the expanded disability qualification. Approximately 70 % of unemployed CCSs had some late effects; independent factors related to unemployed CCS were late effects (OR 6.22) and dropping out of school (OR 8.46). Most unemployed CCSs were likely to seek work, despite their health problems.

Acknowledgments We express our deep appreciation to all the CCSs and their families who participated in this survey. This work was supported by a research grant, "Child support in clinical cancer practice," from the Japanese Ministry of Health, Labour and Welfare. We thank Ms. Mizue Hayashi for secretarial assistance and data management.

Conflict of interest The all authors declare that they have no conflict of interest.

References

1. Maeda M (2008) Late effects of childhood cancer: life-threatening issues. J Nippon Med Sch 75(6):320–324
2. Ishida Y, Honda M, Ozono S et al (2010) Late effects and quality of life of childhood cancer survivors: part 1. Impact of stem cell transplantation. Int J Hematol 91(5):865–876
3. Hudson MM (2008) Survivors of childhood cancer: coming of age. Hematol Oncol Clin North Am 22(2):211–31, v-vi
4. Kirchhoff AC, Krull KR, Ness KK et al (2011) Occupational outcomes of adult childhood cancer survivors: a report from the childhood cancer survivor study. Cancer 117(13):3033–3044
5. Huh WW, Jaffe N, Ottaviani G (2006) Adult survivors of childhood cancer and unemployment: a metaanalysis. Cancer 107(12):2958–9; author reply 9
6. Kirchhoff AC, Leisenring W, Krull KR et al (2010) Unemployment among adult survivors of childhood cancer: a report from the childhood cancer survivor study. Med Care 48(11):1015–1025
7. Asami K, Ishida Y, Sakamoto N (2012) Job discrimination against childhood cancer survivors in Japan: a cross-sectional survey. Pediatr Int 54(5):663–668
8. Gurney JG, Krull KR, Kadan-Lottick N et al (2009) Social outcomes in the Childhood Cancer Survivor Study cohort. J Clin Oncol 27(14):2390–2395
9. Johannsdottir IM, Hjermstad MJ, Moum T et al (2010) Social outcomes in young adult survivors of low incidence childhood cancers. J Cancer Surviv 4(2):110–118
10. Heart Link mutual-aid health insurance program. 2013. http://hartlink.net/
11. Pediatric Brain Tumor Association. 2013. http://www2.pbta.jp/
12. Oeffinger KC, Mertens AC, Sklar CA et al (2006) Chronic health conditions in adult survivors of childhood cancer. N Engl J Med 355(15):1572–1582
13. Ishida Y, Honda M, Kamibeppu K et al (2011) Social outcomes and quality of life (QOL) of childhood cancer survivors in Japan: a cross-sectional study on marriage, education, employment and health related QOL (SF-36). Int J Hematol 93(5):633–644
14. Boman KK, Lindblad F, Hjern A (2010) Long-term outcomes of childhood cancer survivors in Sweden: a population-based study of education, employment, and income. Cancer 116(5):1385–1391
15. Yagci-Kupeli B, Yalcin B, Kupeli S et al (2013) Educational achievement, employment, smoking, marital, and insurance statuses in long-term survivors of childhood malignant solid tumors. J Pediatr Hematol Oncol 35(2):129–133
16. de Boer AGEM, Verbeek JHAM, van Dijk FJH (2006) Adult survivors of childhood cancer and unemployment. Cancer 107(1):1–11
17. Kirchhoff AC, Krull KR, Ness KK et al (2011) Physical, mental, and neurocognitive status and employment outcomes in the childhood cancer survivor study cohort. Cancer Epidemiol Biomarkers Prev 20(9):1838–1849
18. Olson R, Hung G, Bobinski MA, Goddard K (2011) Prospective evaluation of legal difficulties and quality of life in adult survivors of childhood cancer. Pediatr Blood Cancer 56(3):439–443
19. Kunin-Batson A, Kadan-Lottick N, Zhu L et al (2011) Predictors of independent living status in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. Pediatr Blood Cancer 57(7):1197–1203
20. Haupt R, Spinetta JJ, Ban I et al (2007) Long term survivors of childhood cancer: cure and care. The Erice statement. Eur J Cancer 43(12):1778–1780

PEDIATRICS INTERNATIONAL Official Journal of the Japan Pediatric Society

Pediatrics International (2012) ••, ••–••

doi: 10.1111/j.1442-200X.2012.03633.x

Original Article

Job discrimination against childhood cancer survivors in Japan: A cross-sectional survey

Keiko Asami,[1] Yasushi Ishida[2] and Naoko Sakamoto[3]

[1]*Department of Pediatrics, Niigata Cancer Center Hospital, Niigata,* [2]*Department of Pediatrics, St. Luke's International Hospital and* [3]*Department of Epidemiology, National Research Institute for Child Health and Development, Tokyo, Japan*

Abstract ***Background***: The aim of this study was to investigate the policies to identify job discrimination by company recruiters against childhood cancer survivors in Japan.

Methods: We conducted a cross-sectional study using a mailed questionnaire for the Japanese companies that were divided into three groups: companies listed on the stock market, companies not listed on the stock market, and public offices. We randomly selected 2000 of the 4000 listed companies and 2500 of the 4300 unlisted companies. We selected 47 public offices from prefectures and 17 from government ordinance-designated cities. Outcomes were health certificate requirements, how to treat past medical history and present illness, childhood cancer survivors' employment experience, and company's policy for evaluating applicants based on past medical history and present illness.

Results: Response rates were 17.7% for listed companies, 28.9% for unlisted companies, and 56.3% for public offices. A health certificate was required by 86% of listed companies, 77% of unlisted companies, and 75% of public offices. However, 33% of listed companies and 36% of unlisted companies, and none of the public offices demanded it at the time of application. Small numbers of private companies (0.7% of listed companies and 1.0% of unlisted companies) and public offices (4%) reject applicants outright if they have a disease in their past medical history. Using multivariate analysis, we found that large companies and company policies were significantly associated with the demand for a health certificate at the time of job applications.

Conclusions: In Japan, employment-related discrimination still occurs in a small number of companies and public offices.

Key words childhood cancer, health certificate, long-term survivors, job application, social discrimination.

Introduction

Because of advances in treatment, between 70% and 80% of children diagnosed with cancer become long-term survivors. In Japan, the estimated number of pediatric cancer survivors is over 50 000: approximately one out of every 700 adults between the ages of 20 and 39 years. Although an increased number of children have been cured of cancer, many survivors experience various health problems later in life because of their treatments.[1,2] In addition to various physical problems in childhood cancer survivors (CCS),[3] future social outcomes, including marriage, education, and employment, are apparently affected by these late effects, both directly and indirectly. In addition, the CCS have made many efforts to attain educational/ vocational goals; however, a significant proportion of CCS remains at increased risk of developing poor social outcomes and quality of life.[4]

Many articles have noted discrimination against adult cancer survivors in obtaining employment appropriate to their abilities and training or returning to their previous jobs.[5–8] Among CCS, these problems are more complicated, as nearly all CCS have no employment experience before the onset of cancer. These CCS generally have more easily recognizable work-related limitations at the time of their employment examinations than adult cancer survivors do.[9] Many CCS have problems even filling out job applications, and their reactions to employment examinations are far more variable than the reactions of adult cancer survivors are (Asami and Ishida, unpublished data). However, the extent to which CCS in Japan have suffered from job discrimination remains to be determined. In this article, we investigate the policies of private companies and public offices to identify the extent of job discrimination against CCS in Japan by company recruiters.

Correspondence: Yasushi Ishida, MD, St. Luke's International Hospital, Department of Pediatrics, 9-1 Akashi-cho, Chuo-ku, Tokyo 104-8460, Japan. Email: yaishida@luke.or.jp

Received 25 January 2012; accepted 15 March 2012.

