Cancer in adolescents and young adults: treatment and outcome in Victoria

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ABSTRACT

Objectives: To describe the location of treatment, recruitment to clinical trials and outcomes for adolescents and young adults treated for cancer in Victoria.

Design and setting: Retrospective review of all adolescents and young adults aged 10–24 years diagnosed with cancer between 1992 and 1996, identified from the Victorian Cancer Registry.

Main outcome measures: Treatment regimen (clinical trial, treatment protocol or neither), compliance with treatment and 5-year survival.

Results: Questionnaires were completed for 576 of 665 eligible adolescents and young adults (87% response rate). Recruitment into clinical trials decreased with increasing age. Adolescents aged 10–19 years were more likely to be recruited to a clinical trial if treated at a paediatric hospital. For all cancers, 5-year survival was similar across the age groups and was not influenced by the place of treatment. Only 1% of adolescents and young adults failed to complete planned therapy due to non-compliance.

Conclusions: Despite a similar incidence of cancer to that in younger children, adolescents and young adults with cancer are poorly recruited into clinical trials in Victoria. Establishment of a cancer resource network in Victoria may provide information to both paediatric and adult oncologists about currently available clinical trials.

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THE PAST 20 YEARS has seen an increase in the incidence of cancer in all age groups in Victoria. This increase has been more marked in adolescents and young adults than in any other age group. Cancer incidence increased by 30% in those aged 10–24 years between 1993 and 2001.[1,2] A similar trend has been reported overseas.[3] In addition, mortality rates in adolescents and young adults with cancer have been slow to decline.

Published studies have consistently shown that children and adolescents with a variety of cancer types have higher survival rates if treated in clinical trials and at specialised centres.[4-6] Entry into clinical trials appears to be a more important determinant of outcome than the place of treatment.[7,8] Given the poor outcomes for adolescents and young adults with cancer, access to, and treatment in, national clinical trials is of paramount importance in this age group.

The proportion of adolescents and young adults managed at specialised tertiary centres and treated in clinical trials in Victoria is not known. We felt it important to document current management, and to examine the outcomes of adolescents and young adults with cancer who receive their treatment in Victoria.

METHODS

All adolescents and young adults aged 10–24 years, who were diagnosed with cancer between 1 January 1992 and 31 December 1996, were identified from the Victorian Cancer Registry. Eligibility was limited to adolescents and young adults presenting with cancers common in this age group, namely, leukaemia, lymphoma, germ cell tumours, brain tumours, soft tissue tumours and bone tumours. The referring physician for each patient was sent a brief questionnaire to ascertain:

- the location of treatment (adult hospital, paediatric teaching hospital, or private rooms);
- whether the patient received treatment in a clinical trial or according to a treatment protocol;
- if not treated in a trial or according to a protocol, whether the patient received surgery, chemotherapy or radiotherapy;
- whether proposed treatment was completed; and,
- whether compliance with treatment was a problem.

Where required, posted questionnaires were followed up with a reminder letter and telephone call. For some hospitals, clinical notes were reviewed on-site in conjunction with the local data managers.

The reported treatment outcome at the end of 2001 was matched with information from the Registrar of Births, Deaths and Marriages to give 5-year follow-up data for all patients. The χ^2 test was used in comparison of treatment regimens, and 95% confidence intervals for differences in proportions are reported. Five-year survival was examined by means of Kaplan–Meier survival estimates.

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1: The distribution of cancers and location of treatment for 576 adolescents and young adults with cancer

