.1)	3 (0.8)	0
Unspecified malignant intracranial and intraspinal neoplasms	4 (1.1)	3 (0.8)	1 (0.3)	3 (0.8)	1 (0.3)	0
Unspecified ben/border intracranial and intraspinal neoplasms	3 (0.8)	1 (0.3)	2 (0.6)	1 (0.3)	2 (0.6)	0
Osseous and chondromatous neoplasms	19 (5.2)	8 (2.2)	11 (3.0)	12 (3.3)	4 (1.1)	3 (0.8)
Osteosarcoma	12 (3.3)	4 (1.1)	8 (2.2)	9 (2.5)	1 (0.3)	2 (0.6)
Chondrosarcoma	2 (0.6)	0	2 (0.6)	0	1 (0.3)	1 (0.3)
Ewing tumor	3 (0.8)	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.6)	0
Other specified and unspecified bone tumors	2 (0.6)	2 (0.6)	0	2 (0.6)	0	0
Soft Tissue Sarcomas	28 (7.7)	13 (3.6)	15 (4.1)	10 (2.8)	7 (1.9)	11 (3.0)
Fibromatous neoplasms	5 (1.4)	2 (0.6)	3 (0.8)	1 (0.3)	0	4 (1.1)
Rhabdomyosarcoma	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.6)	0	0
Other soft tissue sarcoma	21 (5.8)	10 (2.8)	11 (3.0)	7 (1.9)	7 (1.9)	7 (1.9)
Specified soft tissue sarcoma	19 (5.2)	8 (2.2)	11 (3.0)	7 (1.9)	6 (1.7)	6 (1.7)
Specified (excluding Kaposi sarcoma)	19 (5.2)	8 (2.2)	11 (3.0)	7 (1.9)	6 (1.7)	6 (1.7)
Kaposi sarcoma	0	0	0	0	0	0
Unspecified soft tissue sarcoma	2 (0.6)	2 (0.6)	0	0	1 (0.3)	1 (0.3)
Germ cell and Trophoblastic Neoplasms	27 (7.5)	18 (5.0)	9 (2.5)	14 (3.9)	8 (2.2)	5 (1.4)
Germ cell and trophoblastic neoplasms of gonads	13 (3.6)	7 (1.9)	6 (1.7)	6 (1.7)	4 (1.1)	3 (0.8)
Germ cell and trophoblastic neoplasms of nongonadal sites	14 (3.9)	11 (3.0)	3 (0.8)	8 (2.2)	4 (1.1)	2 (0.6)
Intracranial (all behaviors)	11 (3.0)	8 (2.2)	3 (0.8)	6 (1.7)	4 (1.1)	1 (0.3)
Other nongonadal	3 (0.8)	3 (0.8)	0	2 (0.6)	0	1 (0.3)
Melanoma and Skin Carcinomas	3 (0.8)	3 (0.8)	0	0	1 (0.3)	2 (0.6)
Melanoma	2 (0.6)	2 (0.6)	0	0	1 (0.3)	1 (0.3)
Skin carcinomas	1 (0.3)	1 (0.3)	0	0	0	1 (0.3)

Table I. Continued.