Methods

Study design and companies selection

In 2009, we performed a cross-sectional survey using a questionnaire (see Supplemental Appendix 1). The companies were divided into three groups: companies listed on the stock market, companies not listed on the stock market, and public offices. We randomly selected 2000 of the 4000 listed companies and 2500 of the 4300 unlisted companies in the Japan company handbook *Kaisyasikihou*. We selected 47 public offices from prefectures and 17 from government ordinance-designated cities. Public servants were classified into four groups: general desk workers, schoolteachers, police officers, and medical service providers. We sent a questionnaire to the personnel department of each company or public office under the auspices of the Japanese Ministry of Health, Labour and Welfare with a request that it be filled out and returned anonymously. If the company wanted our report on the survey, we asked them to enclose their company's name and address separately.

Measurement of variables

The questionnaire consisted of 13 items, with four items (question [Q] 4–6, Q12) that included free writing. We evaluated health certificate requirements (Q1 and Q2), how past medical history and present illness are treated (Q3–Q6), employment experience of CCS (Q7), company's policy for evaluating applicants based on past medical history and present illness (Q8), and company's background (Q9–Q11). For Q4 through Q6, free writing sentences were classified using content analysis by two independent researchers and classified into seven answer types: (answer [A] 1) past medical history does not matter (hiring is based on job performance); (A2) if the disease has been cured, it does not matter; (A3) hiring will depend on a physician's determination; (A4) it depends on the applicants (case by case); (A5) hiring will depend on the state of the disease; (A6) hiring will depend on the applicant's performance during the trial period; and (A7) we are concerned that the disease will recur.

Each company was categorized as belonging to a primary, secondary, or tertiary sector of industry. Further, the company's size was classified on the basis of the number of regular workers, with each classified as either a large company (500 workers or more) or a small or intermediate company (fewer than 500 workers). Companies were also classified by location based on whether or not they were located in Kanto District.

Ethics

The study was performed following approval from the ethics committee of the principal investigator's institution (K. Asami, Niigata Cancer Center Hospital).

Statistical analysis

We performed χ^2-tests (or Fisher's exact tests for cells with expected counts of <5) within categorical predictors. We explored the association features of the companies that require a health certificate at the time of the job application limited to private companies. The adjusted odds ratios for the interesting outcome were estimated with logistic regression analysis. As predictors we assessed various typical features of companies; type of stocks, type of business, company sizes, location of the head office, and companies' experience of CCS employment and their policy. Data were analyzed with SPSS software, v. 19.0 (IBM Japan, Tokyo, Japan).

Results

The demographic data of the companies are shown in Supplemental Appendix 2. Completed questionnaire sheets were returned by 354 listed companies (a 17.7% response rate), 720 unlisted companies (28.9%) and 36 public offices (56.3%). Most companies belonged to the secondary or tertiary sector of industry (140:162 in listed companies and 296:343 in unlisted companies, respectively). The number of regular workers in a company depended largely on whether the company was listed or unlisted ($P < 0.001$). The proportion of large companies (500 workers or more) was 48% in listed and 24% in unlisted companies ($P < 0.001$). Many head offices of listed and unlisted companies were located in Kanto (around Tokyo). The distribution of locations of head offices was significantly different between private companies and public offices ($P < 0.001$).

Table 1 shows the main results of this survey (Q0 through Q8). Fifty-seven (16.2%) of the 352 listed companies and 72 (10.1%) of the 716 unlisted companies indicated that they were unable to answer our questions because of confidentiality issues; this difference was significant ($P = 0.004$). Health certificates were required by 86% of listed companies, 77% of unlisted companies, and 75% of public offices. Health certificates were required at the time of application by 33% of listed companies, 36% of unlisted companies, and none of the public offices. This difference between private companies and public offices was significant ($P < 0.001$). Small numbers of private companies (0.7% of listed companies and 1.0% of unlisted companies) and public offices (4%) reject applicants after reviewing their application or because of their internal rules if the applicant listed a disease in his or her past medical history (Q3). Only three private companies had policies in the relevant rule for applicants who listed childhood cancer or other diseases in their past medical history; in contrast, 43% of public offices had pertinent policies (Q4 and Q5). Surprisingly none of the public offices answered definitely that they have ever employed a former childhood cancer patient (Q7). About 40% of private companies (both listed and unlisted) answered that the present illness of applicants is more important than the past history (Q8).

We explored the typical associated characteristics of the companies that require a health certificate at the time of the job application (Table 2). A univariate analysis showed that company size, the importance of past medical history, and company policy for dealing with present illness and past medical history were strongly associated with the demand for a health certificate at the time of the job application. Logistic regression analysis revealed that large companies (500 or more workers) and companies with policies in effect (companies that answered that both present illness and past medical history are important) were significantly more likely to require a health certificate at the time of the job application.

We compared the answers among four kinds of jobs in public offices in Table 3. There were no differences in many questions. However, health certificates were required at the time of application in medical service providers alone ($P = 0.004$).

Table 1 Comparison between listed companies and unlisted companies and between private companies and public offices

	Listed companies (n = 354)	Unlisted companies (n = 720)	Listed vs unlisted (P-value)	Public offices (n = 36)	Private companies vs public offices (P-value)
Q0 Can you publicly answer the following questions?					
1. No	57 (16%)	72 (10%)	0.004		
Q1 Do you require a health certificate at the time of employment testing?					
1. Yes	259 (86%)	493 (77%)	0.002	27 (75%)	0.522
Q2 If so, when do you require it?	(n = 258)	(n = 489)		(n = 27)	
1. At the time of application	85 (33%)	178 (36%)	0.496	0	<0.001*
2. After hiring	128 (50%)	225 (45%)		5 (19%)	
3. It depends (case by case)	45 (17%)	96 (19%)		22 (81%)	
Q3 What are your thoughts when an applicant lists a disease in his or her past medical history?					
1. Past medical history does not matter	108 (39%)	276 (40%)	0.098	4 (15%)	<0.001
2. It depends (case by case)	107 (38%)	172 (25%)		16 (62%)	
3. It depends on desired sections	36 (13%)	68 (10%)		0	
4. It depends on the disease	61 (22%)	123 (18%)		1 (4%)	
5. The decision is entrusted to the interviewers	8 (3%)	28 (4%)		1 (4%)	
6. The applicant will be rejected after being reviewed	0	2 (0.3%)		0	
7. The applicant will be rejected because of the company's internal rules	2 (0.7%)	5 (0.7%)		1 (4%)	
8. Others	8 (3%)	16 (2%)		5 (19%)	
Q4 How would you respond if an applicant has listed childhood cancer in his or her past medical history?					
1. Yes, we have a rule	0	3 (0.4%)	0.061*	15 (43%)	<0.001*
2. No, we don't have a rule	172 (49%)	300 (42%)		10 (29%)	
3. No comment	180 (51%)	413 (58%)		10 (29%)	
Q5 How would you respond if an applicant has listed a disease other than childhood cancer in his or her past medical history?					
1. Yes, we have a rule	0	3 (0.4%)	0.042*	15 (43%)	<0.001*
2. No, we don't have a rule	173 (49%)	299 (42%)		10 (29%)	
3. No comment	179 (51%)	414 (58%)		10 (29%)	
Q6 How would you respond if an applicant were a childhood cancer patient?					
1. Yes, we have a rule	0	3 (0.4%)	0.499*	12 (34%)	<0.001*
2. No, we don't have a rule	253 (72%)	528 (74%)		18 (49%)	
3. No comment	99 (28%)	185 (26%)		5 (17%)	
Q7 Have you ever employed a former childhood cancer patient?					
1. Yes	2 (0.7%)	3 (0.5%)	0.001*	0	0.002*
2. No	45 (15%)	158 (25%)		0	
3. Not sure	253 (84%)	479 (75%)		32 (100%)	
Q8 What is your policy on the past medical history and present illness of applicants?					
1. Present illness is important	126 (42%)	264 (41%)	0.982*	0	<0.001*
2. Past history is important	0	1 (0.2%)		0	
3. Both are important,	51 (17%)	112 (18%)		5 (17%)	
4. It depends (case by case)	121 (41%)	260 (41%)		25 (83%)	

*Fisher's exact test.

