

## BRIEF REPORT

# Incidence and outcomes of cancer in 16- to 17-year-old adolescents

In Finland, the incidence of cancer in adolescents aged 15–19 years is 23 per 100,000.<sup>1</sup> The most common types include typical childhood cancers, such as leukaemia, lymphomas and brain tumours, and adult-type cancers, for instance, melanomas and thyroid cancer.<sup>1</sup> Survival rates for children and adolescents with cancer have improved significantly, but patients aged 15–39 years have poorer rates than children for several cancers that affect both groups.<sup>2</sup>

Multinational and paediatric-type protocols have been successful in treating adolescents and young adults with acute lymphoblastic leukaemia. Enrolling in clinical trials has generally been associated with improved survival, but has been lower among adolescents and young adults than paediatric patients.<sup>3</sup> The reasons include wider variations in cancer types and treatments and the lack of clinical trials for older patients.<sup>4</sup> In contrast to many other Western countries, 16- and 17-year-old adolescents with cancer have been previously treated mainly in adult oncology and haematology departments in Finland.

Our aim was to investigate adolescents aged 16–17 years with cancer, by looking at their tumour characteristics, treatment and response, participation in therapy protocols, prognosis and whether they were treated by an adult or paediatric department.

This retrospective cohort study was conducted at Tampere University Hospital, which is a tertiary referral centre for approximately one million patients in Western and Central Finland. The study was approved by the Director of the Science Center of Pirkanmaa Hospital Region. The subjects were 16–17 years old when they were diagnosed with a primary malignancy between 2000 and 2019. Patients were identified from the hospital's electronic medical records, and clinical data were collected from diagnosis until death or 1 June 2020.

The data comprised the diagnosis and date, treatment, therapy protocol, response, survival, where they were treated and the date of the last follow-up visit. The cancers were grouped into three main diagnostic categories, according to the International Classification of Childhood Cancers, Third Edition: solid, central nervous system or haematopoietic malignancy.

Overall survival (OS) and event-free survival (EFS) were estimated using the Kaplan-Meier method and the log-rank test identified differences between the groups. The relationship between the

treatment sites and therapy protocols was assessed with the chi-squared test. Patient survival was explored with multivariate Cox regression. The cumulative incidence of relapse was estimated using fine-grey modelling, with death as a competing event.

A total of 93 patients (62.3% male) aged 16–17 were diagnosed with a malignant tumour, and 75.2% were solid tumours outside the central nervous system. The most common malignancies were Hodgkin lymphoma (31.2%), acute lymphoblastic leukaemia (14.0%) and gonadal germ cell tumours (9.7%) (Table S1).

The 70 patients who completed their therapy in the referral centre were followed up for a median of 7.9 years (interquartile range 4.0–13.7) (Table 1 and Figure S1). Most achieved complete remission (88.6%), but 21.4% relapsed (Table 1). The 5-year EFS for all cancers was 65% (95% CI 54–79%), and the OS was 84% (95% CI 75–94%) (Figures S2A–C and S3). No statistically significant difference between the sexes ( $p = 0.51$ ) or different tumour types ( $p = 0.21$ ) was observed for EFS (Figure S3). However, OS was worse for males than females (73% versus 100%,  $p = 0.046$ ) (Figure S2). The 5-year OS rate for haematopoietic malignancies was 62% (95% CI 40–96%), for CNS tumours 75% (43–100%) and 91% for solid tumours (95% CI 83–100%) ( $p = 0.017$ ) (Table 1 and Figure S2C).

Most adolescents (68.6%) were treated in adult departments. The complete remission rates were 90.9% for the paediatric department and 87.5% for the adult departments. The 5-year OS rates were 84% (95% CI, 69–100%) and 84% (95% CI, 74–96%), respectively.

Cox regression modelling showed no significantly increased hazard ratio for death by treatment site (Table S3).

Altogether, 22 patients (31.4%) were treated according to a specific clinical trial protocol: at the paediatric department, 54.5% ( $n = 12$ ), and at adult departments, 20.8% ( $n = 10$ ) were treated using a specific trial protocol ( $p = 0.011$ ).

Hodgkin lymphoma, acute lymphoblastic leukaemia, soft tissue and bone sarcomas were the most common diagnoses. The overall range of diagnoses mirrored the transitional phase for the age group, with decreasing haematopoietic malignancies and increasing solid cancers. The 5-year OS of 84% compared well with local and international studies of children and adolescents.<sup>2,5</sup> Males had more unfavourable outcomes, as they accounted for 81.3% of haematopoietic malignancies.

**Abbreviations:** CNS, central nervous system; EFS, event-free survival; OS, overall survival.

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TABLE 1 Characteristics of patients in the main cohort

	All subjects (%)	Solid	Haematopoietic	CNS
N (%)	70	49 (70.0)	16 (22.9)	5 (7.1)
Sex				
Male	45 (64.3)	29	13	3
Female	25 (35.7)	20	3	2
Age				
16-year	38 (54.3)	30	7	1
17-year	32 (45.7)	19	9	4
Treatment site				
Adult	48 (68.6)	33	11	4
Paediatric	22 (31.4)	16	5	1
Treatment modality <sup>f</sup>				
Chemotherapy	56 (80.0)	36	16	4
Surgery	32 (45.7)	29	0	3
Radiation therapy	28 (40.0)	17	7	4
Allo-HSCT <sup>a</sup>	11 (15.7)	3	8	0
Auto-HSCT <sup>b</sup>	8 (11.4)	8	0	0
Best response				
Complete remission	62 (88.6)	43	16	3
Partial remission	3 (4.3)	3	0	0
Stable disease	1 (1.4)	1	0	0
Refractory disease	4 (5.7)	2	0	2
Relapse	15 (21.4)	10	5	0
Death	12 (17.1)	5	6	1
OS, median FU, years, (IQR) <sup>c</sup>	7.9 (4.0–13.7)	8.9 (4.9–13.9)	4.8 (1.7–11.1)	5.6 (2.9–7.0)
EFS, median FU, years, (IQR) <sup>d</sup>	4.1 (2.0–7.4)	4.3 (2.0–8.1)	3.2 (1.0–5.0)	5.9 (2.9–7.2)
OS, 5 years (95% CI) <sup>c</sup>	0.84 (0.75–0.94)	0.91 (0.83–1.00)	0.62 (0.40–0.96)	0.75 (0.43–1.0)
EFS, 5 years (95% CI) <sup>d</sup>	0.65 (0.54–0.79)	0.72 (0.6–0.87)	0.38 (0.18–0.82)	0.75 (0.43–1.0)
CIR, 5 years (95% CI) <sup>e</sup>	0.27 (0.15–0.39)	0.24 (0.11–0.37)	0.47(0.15–0.79)	0

<sup>a</sup>Allogeneic haematopoietic stem cell transplantation.

<sup>b</sup>Autologous haematopoietic stem cell transplantation.

<sup>c</sup>Overall survival; FU, follow-up.

<sup>d</sup>Event-free survival; FU, follow-up.

<sup>e</sup>Cumulative incidence of recurrence.

<sup>f</sup>Subjects might have been treated with multiple different treatment methods.

The overall patient outcomes were similar in adult and paediatric departments, but clinical trial protocols were more common in the latter. Participation in clinical trials improves patient survival, and young patients with cancer should be enrolled in clinical therapy protocols whenever possible.<sup>4</sup>

#### CONFLICT OF INTEREST

None.

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#### SUPPORTING INFORMATION

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