Site group	Total, n (%)	Male, n (%)	Female, n (%)	Age group, 15-19, n (%)	Age group, 20-24, n (%)	Age group 25-29, n (%)
Carcinomas	176 (48.6)	35 (9.7)	141 (39.0)	15 (4.1)	45 (12.4)	116 (32.0)
Thyroid carcinoma	17 (4.7)	4 (1.1)	13 (3.6)	3 (0.8)	6 (1.7)	8 (2.2)
Other carcinoma of head and neck	12 (3.3)	5 (1.4)	7 (1.9)	0	7 (1.9)	5 (1.4)
Nasopharyngeal carcinoma	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0
Other sites in lip, oral cavity and pharynx	10 (2.8)	4 (1.1)	6 (1.7)	0	5 (1.4)	5 (1.4)
Nasal cavity, mid ear, sinuses, larynx, other ill-defined head/neck	1 (0.3)	0	1 (0.3)	0	1 (0.3)	0
Carcinoma of trachea, bronchus, and lung	0	0	0	0	0	0
Carcinoma of breast	7 (1.9)	0	7 (1.9)	0	1 (0.3)	6 (1.7)
Carcinoma of genitourinary tract	68 (18.8)	0	68 (18.8)	1 (0.3)	12 (3.3)	55 (15.2)
Carcinoma of kidney	2 (0.6)	0	2 (0.6)	0	1 (0.3)	1 (0.3)
Carcinoma of bladder	0	0	0	0	0	0
Carcinoma of gonads	4 (1.1)	0	4 (1.1)	0	4 (1.1)	0
Carcinoma of cervix and uterus	62 (17.1)	0	62 (17.1)	1 (0.3)	7 (1.9)	54 (14.9)
Carcinoma of other and ill-defined sites, genitourinary tract	0	0	0	0	0	0
Carcinoma of gastrointestinal tract	18 (5.0)	12 (3.3)	6 (1.7)	2 (0.6)	6 (1.7)	10 (2.8)
Carcinoma of colon and rectum	7 (1.9)	5 (1.4)	2 (0.6)	1 (0.3)	3 (0.8)	3 (0.8)
Carcinoma of stomach	5 (1.4)	3 (0.8)	2 (0.6)	0	1 (0.3)	4 (1.1)
Carcinoma of liver and intrahepatic bile ducts	2 (0.6)	2 (0.6)	0	1 (0.3)	1 (0.3)	0
Carcinoma of pancreas	3 (0.8)	1 (0.3)	2 (0.6)	0	1 (0.3)	2 (0.6)
Carcinoma other and ill-defined sites, gastrointestinal tract	1 (0.3)	1 (0.3)	0	0	0	1 (0.3)
Carcinoma of other and ill-defined sites	54 (14.9)	14 (3.9)	40 (11.0)	9 (2.5)	13 (3.6)	32 (8.8)
Adrenocortical carcinoma	1 (0.3)	0	1 (0.3)	0	0	1 (0.3)
Carcinoma of other and ill-defined sites, NOS	53 (14.6)	14 (3.9)	39 (10.8)	9 (2.5)	13 (3.6)	31 (8.6)
Miscellaneous specified neoplasms, NOS	12 (3.3)	3 (0.8)	9 (2.5)	2 (0.6)	1 (0.3)	9 (2.5)
Other pediatric and embryonal tumors, NOS	3 (0.8)	1 (0.3)	2 (0.6)	1 (0.3)	0	2 (0.6)
Wilms tumor	0	0	0	0	0	0
Neuroblastoma	0	0	0	0	0	0
Other pediatric and embryonal tumors, NOS	3 (0.8)	1 (0.3)	2 (0.6)	1 (0.3)	0	2 (0.6)
Other specified and embryonal tumors, NOS	9 (2.5)	2 (0.6)	7 (1.9)	1 (0.3)	1 (0.3)	7 (1.9)
Paraganglioma and glomus tumors	0	0	0	0	0	0
Other specified gonadal tumors	0	0	0	0	0	0
Myeloma, mast cell, miscellaneous lymphoreticular neoplasms, NOS	2 (0.6)	0	2 (0.6)	0	0	2 (0.6)
Other specified neoplasms, NOS	7 (1.9)	2 (0.6)	5 (1.4)	1 (0.3)	1 (0.3)	5 (1.4)
Unspecified Malignant Neoplasms	1 (0.3)	0	1 (0.3)	0	0	1 (0.3)
# Unclassified	4 (1.1)	3 (0.8)	1 (0.3)	2 (0.6)	1 (0.3)	1 (0.3)
Total	362 (100)	119 (32.9)	243 (67.1)	79 (21.8)	99 (27.3)	184 (50.8)

treatments (n=5). Radiation included total body irradiation (n=16) for leukemia and lymphoma. Other treatments included thermal therapy (1 case), WT1 antigen vaccination (1 case), immunotherapy (1 case), and steroid ointment treatment (2 cases). Fig. 4A shows the treatments involving combined modes. Surgery + chemotherapy (n=44) was the most common

combined modality, followed by chemotherapy + radiation (n=28), surgery + chemotherapy + radiation (n=28), surgery + radiation (n=15), surgery + endocrine treatment (n=13), and others (n=12).

Of the patients, 20.3% underwent fertility preservation (Fig. 4B). More females underwent fertility preservation