Figure 1 shows the detailed answers for Q4, Q5, and Q6. Q4 focused on treatment of childhood cancer in the past. Q5 focused on treatment of some childhood disease other than cancer in the past. Q6 focused on treatment of workers who turned out to be childhood cancer survivors after hiring. All three groups surveyed showed the same tendency in their answers. In the listed company and public office groups, A1 (past medical history does not matter) and A4 (case by case) were the main answers, while A1 (hiring is based on job performance) was predominant in the unlisted company group. In addition, A3 (hiring will depend on a physician's determination) was also more common in the public office group. Of note was that neither A2 (if the disease has been cured, it does not matter) nor A5 (hiring will depend on the state of the disease) existed exclusively in the public office group.

Discussion

In this survey of Japanese companies, we found that a very small number of private companies or public offices would reject applicants on the basis of their history of cancer. Although large companies and the companies in effect (companies that answered that both present illness and past medical history are important) were significantly more likely to demand a health certificate at the time of the job application.

In our study there were significant varieties in company size and location of head offices among three groups. The Kanto district is located around Tokyo, in which most of the social rules are expected to be standardized, but the difference was marginal, as shown in Table 2. It is noteworthy that a substantial proportion of private companies (16% of the listed companies and 10% of

Table 2 Typical features of the companies that required health certificate at the time of application

	Required at application		χ^2/Fisher (P-value)	Logistic regression analysis	
	Yes	No		Odds ratio (95%CI)	P-value
Type of stock					
Listed companies	64 (37%)	223 (29%)	0.151	1.03 (0.69–1.52)	0.896
Unlisted companies	111 (63%)	498 (71%)		Reference	
Q9 Type of business					
Primary sector (A1–A3)	0	1 (0.1%)	0.288 (0.291*)	–	
Secondary sector (A4–A6)	88 (51%)	319 (45%)		1.12 (0.78–1.60)	0.550
Tertiary sector (A7–A20)	86 (49%)	396 (55%)		Reference	
Q10 Company size					
Less than 500 workers (A7–A8)	88 (51%)	519 (72%)	<0.001	Reference	
500 or more workers (A1–A6)	86 (49%)	201 (28%)		2.66 (1.81–3.90)	<0.001
Q11 Location					
Kanto (A3)	78 (45%)	363 (50%)	0.180	0.73 (0.51–1.05)	0.094
Non-Kanto (not A3)	96 (55%)	356 (50%)		Reference	
Q3 Importance of past history					
Past medical history does not matter (A1)	46 (26%)	331 (49%)	<0.001	0.73 (0.26–2.08)	0.554
It depends (A2–A4)	117 (67%)	315 (46%)		1.52 (0.56–4.15)	0.412
The decision is entrusted to interviewers (A5)	8 (5%)	28 (4%)		0.83 (0.32–2.15)	0.697
The applicant will be rejected (A6,A7)	4 (2%)	5 (1%)		2.39 (0.56–10.2)	0.241
Q7 Employment experience of the childhood cancer survivors					
No (A2)	48 (28%)	151 (21%)	0.063	Reference	
Not sure (A3)	125 (72%)	562 (79%)		0.78 (0.51–1.20)	0.250
Q8 Companies' policy of dealing with present illness and past history					
Present illness is very important (A1)	65 (38%)	312 (44%)	<0.001 (<0.001*)	Reference	
Past medical history is very important (A2)	1 (0.6%)	0		–	
Both are very important (A3)	58 (33%)	102 (14%)		2.06 (1.30–3.28)	0.002
It depends (case by case) (A4)	50 (29%)	299 (42%)		0.85 (0.55–1.30)	0.444

*Fisher's exact test.

the unlisted companies) indicated that they were unable to answer our questions on employment policy because of confidentiality issues.

It is a considerable problem that about one-third of private companies demand health certificates at the time of job application and small numbers of private companies as well as public offices reject applicants after reviewing their application or because of their internal rules if the applicant listed a disease in his or her past medical history in Table 1. In Japan, the Ministry of Health, Labour and Welfare prohibits companies from using an applicant's health certificate for his or her employment test and recommends using it instead for appropriate assignment after hiring.[10] Logistic regression analysis demonstrated that large companies (500 or more workers) and companies with policies in effect (companies that answered that both present illness and past medical history are important) were significantly more likely to require a health certificate at the time of the job application. The Kanto head offices made a marginal negative effect on it.

In Figure 1, it is interesting that A1 (hiring is based on job performance) was the predominant answer in the unlisted company group, which suggests that job performance by itself is crucial for the unlisted companies. On the other hand, A4 (case by case) was the main answer in the listed companies and public offices. In addition, it is also interesting that they might avoid the absolute evaluation like A2 (if the disease has been cured, it does not matter) or A5 (hiring will depend on the state of the disease) in the public office group.

Employment outcomes can be improved with improved quality of medical treatment and with clinical and supportive services designed for better management of symptoms, rehabilitation, and reasonable accommodation for disabilities.[8,11] In the USA, employment-related discrimination was, at one time, rather common.[5,8] However, four federal laws now provide some job protection to cancer patients and survivors:[8] the Americans with Disabilities Act (ADA), the Federal Rehabilitation Act, the Family and Medical Leave Act (FMLA), and the Employee Retirement and Income Security Act (ERISA).[9] If a cancer survivor needs extra time or help to do his or her job, the ADA requires the employer to provide a "reasonable accommodation," which may involve a change in working conditions, including hours or duties.

In adult cancer survivors, the inability to return to work after cancer treatment, frequent or prolonged work absenteeism, or problems with work performance may have a substantial economic impact on the survivor and his or her family.[12,13] Work changes also may have a substantial impact on self-esteem, quality of life, and social and family roles. De Boer *et al.*[14] conducted a meta-analysis and found that cancer survivorship was associated with unemployment, as cancer survivors were more likely to be unemployed than healthy control participants were (33.8% vs 15.2%; pooled relative risk [RR], 1.37; 95% confidence interval [CI], 1.21–1.55). Survivors (10.4%) reported health-related unemployment more often than their siblings did (1.8%; RR, 6.07; 95%CI, 4.32–8.53). In the same manner, the Childhood Cancer Survivors Study showed that CCS (5.7%) were more likely to