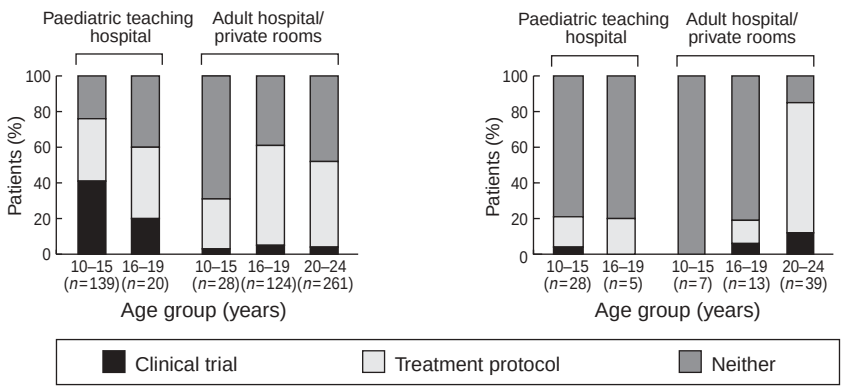
	Age group		
	10–15 years	16–19 years	20–24 years
Completed questionnaires	167/177* (94%)†	144/165* (87%)†	265/323* (82%)†
Distribution of cancers (No. [%]‡)			
Bone tumours	26 (16%)	18 (13%)	16 (6%)
Brain tumours	35 (21%)	19 (13%)	41 (16%)
Germ cell tumours	10 (6%)	28 (19%)	72 (27%)
Leukaemia	43 (26%)	23 (16%)	26 (10%)
Lymphoma	40 (24%)	49 (34%)	90 (34%)
Soft tissue tumours	13 (8%)	7 (5%)	20 (8%)
Treatment location†			
Paediatric hospital	139 (83%)	20 (14%)	4 (2%)
Adult hospital	25 (15%)	121 (84%)	253 (96%)
Private rooms	3 (2%)	3 (2%)	8 (3%)

*Denominator is total number of eligible patients. † $P = 0.023$. ‡Percentage of patients with completed questionnaires.

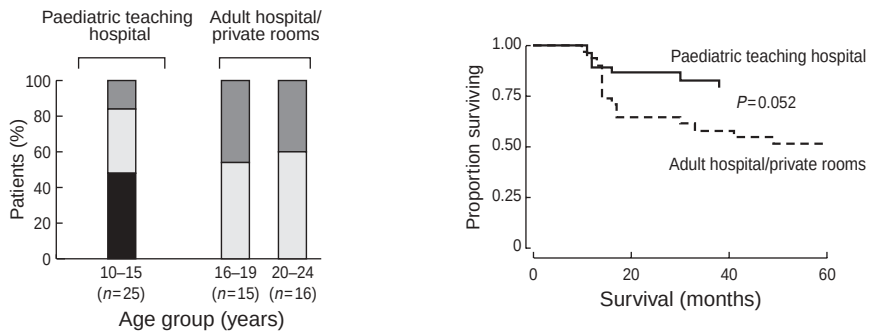
2: Management of all 576 adolescents and young adults with cancer, those with bone tumours (survival also shown) and those with brain tumours according to treatment regimen and place of treatment

(a) Treatment regimen and place of treatment for 576 adolescents and young adults with cancer

(b) Treatment regimen and place of treatment for 95 adolescents and young adults with brain tumours*



(c) Treatment regimen and place of treatment, and Kaplan–Meier survival curves for 60 adolescents and young adults with bone tumours*



*Groups totalling three patients or fewer (eg, three patients aged 16–19 years with bone tumours treated at a paediatric hospital; one patient aged 10–15 years with a bone tumour treated at an adult hospital) were not included.

Ethical approval for the study was granted by the Human Research Ethics Committee of the Cancer Council Victoria, the Human Research Ethics Committee of the Royal Children's Hospital, and the Human Research Ethics Committee of the Peter MacCallum Cancer Institute. Formal ethics approval was not required at other participating hospitals. Approval was granted by the Heads of Department at all other participating institutions.

RESULTS

A total of 679 adolescents and young adults with cancer were identified from the Victorian Cancer Registry for the 5 years from 1992 to 1996. Fourteen patients were excluded: eight were not treated in Victoria; five had an incorrect diagnosis of cancer; and one received no treatment. This left 665 patients eligible for study entry. Questionnaires were completed for 576 (357 male, 219 female) eligible patients (87%).

The distribution of cancers and location of treatment for each age group is shown in Box 1.