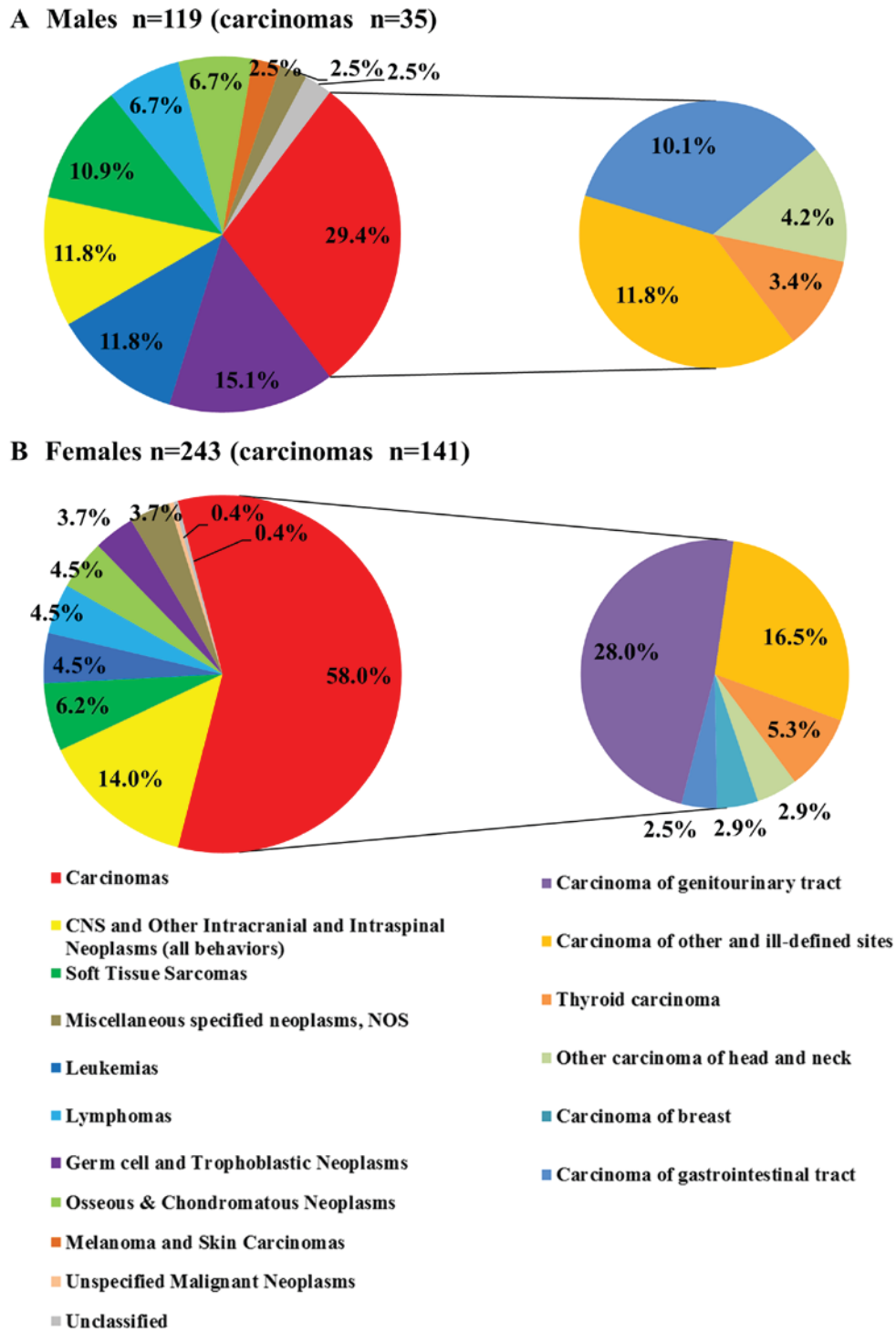


Figure 2. Distribution of cancer types in adolescents and young adults by sex. (A) Males (n=119), carcinomas (n=35). (B) Females (n=243), carcinomas (n=141).

(females 24.7%, males 9.2%). Fertility-sparing surgery (16.0%) was the most common method of fertility preservation, mainly for cervical cancers, followed by sperm banking (3.1%).

Fig. 5 shows the treatment outcomes of the cancers in AYAs. The 5-year survival rate was 85.6% in all AYA cases (n=350) and was better in females (88.4%) than in males (79.9%). Overall survival curves were drawn for several factors, including sex, age group, and cancer types (Fig. 5). The treatment outcomes were significantly (P<0.05) better in females (Fig. 5A). Comparing the age groups, the 15-19 years group had a significantly (P<0.017) worse outcome than the

25-29 years group (Fig. 5B). Cancer types were categorized as i) leukemias/lymphomas; ii) CNS and other intracranial and intraspinal neoplasms (all behaviors); iii) osseous and chondromatous neoplasms/soft tissue sarcomas; iv) germ cell and trophoblastic neoplasms; v) melanoma and skin carcinomas/miscellaneous specified neoplasms, NOS/unspecified malignant neoplasms/unclassified; and vi) carcinomas. Comparing cancer types, the treatment outcomes were not significantly different among the six groups (Fig. 5C). Carcinomas (n=168) were further classified and analyzed separately, as shown in Fig. 5D. No patients died of thyroid