Table 3 Four kinds of jobs in public offices

	General desk workers (n = 35)	Schoolteachers (n = 35)	Police officers (n = 35)	Medical service providers (n = 35)	χ^2/Fisher (P-value)
Q1 Do you require a health certificate at the time of employment testing?					
1. Yes	27 (75%)	24 (89%)	26 (77%)	28 (85%)	0.900
Q2 If so, when do you require it?					
1. At the time of application	0	0	0	4 (14%)	0.004*
2. After hiring	5 (19%)	9 (38%)	1 (4%)	5 (18%)	
3. It depends (case by case)	22 (81%)	15 (62%)	25 (96%)	19 (68%)	
Q3 What are your thoughts when an applicant lists a disease in his or her past medical history?					
1. Past medical history does not matter	4 (15%)	10 (42%)	3 (11%)	4 (14%)	0.461
2. It depends (case by case)	16 (62%)	9 (38%)	19 (68%)	16 (55%)	
3. It depends on desired sections	0	0	0	1 (3%)	
4. It depends on the disease	1 (4%)	3 (13%)	2 (7%)	1 (3%)	
5. The decision is entrusted to the interviewers	1 (4%)	0	2 (7%)	2 (7%)	
6. The applicant will be rejected after being reviewed	0	0	0	0	
7. The applicant will be rejected because of the company's internal rules	1 (4%)	0	1 (4%)	1 (4%)	
8. Others	5 (19%)	4 (17%)	4 (14%)	6 (21%)	
Q4 How would you respond if an applicant has listed childhood cancer in his or her past medical history?					
1. Yes, we have a rule	15 (43%)	14 (40%)	15 (43%)	15 (43%)	0.999
2. No, we don't have a rule	10 (29%)	11 (31%)	10 (29%)	10 (29%)	
3. No comment	10 (29%)	10 (29%)	10 (29%)	10 (29%)	
Q5 How would you respond if an applicant has listed a disease other than childhood cancer in his or her past medical history?					
1. Yes, we have a rule	15 (43%)	14 (40%)	15 (43%)	15 (43%)	0.999
2. No, we don't have a rule	10 (29%)	11 (31%)	10 (29%)	10 (29%)	
3. No comment	10 (29%)	10 (29%)	10 (29%)	10 (29%)	
Q6 How would you respond if an applicant were a childhood cancer patient?					
1. Yes, we have a rule	12 (34%)	12 (34%)	11 (31%)	13 (37%)	0.994
2. No, we don't have a rule	18 (51%)	17 (49%)	18 (51%)	18 (51%)	
3. No comment	5 (14%)	6 (17%)	6 (17%)	4 (11%)	
Q7 Have you ever employed a former childhood cancer patient?					
1. Yes	0	0	0	0	0.045*
2. No	0	5 (19%)	2 (6%)	2 (6%)	
3. Not sure	32 (100%)	21 (81%)	30 (94%)	29 (94%)	
Q8 What is your policy on the past medical history and present illness of applicants?					
1. Present illness is very important	0	3 (13%)	2 (7%)	2 (7%)	0.177*
2. Past history is very important	0	1 (4%)	0	0	
3. Both are very important,	5 (17%)	2 (8%)	9 (31%)	5 (17%)	
4. It depends (case by case)	25 (83%)	18 (75%)	18 (62%)	23 (77%)	

*Fisher's exact test.

report that they were unemployed and seeking work than siblings were (2.7%; RR, 1.90; 95%CI, 1.43–2.54).[15]

Our previous study also showed a high unemployment rate (from 5% to 9%) among CCS, with some late effects experienced after receiving stem cell transplantation or radiotherapy.[4] This is important, as Japan's national healthcare and social support systems must address these groups of CCS. High-risk CCS may need specific vocational assistance before they can apply for jobs.[16] While the Children's Cancer Association of Japan (http://www.ccaj-found.or.jp/english/) now tries to provide assistance and job training to CCS, more effective job training systems for CCS are still needed.[17]

The limitations of our study include the potential for selection bias despite the use of random sampling because response rates were relatively low, especially from listed companies (those with a stronger interest in the topic may have been more likely to respond to our survey). In fact, it is highly possible that the data presented here are an underestimate of discrimination rates. It is possible that companies who chose not to respond were more likely to have discriminatory policies. Second, our results were reliant on companies' statements. It is important to note that this study assessed formal company policy regarding this issue, rather than what actually occurs in the real workplace (which might be quite different). Thus, these results may not represent what actually occurs. Nonetheless, our report fills a gap between Japan and Western countries, and it is valuable because it is the first survey on job discrimination against CCS in Japan.

Conclusions

A health certificate was required by 33% of listed companies, 36% of unlisted companies, and none of the public offices at the time of job application. Small numbers of private companies (0.7% of listed companies and 1.0% of unlisted companies) and public offices (4%) reject applicants outright if they have a disease in their past medical history. Our study revealed that employment-related discrimination still takes place in a small

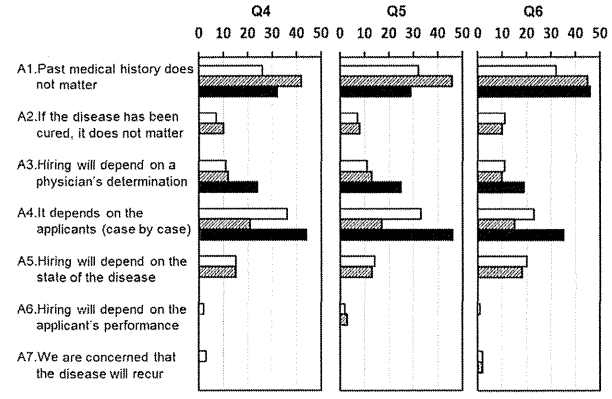

Fig. 1 Comparison of detailed answers to question (Q) 4–Q6 among three groups. Q4. How do you deal with childhood cancer in the applicant's medical history? Q5. How do you deal with some childhood disease other than cancer in the applicant's medical history? Q6. How do you deal with workers who turn out to be childhood cancer survivors after hiring? Answer (A) 1: past medical history does not matter (hiring is based on job performance). A2. If the disease has been cured, it does not matter. A3. Hiring will depend on a physician's determination. A4. It depends on the applicants (case by case). A5. Hiring will depend on the state of the disease. A6. Hiring will depend on the applicant's performance during the trial period. A7. We are concerned that the disease will recur. □, listed companies; ▨, unlisted companies; ■, public offices (general desk workers).

number of companies and even public offices. Opportunities to provide specific vocational assistance to high-risk CCS should be advocated and advanced.

Acknowledgments

Drs Asami and Ishida participated in the conception and design of the study, analysis and interpretation of data, statistical analysis and drafting the manuscript; Dr Sakamoto participated in the conception and design of the study, acquisition of data, analysis and interpretation of data and critical revision of the manuscript. Final approval was made by all co-authors. The authors indicated no potential conflicts of interest. This study was supported by a research grant (No. 18-14) from the Japanese Ministry of Health, Labour and Welfare ("Study of quality of life and prognosis in childhood cancer survivors and establishment of the long-term follow-up system" (principal investigator: Yasushi Ishida).