Treatment regimen

Treatment was categorised according to management in a clinical trial, according to a treatment protocol, or neither. The results for each age group and all cancers are shown in Box 2 (a). Significantly more adolescents aged 10–19 years were treated within clinical trials in paediatric teaching hospitals than adult hospitals (38% and 3%, respectively; $P < 0.005$; 95% CI for difference, 25%–41%). Only 4% of young adults aged 20–24 years were treated within clinical trials.

Overall 5-year survival

There was no significant difference in overall 5-year survival between the three age groups for all cancers combined.

Treatment and 5-year survival were examined separately for each of the six cancers studied. Overall survival did not differ significantly between age groups for each cancer (Box 3).

Brain tumours: Few adolescents and young adults with brain tumours were

3: Percentage of adolescents and young adults in clinical trials, and overall 5-year survival in all age groups by tumour type

	Age group		
	10–15 years	16–19 years	20–24 years
Bone tumours			
Number	26	18	16
Clinical trial	12 (46%)*	1 (5.5%)*	0*
Overall survival (95% CI)	81% (59%–91%)	44% (22%–65%)	63% (35%–81%)
Brain tumours			
Number	35	19	41
Clinical trial	1 (3%)	1 (6%)	1 (2%)
Overall survival (95% CI)	83% (66%–92%)	58% (33%–76%)	68% (52%–80%)
Germ cell tumours			
Number	10	28	72
Clinical trial	0	0	4 (6%)
Overall survival (95% CI)	80% (41%–95%)	93% (74%–98%)	85% (74%–91%)
Leukaemias			
Number	43	23	26
Clinical trial	28 (65%)*	3 (13%)*	3 (12%)*
Overall survival (95% CI)	56% (40%–69%)	61% (38%–77%)	50% (30%–67%)
Lymphomas			
Number	40	49	90
Clinical trial	16 (40%)*	5 (10%)*	2 (2%)*
Overall survival (95% CI)	85% (70%–93%)	80% (65%–88%)	82% (73%–89%)
Soft tissue tumours			
Number	13	7	20
Clinical trial	1 (8%)	0	1 (5%)
Overall survival (95% CI)	77% (44%–92%)	71% (26%–92%)	75% (50%–89%)

* $P < 0.05$

treated within clinical trials (Box 2 [b]).

Bone tumours: Significantly more adolescents aged 10–15 years than those aged 16–19 years were treated within clinical trials (46% v 5.5%; $P = 0.003$; 95% CI for difference, 21%–64%; Box 2 [c]). Survival appeared to be improved if patients were treated at a paediatric hospital (Box 2 [c]), although these differences are completely confounded with age differences (almost all patients over 16 years were treated at adult hospitals).

Germ cell tumours: Few patients were treated in clinical trials (Box 3). There were no major differences in survival according to place of treatment.

Leukaemia and lymphoma: Recruitment into clinical trials decreased significantly with increasing age (Box 3). Survival was not associated with place of treatment.

Soft tissue tumours: There were insufficient numbers of patients with soft tissue tumours for statistical analysis.

Failure to complete treatment

About 10% of patients eligible for our study (67/665) did not complete treatment. This was more commonly because of relapse (37 patients) than non-compliance with therapy (seven patients). Other reasons included toxicity or sepsis (6), death (12), changed diagnosis (1), paraplegia (1), acute psychosis (1), or were not recorded.

DISCUSSION

Several international studies have shown that the outcome for adolescents and young adults with cancer is worse than for younger children.[3,9] Our study has provided previously unavailable information on the patterns of management and outcomes of adolescents and young adults with cancer in Victoria. The study was not designed to examine factors other than recruitment to clinical trials that might be associated with cancer outcomes in this population, as differences between treatment locations were heavily confounded with age differences. Possible effects of treatment regimens are better examined within the context of randomised trials.

In our study, the overall 5-year survival in adolescents aged 16–19 years was not significantly different from that of patients aged 10–15 and 20–24 years.