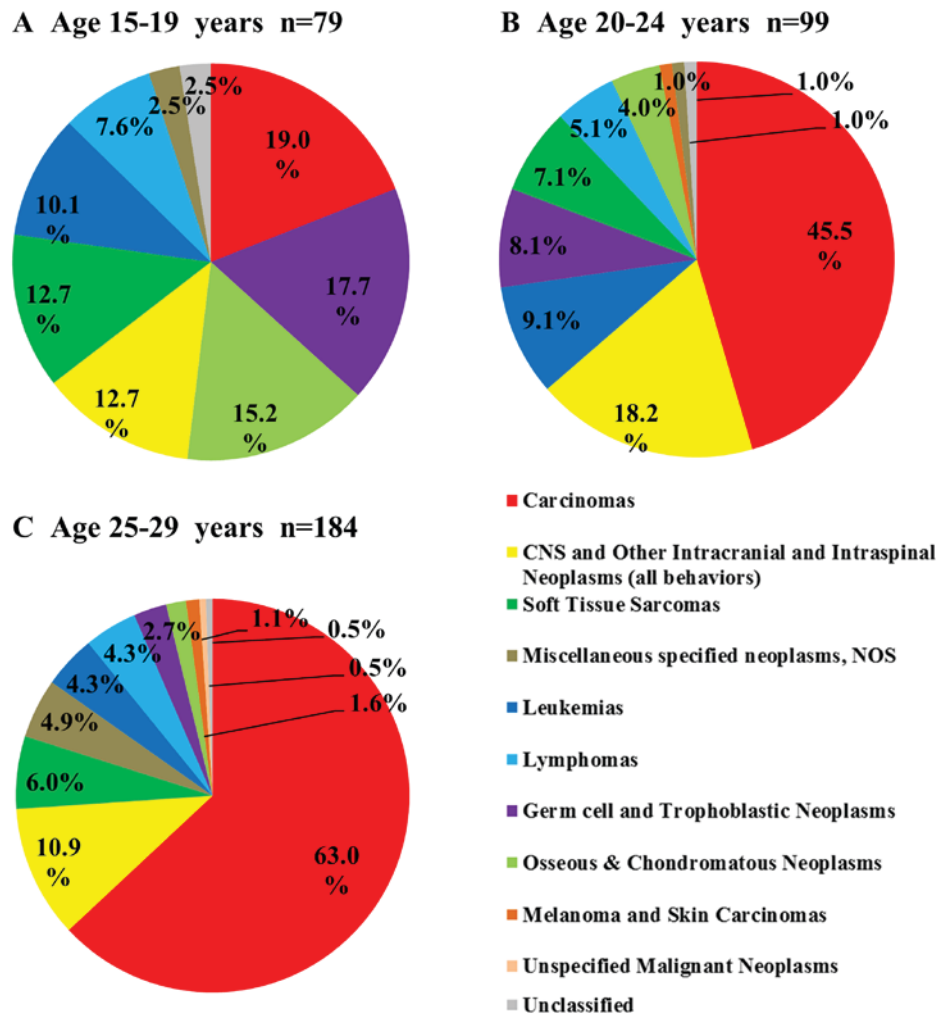


Figure 3. Distribution of cancer types in adolescents and young adults by age group. (A) Age 15-19 years (n=79). (B) Age 20-24 years (n=99). (C) Age 25-29 years (n=184).

carcinoma or other carcinoma of head and neck. Carcinoma of gastrointestinal tract had a significantly worse outcome than that of carcinoma of other and ill-defined sites ($P<0.0033$, Fig. 5D).

Family and social status. At the date last confirmed, the proportion of married AYAs significantly increased with age group (married vs. all other marital statuses, 15-19, 20-24, 25-29 years old, $P<0.017$). The proportion of married cases at a diagnosis of cancer was 0, 9.5, and 29.9% in the 15-19, 20-24, and 25-29 years groups, respectively (Fig. 6A); at the date last confirmed, these values were 2.6, 21.1, and 44.1%. The percentage of patients raising children increased with age group and was 0/1.3% (at diagnosis/date last confirmed), 7.4/15.8, and 19.8%/33.9%, respectively (Fig. 6B). When marriage status and parenting status were compared by sex, the proportions of patients who were married and raising children were higher among females than males both at diagnosis and at date last confirmed ($P<0.01$; Fig. 6A and B). The proportion of patients who were married or raising children was higher at date last confirmed than at diagnosis among females ($P<0.001$), but not among males (Fig. 6A and B). Patients with carcinoma of genitourinary tract were more likely to be married (60.0%) or raising children (47.7%) compared with the other types of cancer (21.4,

15.8%; $P<0.001$). Patients with fertility preservation were also more likely to be married (50.7%) or raising children (39.4%) compared with the other groups (no fertility preservation and unknown status, 22.9 and 17.2%, respectively; $P<0.001$).