References

1 Schwartz C, Hobbie W, Constine L, Ruccione K. *Survivors of Childhood and Adolescent Cancer*. Springer-Verlag, Berlin, 2005.
2 Wallace H, Green D. *Late Effects of Childhood Cancer*. Arnold, London, 2004.
3 Oeffinger KC, Mertens AC, Sklar CA *et al.* Chronic health conditions in adult survivors of childhood cancer. *N. Engl. J. Med.* 2006; **355**: 1572–82.
4 Ishida Y, Honda M, Kamibeppu K *et al.* Social outcomes and quality of life (QOL) of childhood cancer survivors in Japan: a cross-sectional study on marriage, education, employment and health related QOL (SF-36). *Int. J. Hematol.* 2011; **93**: 633–44.
5 Hays DM. Adult survivors of childhood cancer. Employment and insurance issues in different age groups. *Cancer* 1993; **71**: 3306–9.
6 de Boer AG, Verbeek JH, van Dijk FJ. Adult survivors of childhood cancer and unemployment: a metaanalysis. *Cancer* 2006; **107**: 1–11.
7 Ashford NA. Low-level chemical sensitivity: implications for research and social policy. *Toxicol. Ind. Health* 1999; **15**: 421–7.
8 Hoffman B. Cancer survivors at work: a generation of progress. *CA Cancer J Clin* 2005; **55**: 271–80.
9 Hoffman B. Legal issues. In: Schwartz C, Hobbie W, Constine L, Ruccione K (eds). *Survivors of Childhood and Adolescent Cancer*. Springer-Verlag, Berlin, 2005; 305–20.
10 Ministry of Health, Labour and Welfare of Japanese Government. The employment bureau. Health certificate at the time of job application. *The Ministry of Health, Labour and Welfare*. 1993.
11 Feuerstein M, Luff GM, Harrington CB, Olsen CH. Pattern of workplace disputes in cancer survivors: a population study of ADA claims. *J. Cancer Survivorship Res. Pract.* 2007; **1**: 185–92.
12 McGrath PD, Hartigan B, Holewa H, Skarparis M. Returning to work after treatment for haematological cancer: findings from Australia. *Support. Care Cancer* 2011 (in press).
13 Hoving JL, Broekhuizen ML, Frings-Dresen MH. Return to work of breast cancer survivors: a systematic review of intervention studies. *BMC Cancer* 2009; **9**: 117–126.
14 de Boer AG, Taskila T, Ojajarvi A, van Dijk FJ, Verbeek JH. Cancer survivors and unemployment: a meta-analysis and meta-regression. *JAMA* 2009; **301**: 753–62.
15 Kirchhoff AC, Leisenring W, Krull KR *et al.* Unemployment among adult survivors of childhood cancer: a report from the childhood cancer survivor study. *Med. Care* 2010; **48**: 1015–25.
16 Barrera M, Schulte F. A group social skills intervention program for survivors of childhood brain tumors. *J. Pediatr. Psychol.* 2009; **34**: 1108–18.
17 Tamminga SJ, de Boer AGEM, Verbeek JHAM, Frings-Dresen MHW. Return-to-work interventions integrated into cancer care: a systematic review. *Occup. Environ. Med.* 2010; **67**: 639–48.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Questionnaire.

Appendix S2 Background information of the companies and public offices.

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Japanese Journal of Clinical Oncology Advance Access published March 28, 2012

JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2012
doi:10.1093/jjco/hys038

Original Article

Physician Preferences and Knowledge Regarding the Care of Childhood Cancer Survivors in Japan: A Mailed Survey of the Japanese Society of Pediatric Oncology

Yasushi Ishida[1,*], Miyako Takahashi[2], Mitsue Maru[3], Michiko Mori[4], Tara O. Henderson[5], Christopher K. Daugherty[6] and Atsushi Manabe[1]

[1]Department of Pediatrics, St Luke's International Hospital, Tokyo, [2]Department of Public Health, Dokkyo Medical University, Tochigi, [3]Department of International Nursing Development, Tokyo Medical and Dental University, Tokyo, [4]The Japanese Red Cross Akita College of Nursing, Akita, Japan, [5]Department of Pediatrics, University of Chicago Pritzker School of Medicine, Chicago, IL and [6]Department of Medicine, University of Chicago Pritzker School of Medicine, Chicago, IL, USA

*For reprints and all correspondence: Yasushi Ishida, Department of Pediatrics, St Luke's International Hospital, 9-1 Akashi-cho, Chuo-ku, Tokyo 104-8560, Japan. E-mail: yaishida@luke.or.jp

Received December 24, 2011; accepted February 27, 2012

Objective: Japanese physicians' attitudes regarding the health-care needs of young adult childhood cancer survivors (CCSs) are not well described. Thus, we examined the self-reported preferences and knowledge of pediatric oncologists and surgeons.

Methods: A mailed survey was sent to 858 physician members of the Japanese Society of Pediatric Oncology. We compared the responses of pediatric oncologists and pediatric surgeons.

Results: The pediatric oncologists' response rate was 56% (300 out of 533) and that of pediatric surgeons 32% (105 out of 325). The median age of respondents was 46 and 48 years, respectively; 79 and 84% were men. When comfort levels in caring for CCSs were described (i.e. 1 = very uncomfortable; 7 = very comfortable), the mean levels were 4.4 and 3.8 with CCSs $\leq$ 21 years, 3.6 and 3.6 with 21 years $<$ CCSs $\leq$ 30 years, and 2.8 and 3.3 with CCSs $>$ 30 years, respectively. In clinical vignette questions, 62% of the pediatric oncologists and 43% of the surgeons answered three or more questions appropriately. Pediatric surgeons reported significantly lower familiarity with long-term follow-up guidelines than pediatric oncologists. Most pediatric oncologists and many surgeons conducted truth-telling of cancer diagnosis to adult CCSs now. They thought that the most important issues are an original long-term follow-up guideline suitable for the Japanese situation and collaborations with adult-based general physicians.

Conclusions: Many Japanese pediatric oncologists are uncomfortable with caring for survivors as they age and have suboptimal knowledge regarding late effects. The change in truth-telling situation and preference for collaboration with adult-based physicians was demonstrated also in Japan.

Key words: pediatric cancer – long-term survivors – transition to adult care – pediatric oncologist – pediatric surgeon

INTRODUCTION

As a result of treatment advances, almost 80% of children diagnosed with cancer become long-term survivors (1). In Japan, there are over 50 000 childhood cancer survivors (CCSs), or approximately 1 in 700 adults between the ages of 20 and 39 years has cancer experience (2). Many of these survivors face significant life-long health risks (3) and early mortality (4). Treatment-related late effects are often clinically insidious for years or decades after the completion of cancer treatment (5,6). Promotion of healthy lifestyle behaviors and provision of regular risk-based medical care and surveillance may modify the evolution of these late effects. However, many CCSs engage in risky health behaviors and do not receive adequate risk-based medical care (7).

In 2007, the members of the International Berlin-Frankfurt-Munster (I-BFM) Early and Late Toxicity Educational Committee (ELTEC) published the Erice statement to summarize what the group considers essential for the care of survivors (8). Included in the Erice statement was the following point: 'when the survivor enters adulthood, he/she should be referred to an appropriate health care provider who coordinates long-term care' (8). Despite these recommendations, many reports suggest that effective transitions from the pediatric to the adult-focused health-care system are difficult (9–11).

One well-described barrier to risk-based long-term healthcare is that CCSs themselves are not well informed regarding their previous therapies or their potential risks for late effects (12,13). In the past study, CCSs in Japan did not always know the precise diagnosis of cancer itself (14). We recently reported that the previous treatment hospitals (where CCSs were treated for their cancer) were the most commonly visited medical facilities for the CCS group (74% for females and 64% for males) and more than half of CCSs preferred to continue visiting the previous treatment hospitals with full satisfaction in Japan (15). Recently, Henderson et al. (16) published a comprehensive report on physicians' attitudes and knowledge regarding the health-care needs of CCSs in the USA. On the other hand, there is no information in Japan regarding whether the pediatric oncologists in the previous treatment hospitals are comfortable with these adult-aged CCSs and have knowledge of the published guidelines or recommendations for late-effect surveillance (17,18). In addition, many CCSs have received long-term follow-up not only with pediatric oncologists but also with pediatric surgeons in Japan. To further understand physician attitudes and knowledge regarding the care of CCSs as they transition into adulthood in Japan, we conducted a comparative survey of pediatric oncologists and pediatric surgeons who belonged to the Japanese Society of Pediatric Oncology (JSPO).

PATIENTS AND METHODS

Participants

The approval of both St Luke's International Hospital review board and the director board in JSPO was obtained before initiation of this study. Candidate participants were selected from the 2010 JSPO Membership Directory. From the available directory, 1381 potential survey members with sufficient addresses for survey mailings were identified. Of those, we identified 1022 members specialized in pediatric hematology/oncology or pediatric surgical oncology.

Survey Mailings

A self-addressed survey was mailed to the 1022 eligible members. Through the initial mailing, 16 physicians were eliminated because of incorrect mailing addresses or because physicians were no longer clinically active, yielding a final sample of 1006 survey members. A second mailing was sent to all potential participants 4 weeks after the initial mailing.