Adolescents and young adults with cancer are treated at both adult and paediatric centres. In keeping with reports from the United States,[10] 83% of Victorian adolescents aged 10–15 years, and 14% of those aged 16–19 years are treated at paediatric institutions and have access to paediatric clinical trials. We found significantly fewer adolescents and young adults aged 16–19 years and 20–24 years were recruited to clinical trials when compared with those aged 10–15 years. Again, this result is in keeping with US reports, showing enrolment into both paediatric and adult cooperative group clinical trials was consistently lower in adolescents aged 15–21 years than in children aged 0–14 years.[11] It is unclear why adolescents and young adults with cancer have such low rates of recruitment into clinical trials.

A recent British study confirmed that most oncologists and haematologists are committed to the concept of prospective randomised clinical trials.[12] However, despite this, less than half the eligible patients aged 15–29 years were actually enrolled in national leukaemia trials. Reasons for lack of recruitment included clinician preference for one arm of a national trial, concurrent regional studies or non-trial protocols, and concerns about administrative issues. In our study, which includes patients enrolled in regional trials, we did not explore the reasons for lack of recruitment into clinical trials, but it is clear that barriers do exist.

In adolescents and young adults with acute lymphoblastic leukaemia, improved survival has been reported for patients treated on intensive paediatric protocols, suggesting that adolescents and young adults with this cancer may benefit from an "aggressive" paediatric-type regimen.[13] In our study, the number of adolescents and young adults with cancer was too small to examine the influence of treatment on outcome. However, Kaplan–Meier survival analysis showed the 5-year survival for all cancers combined was similar across all age groups and was independent of place of treatment.

In adolescents and young adults with bone tumours, we demonstrated that treatment at a paediatric teaching hospital, where recruitment into clinical trials was more common, was associated with improved outcome. The pathophysiology, natural history and response to treatment in osteosarcoma is not influenced by age,[14] but the prognosis in Ewing's sarcoma does appear to worsen with age.[15] In our study it was not possible to separate the influence of increasing age from the potentially adverse influence of poor recruitment into clinical trials on patient survival.

For some tumour types, such as germ cell tumours and lymphoma, where well established treatment protocols are in place, recruitment into clinical trials appears to have less effect on overall survival. In Victoria, most patients with germ cell tumours and lymphomas were treated according to well-established protocols. Survival appeared uniformly high across all age groups and settings.

About 1% of adolescents and young adults in our study failed to complete planned therapy because of non-compliance with treatment. We probably underestimated the extent of the problem. Despite completing planned therapy, adolescents and young adults may not have complied with oral self-administered chemotherapy, which can be a significant component of therapy for some cancers. Published studies of non-compliance with oral chemotherapy in children and adolescents have reported rates between 10%[16] and 59%.[17] Compliance is known to decrease with duration of therapy,[18] and has a significant effect on patient survival.[19] Non-compliance may account, in part, for the poor survival rates reported in adolescents and young adults with cancer.

We examined outcome in terms of survival, and did not attempt to address treatment-related morbidity or quality-of-life, both of which are major concerns for adolescents and young adults. Although short-term and long-term adjustment difficulties have been described,[11] there is a paucity of information on quality-of-life in adolescents and young adults with cancer. Increasingly, clinical trials are incorporating measures of quality-of-life and, as survival improves, these will become a more important focus of outcome.

Our study has confirmed that, in Victoria, adolescents and young adults are less likely to be enrolled in clinical cancer trials than younger children. There is clearly a need to address this problem.

One reason for lack of recruitment into clinical trials might be the absence of suitable open studies.[20] Many of the cancers seen in patients aged 10–24 years are common in the paediatric age group, but more than 25% of young adults will have tumours not routinely studied or treated by paediatric oncology cooperatives, and which adult oncologists regularly manage. Enrolment into appropriate adult trials should be encouraged. Appropriate management of adolescents and young adults requires communication and cooperation between all adult and paediatric specialists involved in cancer treatment. This could be achieved by developing a cancer resource network to provide information about current clinical studies to paediatric and adult oncologists, other specialists, adolescents and young adults with cancer and their families.[9]

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COMPETING INTERESTS

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