The proportion of unemployed patients significantly increased after cancer treatment in the 15-19 and 20-24 year age groups (unemployed vs. all other employment statuses, $P<0.05$), but not in the 25-29 year age group, and was greatest in the 20-24 year age group at the date last confirmed (at diagnosis/date last confirmed: 1.3/9.0, 3.2/12.6, and 4.5%/7.9% in the 15-19, 20-24, and 25-29 year age groups; Fig. 6C). At the date last confirmed, the proportion of unemployed patients was not significantly different among the three age groups (unemployed vs. all other employment statuses).

Discussion

This study analyzed 362 AYAs (15 to 29 years old) with cancer seen in Niigata University Medical and Dental Hospital between 2007 and 2015. The most common cancers in both males and females were carcinomas. The 5-year survival was 79.9% in males and 88.4% in females. More than 40% of the patients in the 25-29 years group were married, at the date last confirmed.

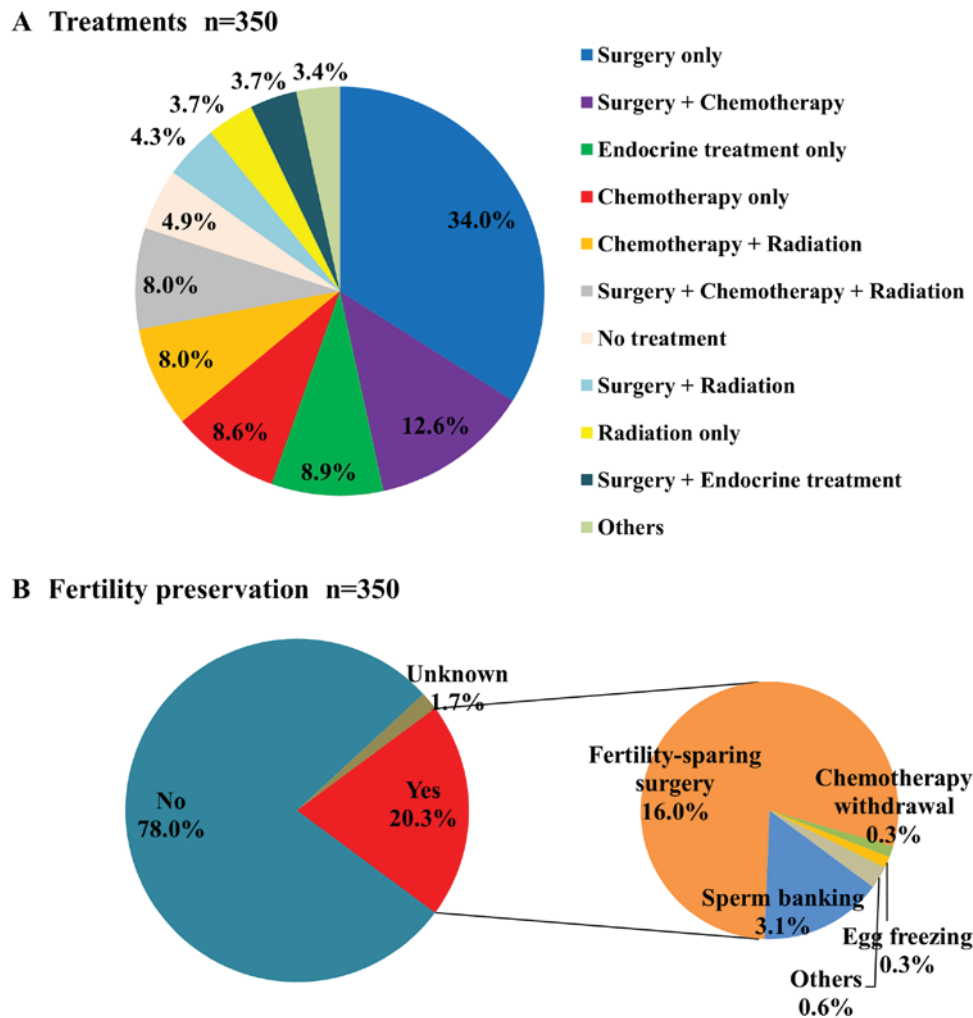


Figure 4. Treatment method and fertility preservation in cancers in adolescents and young adults. (A) Treatments (n=350). (B) Fertility preservation (n=350).

We compared our data with relatively old SEER data from 1975 to 2000 (3), due to the recent widening of the definition of AYA by SEER. In the older SEER data, 2.0% of AYAs (15-29 years) had cancers, compared to 2.3% in Korea (1999 to 2010) (11). At our institution, 1.9% of AYAs (15-29 years) had cancers. Overall, the incidence of cancers in AYAs was similar in Japan, the USA, and Korea.