Survey Method

The survey instrument was developed originally. Survey content and format was based on a previous study (16) regarding physician preferences and knowledge. The survey included 14 questions and used both quantitative (i.e. closed-ended questions) and qualitative (i.e. open-ended questions that asked for short responses) items (Supplementary data 1). The survey sought demographic information about participant's age, sex, practice environment, years since completion of formal training, estimated number of patients with cancer and cancer survivors seen per week in clinical practice, and information regarding prior learning with regard to childhood cancer survivorship. The definition of CCS was a patient who was at least 5 years from the completion of cancer therapy and was malignancy free.

Quantitative survey items queried participants regarding whether their practices were affiliated with a long-term follow-up program for cancer survivors and if it was routine practice to eventually refer their long-term survivors to other physicians. By using a seven-point Likert scale, physicians were asked about their comfort with caring for survivors at varying ages and were asked about their familiarity with the available monitoring guidelines for adolescent and young adult cancer survivors. Quantitative questions queried self-reported attitudes toward caring for long-term CCSs, referral pattern practices for their CCSs and their opinion of the best trajectory of care for CCSs.

The survey included a vignette of a 25-year-old woman treated at age 1 year for acute lymphoblastic leukemia whose treatment included prophylactic cranial radiation (24 Gy) and anthracycline and cyclophosphamide chemotherapy in Supplementary data 2. Three follow-up questions sought physicians' self-reports of the knowledge of health risks caused by pediatric cancers and the physicians' understanding of appropriate surveillance for these health risks on the basis of Japanese leukemia/lymphoma study group (JPLSG)'s recommendation (19).

Finally, participants were asked to give a free description whether they had anything else to add about their

Table 1. Demographic and practice characteristics of eligible study respondents

Characteristic	Pediatric oncologists ($n = 300$)		Pediatric surgeons ($n = 105$)		χ^2 (P value)
	No.	Per cent	No.	Per cent	
Age, years					
39 years of age or younger	87	30	22	21	0.180
40–47 years of age	79	27	24	23	
48–53 years of age	69	24	29	28	
54 years of age or older	58	20	28	27	
Gender					
Male	233	79	87	84	0.279
Female	63	21	17	16	
Years in practice					
14 years or shorter	82	28	26	26	0.316
15–21 years	74	25	22	22	
21–27 years	80	28	25	25	
28 years or longer	55	19	28	28	
Childhood cancer patients in outpatient clinic per week					t-test
Mean ± SD (median, range)	8.3 ± 11.8 (5.0, 0–100)		1.5 ± 2.4 (0.5, 0–10)		<0.001
Position					
Professor/Head	76	26	27	26	0.441
Associate Prof./Lecturer/Chief	103	35	42	41	
Assistant Prof./Fellow	87	30	25	24	
Resident/Doctor course	10	3	1	1	
Other (Clinics etc.)	16	6	8	8	
Living place (Post stamp)					
Hokkaido	15	5	4	4	0.001
Touhoku	21	7	4	4	
Kantou-Koushinetsu	78	26	34	32	
Toukai-Hokuriku	31[a]	10	3	3	
Kinki	51[a]	17	8	8	
Chu-Shikoku	20	7	11	10	
Kyusu-Okinawa	16	5	17[a]	16	
Unknown	68	23	24	23	
Practice environment					
Children's Hospital	24	8	12	11	0.152
University Hospital	154	52	52	50	
General Hospital	93	31	38	36	
Cancer Center	12[a]	4	0	0	
Private practice/others	15	5	3	3	
LT-FU Clinic at Hospital					
Yes	63	21	14	13	0.008
No	230	77	83	79	
Not sure	7	2	8[a]	8	

Continued

Table 1. *Continued*

Characteristic	Pediatric oncologists ($n = 300$)		Pediatric surgeons ($n = 105$)		χ^2 (P value)
	No.	Per cent	No.	Per cent	
Received Education or Learned about Late effects					
Yes	168[a]	56	21	20	<0.001
No	106	36	80[a]	77	
Not sure	24	8	3	3	
Educational experiences in the evaluation and management of childhood cancer survivors					
Government-sponsored meeting	70	23	1	1	<0.001
Symposium/Workshop	113	38	15	14	<0.001
Special Lecture	64	21	3	3	<0.001
Journal article(s)	104	35	12	11	<0.001
Book(s)	82	27	6	6	<0.001
Other	3	1	0	0	0.571

[a]Adjusted standardized residual $> +1.96$.

experiences with CCSs or the survey itself. After conducting a pilot testing with five pediatric oncologists, revisions were made. The survey questions were mailed with a cover letter to explain the purpose of the study and how to return the survey and introduce the original article (16). The survey was designed to be sealed within an envelope and mailed back to the study investigator (Y.I.) anonymously.

Statistical Analyses

All survey data were coded and entered into a database by using standard SPSS statistical software, ver. 19.0 (IBM Japan Co. Ltd, Tokyo, Japan). Descriptive statistics reported included the following: proportions, means and standard deviations, or medians and ranges. For between-group comparisons of continuous or ordinal variables, t-tests or non-parametric Wilcoxon's rank-sum tests were used as appropriate. For comparisons of categorical variables, χ^2 tests were used. As for cross-table comparisons, we used adjusted standardized residuals to evaluate the difference between the observed and expected values; the columns which give more than 1.96 of the adjusted standardized residual were considered as significant.

RESULTS

The two survey mailings were completed between October 2010 and January 2011. Four hundred fifty surveys returned; we excluded 45 sheets from non-pediatricians or non-pediatric surgeons. The total final survey response rate was 47% (405 out of 858): pediatric oncologists 56% (300 out of 533) and pediatric surgeons 32% (105 out of 325).

Demographic Data

Respondent demographic characteristics are listed in Table 1. The median age of respondents was 46 years (range: 29–78) for pediatric oncologists and 48.5 years of age (range: 29–71) for pediatric surgeons. Respondents had been in clinical practice a median of 20 years for pediatric oncologists and 22.5 years for pediatric surgeons. They saw a median of 5.0 and 0.5 CCS patients per week, respectively. A total of 19% of respondents reported that their hospital had a long-term follow-up clinic for CCSs. Pediatric surgeons had significant fewer learning experiences for care about CCSs in any type than pediatric oncologists did. The most popular educational or learning experience consisted of symposiums or workshops at the annual meeting and journal article for pediatric oncologists.

Physician Preferences in Care of CCSs and Optimal (Ideal) Care of Long-term CCSs

Physicians were asked to choose one of four responses that best summarized their current attitudes toward caring for long-term CCSs. As depicted in Table 2, 38% of the pediatric oncologists and 32% of the pediatric surgeons preferred following long-term CCSs as long as possible. There was no statistically significant difference between pediatric oncologists and pediatric surgeons.

As the optimal care of long-term CCSs, 51% of the pediatric oncologists and 42% of the pediatric surgeons answered that a CCS stays in their care until age 21 and then is referred. More pediatric surgeons answered that a CCS stays in their care anywhere between 2 and 5 years after the completion of therapy and then is referred regardless of his/her age.

Table 2. Responses to survey question

Response (select only one)	Pediatric oncologists (%)	Pediatric surgeons (%)	χ^2 (*P* value)
About current attitude toward care for long-term survivors of childhood cancer			
(a) I prefer to be their doctor as long as possible	115 (38)	34 (32)	0.211
(b) Although I enjoy some of the social aspects of their clinic visits, I prefer these patients be seen by a physician other than myself	23 (8)	14 (13)	
(c) I prefer to refer them and/or discharge them from my clinic at the first opportunity	19 (6)	7 (7)	
(d) I am willing to see them and continue to care for them in the absence of a more suitable clinician	129 (43)	50 (48)	
(e) Other	14[a] (5)	0	
About the trajectory which best summarizes your opinion of the OPTIMAL care of long-term cancer survivors			
(a) The patient stays in my care forever (throughout childhood and adulthood)	60 (21)	23 (23)	0.089
(b) The patient stays in my care anywhere between 2 and 5 years after the completion of therapy and then is referred regardless of his/her age	67 (23)	34[a] (34)	
(c) The patient stays in my care until age 21 and then is referred	148 (51)	42 (42)	
(d) Other	15 (5)	2 (2)	

[a]Adjusted standardized residual $>+1.96$.

Referral Preferences

Respondents were asked to report if it was their practice to eventually refer their long-term cancer survivors to other physicians and 31% of respondents answered yes. One-third (34%) of these respondents reported referring long-term survivors to a long-term follow-up program, 23% reported referring them to a primary care physician, 29% responded that they referred them to adult oncologists and 13% reported referring them to some other physician or healthcare provider.

Comfort Levels of Caring for CCSs

Three survey items queried participants' comfort levels with caring for pediatric cancer survivors within three different age groups (Fig. 1). Respondents were asked to report their comfort levels on a seven-point Likert scale. A score of 1 was associated with very uncomfortable; a score of 7 was associated with being very comfortable. Both pediatric oncologists and pediatric surgeons reported being most comfortable with caring for survivors who were 21 years of age or younger (mean $\pm$ SD, 4.4 $\pm$ 1.3 and 3.8 $\pm$ 1.4 level, respectively), being less comfortable with survivors older than 21 years and <30 years (3.6 $\pm$ 1.4 and 3.6 $\pm$ 1.4 level, respectively) and being most uncomfortable caring for survivors 30 years or older (2.8 $\pm$ 1.5 and 3.3 $\pm$ 1.6 level, respectively). While pediatric oncologists became less comfortable with survivors as they aged out of the pediatric age range, pediatric surgeons' comfort levels remained relatively consistent throughout all age groups.

Knowledge of Recommendations for Late Effects

Participants' knowledge of the current JPLSG recommendations for surveillance of late effects was examined through a vignette that described a 25-year-old woman treated at age 1 year for ALL with 24 Gy cranial radiation and anthracyclines (cumulative dose: 180 mg/m^2). Respondents were asked about the follow-up frequency and method, hepatitis C infection and late effects of cranial radiation (Supplementary data 2). On the basis of the JPLSG recommendations, 78% of the pediatric oncologists and 70% of the pediatric surgeons appropriately recommended the follow-up frequency and method (not significant); however, 53% of the pediatric oncologists and 38% of the pediatric surgeons appropriately recommended hepatitis C infection treatment; this difference was significant. Lastly, 92/49% of the pediatric oncologists and 77/36% of the pediatric surgeons appropriately answered the questions related with the late effects of cranial radiation (statistically significant, respectively). Overall, only 47% of the respondents (62% of the pediatric oncologists and 43% of the pediatric surgeons) answered three or more questions appropriately.

Familiarity with Long-term Follow-up Guidelines

Participants were queried about their familiarity with the available monitoring guidelines for adolescent and young adult cancer survivors by using a seven-point Likert scale. The definition of familiarity was left to the discretion of the individual respondent. A score of 1 meant a respondent was very unfamiliar, a score of 4 meant they were somewhat familiar and a score of 7 reflected that a respondent was very familiar. Overall, surveyed pediatric oncologists were significantly more familiar with the available guidelines than pediatric surgeons; the mean score ($\pm$ SD) was 2.8 ($\pm$ 1.4) for pediatric oncologists and 1.5 ($\pm$ 1.4) for pediatric surgeons ($P < 0.001$).

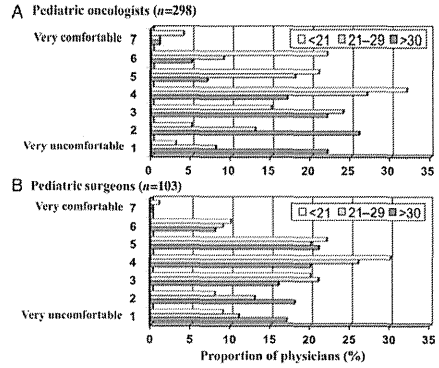

Figure 1. How comfortable are you in managing and caring for adolescent and young adult survivors of childhood cancer depending age? Respondents were asked to report their comfort levels on a seven-point Likert scale. A score of 1 was associated with very uncomfortable; a score of 7 was associated with being very comfortable. (A) Pediatric oncologists and (B) pediatric surgeons.

The Proportion of Truth-telling of Cancer Diagnosis in Adult CCSs

Seventy percent of the pediatric oncologists and 62% of the pediatric surgeons in this study reported that the proportion of truth-telling of cancer was 80–100% (Fig. 2). There was a statistical significant difference in distribution between pediatric oncologists and pediatric surgeons ($P < 0.001$).

Level of Interest in Collaborations with Adult-based Clinicians to Care for CCS

Participants were queried about their interest in collaborations with adult-based clinicians to care for CCSs by using a seven-point Likert scale. Overall, both pediatric oncologists and pediatric surgeons were much interested in collaborations with adult physicians, as the mean score ($\pm$ SD) was 3.1 ($\pm$ 1.6) for pediatric oncologists and 3.0 ($\pm$ 1.5) for pediatric surgeons.

Important Issues for a Long-term Follow-up of Adult CCSs

The most important issues for long-term follow-up for adult CCSs cited by both pediatric oncologists and pediatric surgeons were an original long-term follow-up guideline suitable for the Japanese situation and a passport (individualized clinical records) to share information (Table 3). There was no significant difference in distribution between pediatric oncologists and pediatric surgeons with regard to the most important issues. However, as for important issues for collaboration with adult-based general physicians, both pediatric oncologists and surgeons think that it is of prime importance to have enough knowledge about late effects. More pediatric oncologists than pediatric surgeons demanded sympathy with CCSs and/or their parents, and the ability to introduce organ-specific specialists.

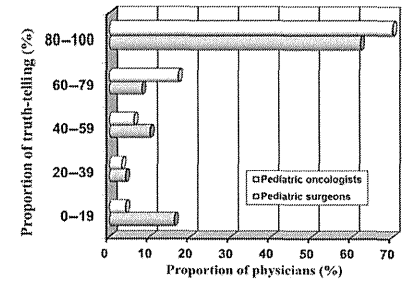

Figure 2. The proportion of truth-telling of cancer diagnosis in adult survivors with childhood cancer. The percentage of adult survivors with childhood cancer giving truth-telling of cancer diagnosis was categorized into five groups: *0–19*, *20–39*, *40–59*, *60–79* or *80–100%*.

DISCUSSION

We found that pediatric oncologists in Japan were increasingly uncomfortable with caring for adult survivors as they age, and the preference and knowledge with regard to long-term follow-up care of young-adult CCSs were different between pediatric oncologists and surgeons in Japan. To our knowledge, our survey is the first large study in Japan that examines physician attitudes toward and knowledge of risk-based healthcare, including surveillance of late effects of CCSs.