At our institution, the most common cancers were carcinomas, particularly in females, followed by germ cell and trophoblastic neoplasms in males and CNS and other intracranial and intraspinal neoplasms in females. In comparison, in a national incidence study in Japan (7), leukemia and germ cell and other gonadal tumors were most common in the 15-19 and 20-29 years groups, respectively, although the disease classification differed slightly. This difference could be specific to our institution. In Korea, the most common cancer was carcinoma, followed by leukemias. In the USA, lymphoma was most common, followed by invasive skin cancer.

At our institution, carcinoma of genitourinary tract was most common and accounted for 28.0% of the cancers in female AYAs. Most such cancers were cervical cancer, including carcinoma *in situ*. Cervical cancer is caused by human papilloma virus (HPV) infection (12), and is preventable by vaccination (13-15). However, the Japanese Ministry

of Health, Labor and Welfare withdrew its recommendation for vaccination against HPV because of controversy regarding its adverse effects (16,17). Consequently, the high incidence of cervical cancer will continue. Screening for cervical cancer in women over 20 years old should be continued in Japan.

Surgery was the most common treatment modality because of the high percentage of carcinomas in AYAs. While 20.3% of the patients underwent fertility preservation, mainly due to fertility-sparing surgery for cervical cancer in females and sperm banking in males, 80% of the patients did not receive any fertility preservation. Sperm banking was performed only in 9.2% of males, which was markedly lower than the 17.8% in male AYAs reported in the USA (18). Egg freezing was performed in one case only. Sperm banking and egg freezing should be performed widely in AYA cancer patients in Japan. The National Comprehensive Cancer Network (19) and American Society of Clinical Oncology (20) guidelines recommend discussing the possibility of infertility and use of fertility preservation before initiating treatment.

The 5-year survival was better in females (88.4%) than in males (79.9%), and was better than those for cancer at all ages (males 59.1%, females 66.0%) (9). The treatment outcome was worse in the 15-19 years age group, probably due to the high percentage of soft tissue sarcoma, osseous and trophoblastic

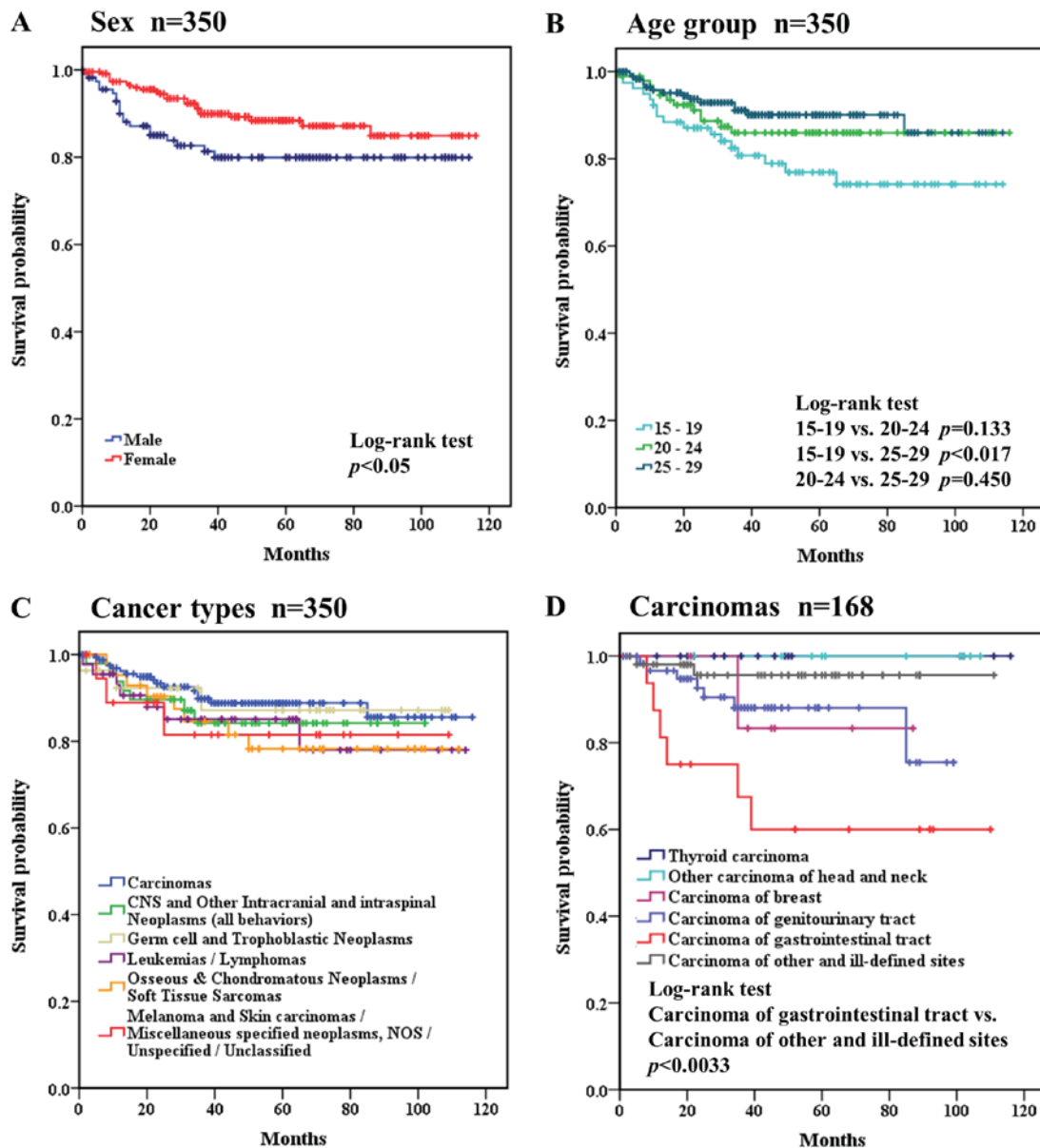


Figure 5. Outcome of cancer treatments in adolescents and young adults. Overall survival curves were drawn based on several factors. (A) Sex (n=350), $P < 0.05$. (B) Age group (n=350), 15-19 vs. 20-24; $P = 0.133$; 15-19 vs. 25-29, $P < 0.017$; 20-24 vs. 25-29, $P = 0.450$. (C) Cancer type (n=350). (D) Carcinomas (n=168), carcinoma of gastrointestinal tract vs. carcinoma of other and ill-defined sites, $P < 0.0033$.

neoplasms, and leukemia/lymphoma. The 10-year relative survival in AYAs (15-29 years) (males 66.0%, females 75.3%) is worse than those in children (0-14 years) (males 73.2%, females 79.3%) in Japan (21). The treatment outcomes for cancer in AYAs is worse than that in pediatric patients with leukemia.²¹ However, acute lymphoblastic leukemia in AYAs has an improved prognosis with intensive chemotherapy (22). The chemotherapy regimens used for pediatric cancer should be applied to these cancers in AYAs because such regimens have better prognoses than adult regimens for cancer in AYAs (23). Among the cancer types, carcinomas and germ cell and trophoblastic neoplasms had better prognoses. None of the patients with thyroid carcinoma or other carcinoma of head and neck died. In many countries, the incidence of thyroid cancer has increased (24-26). Although the reason for the increased incidence of thyroid cancer in AYAs is unclear, improved screening technology, including ultrasound,

which can detect early thyroid cancer, might have led to the increased detection of thyroid cancer (27). In AYAs, we might over-diagnose thyroid cancer, which is not malignant and not lethal (28). Carcinoma of gastrointestinal tract and breast cancers had poorer prognoses in AYAs than in older patients, which suggests that these carcinomas have different biological features in AYAs and need different approaches for detection and treatment (29).

In terms of marital status, the proportion of married patients at diagnosis increased with age group and was 0, 9.5, and 29.9%, respectively. These proportions are similar to those in healthy individuals at similar ages (0.4, 6.6, and 31.5%) based on the 2015 welfare survey in Japan (30). In addition, many patients married after their diagnoses.

The percentage with children increased after diagnosis in all three age groups, which suggests that fertility was maintained in many cases. The high proportion of genitourinary tract

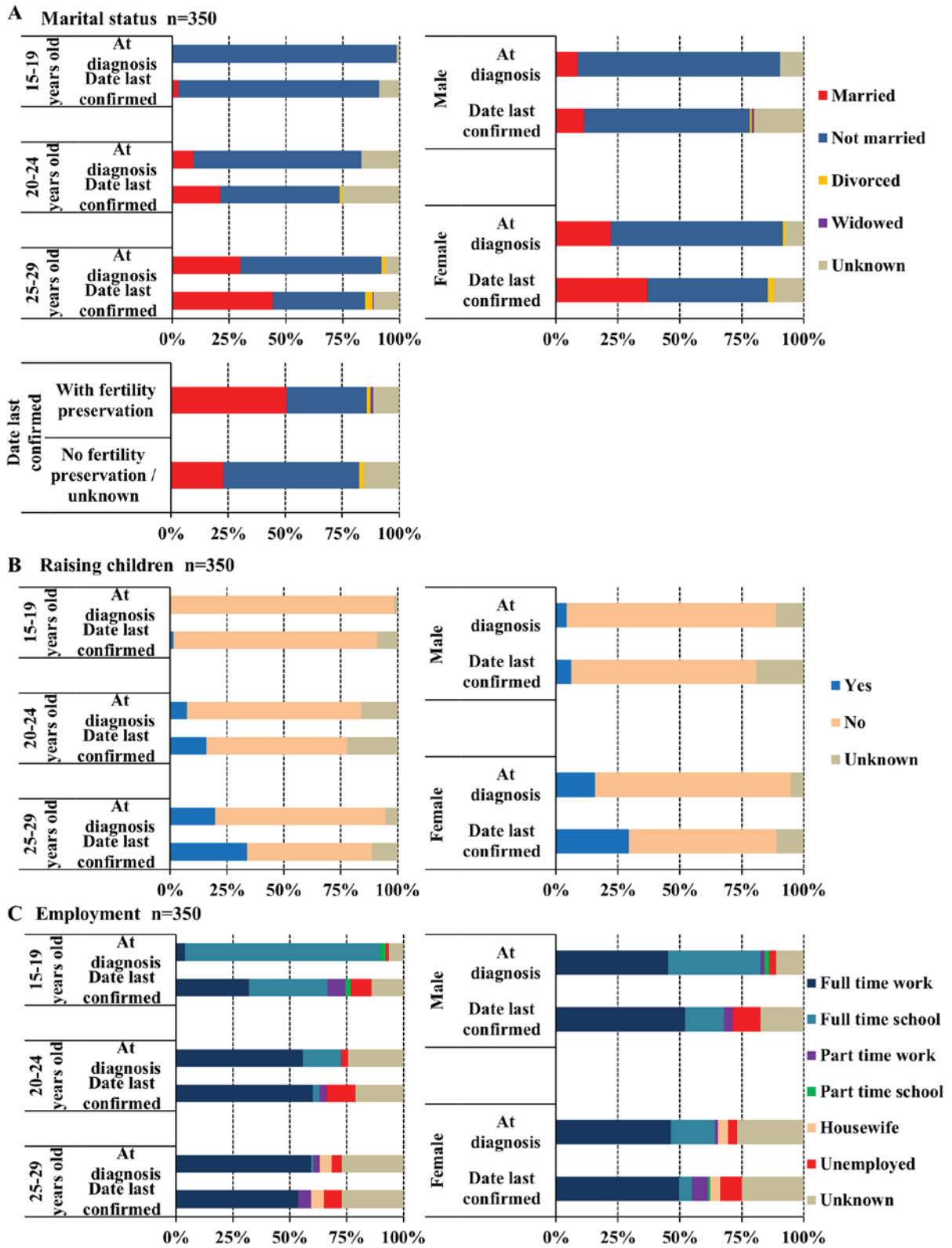


Figure 6. Family and social status of adolescents and young adults by age group and sex. (A) Marital status (n=350): Married at diagnosis (male vs. female), $P < 0.01$; date last confirmed, $P < 0.001$ /married (at diagnosis vs. date last confirmed): male, $P = 0.33$; female, $P < 0.001$. (B) Raising children (n=350): Yes (male vs. female) at diagnosis, $P < 0.001$, date last confirmed, $P < 0.001$ /yes (at diagnosis vs. date last confirmed): Male, $P = 0.38$; female, $P < 0.001$. (C) Employment (n=350): Unemployed (at diagnosis vs. date last confirmed): 15-19 years, $P < 0.05$; 20-24 years, $P < 0.05$; 25-29 years, $P = 0.135$.

carcinoma patients who were married and raising children at the date last confirmed could be due to fertility-sparing surgery for cervical cancers. In this context, fertility preservation is important for marriage and childbirth in AYA cancer survivors.

Employment is a very important issue in AYA cancer patients. The proportion employed (full time or part time) at the date last confirmed was 56.0% (196/350) at our institution. This is similar to the results of Tai *et al* (31), who found that

49.4% of AYA cancer survivors were employed for wages. Financial support and job training are definitely needed for AYA cancer survivors.

The cancers in AYAs varied. There was a high incidence of carcinoma, particularly genitourinary tract carcinomas in females, and a low incidence of melanoma and skin carcinomas among AYAs in Japan compared to the SEER data. Fertility-sparing surgery was the most common method of fertility preservation. Social and economic support is need for AYAs with cancer.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

KK drafted the manuscript. KK, YM and QZ contributed to the collection and analysis of the data. MM and YS conceived and designed the study, and edited the manuscript. All authors approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Review Committee of the School of Medicine of Niigata University (Niigata, Japan; no. 2611).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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