The results of our study are consistent with Henderson et al.'s study of US pediatric oncologists (16). First, as the age of CCSs increases, pediatric oncologist-reported comfort levels in caring for them decrease. However, in contrast to the Henderson study, more physicians report that they prefer to observe their CCSs for as long as possible when compared with US physicians (16). Japanese physicians have had profound attachment with their patients, which is observed in doctor–patient relationships in chronically or severely ill children as reported also in western countries (20–22). In this study, many Japanese physicians had felt uncomfortable to follow adult CCSs by themselves. Systematic efforts should be made after cancer treatment not only to empower the CCSs/families by making available age-appropriate

Table 3. Important issue when you conduct a long-term follow-up for adult childhood cancer survivors and collaboration with adult-based general physicians

Issues	Pediatric oncologists (%)	Pediatric surgeons (%)	*P* value
Long-term follow-up of adult CCSs (select only one)			
(a) An original long-term follow-up guideline suitable to Japan situation	110 (39)	50 (50)	0.494
(b) A passport (individualized clinical records) to share with information	100 (38)	30 (30)	
(c) Provide information to adult-based physician	24 (9)	7 (7)	
(d) Education and empowerment for CCSs	41 (15)	13 (13)	
(e) Other	1 (0.4)	0	
Collaboration with adult-based general physicians (select all that apply)?			
(a) Enough knowledge about late effects of CCSs	270 (90)	82 (98)	0.495
(b) Sympathy with CCSs and/or their parents	238 (79)	73 (70)	0.040
(c) Ability to introduce organ-specific specialists if needed	184 (61)	46 (44)	0.002
(d) Equipment of enough machines for further examination	35 (12)	15 (14)	0.483
(e) Experience as a pediatrician	18 (6)	12 (11)	0.068
(f) Other	3 (0.1)	0	—

information but also to provide adult-based physicians the necessary information (8). These efforts will be especially important in dealing with the sustainable transition from the pediatric to the adult-focused health-care system. A specific program will be needed to facilitate these transitions (10,23,24).

Secondly, the survey results suggest that many pediatric oncologists in Japan are not familiar with available long-term follow-up guidelines compared with US pediatric oncologists (16), mainly because there is no available long-term follow-up guideline for CCSs in Japanese today. Recently, we formulated the Japanese translated version of COG long-term follow-up guidelines in JPLSG homepage (http://www.jplsg.jp/) (19). Only 62% of the pediatric oncologists and 43% of the pediatric surgeons answered three or more of our four vignette-based questions regarding late effects on the basis of available JPLSG recommendations (19).

To achieve effective follow-up for CCSs, truth-telling is an indispensable process for CCSs (12,13). In 2007, Parsons et al. (14) reported that US physicians had a consistent pattern of telling children (65% always told the child; <1% rarely or never told), while Japanese physicians had greater variability in their patterns of telling (with only 9.5% always telling and 34.5% rarely or never telling). During these 10 years, the situation around truth-telling to children with cancer has been dramatically changed in Japan. Our study demonstrated that most pediatric oncologists conduct truth-telling of cancer diagnosis at least to adult CCSs now, and there are no barriers to facilitating effective follow-up.

The most important issues for long-term follow-up for adult CCSs cited by both pediatric oncologists and pediatric surgeons in this survey were an original long-term follow-up guideline suitable for the Japanese situation and a follow-up passport to share information. The long-term follow-up committee of JPLSG has been developing new original guidelines and a long-term follow-up diary now.

It is very interesting that most pediatric oncologists and pediatric surgeons demand not only enough knowledge about late effects of CCSs but also 'sympathy' with CCSs and/or their parents from adult-based general physicians for the purpose of collaboration. There were a lot of opinions to list 'sympathetic ability' as an indispensable nature to succeed transition though semi-structured interviews of the pediatricians in long-term follow-up (25). To our knowledge, many CCSs who were once introduced to an adult department returned to the pediatric department again because of the reasons: 'an adult-based physician is cold' or 'he/she doesn't listen to my story enough', and many CCSs had a sense of hesitation in consulting the adult-based physician.

This study has important strengths. First, this study is based on a national study including not only pediatric oncologists but also pediatric surgeons involved in pediatric oncology practice in JSPO. We can compare between pediatric oncologists and pediatric surgeons with regard to their preference and knowledge about adult CCSs. Secondly, this study revealed for the first time the change in the truth-telling situation in Japan and the preference for collaboration with adult-based physicians to care for adult CCSs.

There are, however, some limitations to our study. First, the response rates were not satisfactory especially for pediatric surgeons. These results may be subject to a response bias (i.e. those with a stronger interest in the topic may have been more likely to have responded to our survey). Conversely, there was no statistically significant difference in the gender or geographic location of responders compared with non-responders, age and time in practice of non-responders by the available JSPO member's information. Secondly, the

results were entirely based on pediatric oncologists' self-report of comfort levels with caring for and transitioning care for CCSs. Thus, these results cannot necessarily be relied on to represent what occurs in actual pediatric oncologist clinical practice. In addition, these results cannot be relied on to represent the experiences of other physicians who may be involved in caring for long-term CCSs (e.g. primary care physicians). Given the limitations, it is important that additional studies be undertaken to explore physician attitudes and knowledge outside the cancer center-based pediatric oncology specialty to include physicians in adult oncology as well as in primary care, including pediatrics, internal medicine and family medicine. Lastly, it must be highlighted that the current JPLSG recommendations, on which our clinical vignette questions were created, are based on limited data and, in many cases, expert opinion.

In conclusion, our study suggests that pediatric oncologists are increasingly uncomfortable with caring for survivors as they age and have suboptimal knowledge regarding the current recommendations for late effects. Preference and knowledge with regard to long-term follow-up care of young-adult CCSs are different between pediatric oncologists and pediatric surgeons in Japan. Findings from this study should provide a foundation for additional research and possible targeted interventions that hope to improve physician knowledge.

Authors' contributions

Conception and design: Y.I., M.T. and M.Ma.; financial support: Y.I., M.Mo. and A.M.; administrative support: Y.I.; provision of study materials or patients: Y.I. and A.M.; collection and assembly of data: Y.I.; data analysis and interpretation: Y.I., M.T., M.Ma., T.O.H. and C.K.D.; manuscript writing: Y.I., M.T., T.O.H. and A.M.; final approval of manuscript: Y.I., M.T., M.Ma., M.Mo., T.O.H., C.K.D. and A.M.

Supplementary data

Supplementary data are available at http://www.jjco.oxfordjournals.org.

Acknowledgements

We express our deep appreciation to all members of the Japanese Society of Pediatric Oncology (JSPO) who participated in this survey. We thank Dr Junich Hara (President of JSPO) for permission of this survey, Kayo Ichikawa for excellent secretarial assistance and Kazumi Ishida for kindly preparing data.

Funding

This work was supported by research grants 'A comprehensive support for families having children with cancer' and 'A study on the cooperation of nurse practitioners with a comprehensive range of health-care workers engaged in cancer therapy, such as certified oncologists and cancer pharmacists, to improve the QOL of cancer patients by promoting home care' from Japanese Ministry of Health, Labor and Welfare.

Conflict of interest statement

None declared.

References

1. Schwartz C, Hobbie W, Constine L, Ruccione K. *Survivors of Childhood and Adolescent Cancer*. Berlin: Springer-Verlag 2005.
2. Maeda M. Late effects of childhood cancer: life-threatening issues. *J Nippon Med Sch* 2008;75:320–4.
3. Hudson MM, Mulrooney DA, Bowers DC, et al. High-risk populations identified in Childhood Cancer Survivor Study investigations: implications for risk-based surveillance. *J Clin Oncol* 2009;27:2405–14.
4. Armstrong GT, Liu Q, Yasui Y, et al. Late mortality among 5-year survivors of childhood cancer: a summary from the Childhood Cancer Survivor Study. *J Clin Oncol* 2009;27:2328–38.
5. Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med* 2006;355:1572–82.
6. Diller L, Chow EJ, Gurney JG, et al. Chronic disease in the Childhood Cancer Survivor Study cohort: a review of published findings. *J Clin Oncol* 2009;27:2339–55.
7. Nathan PC, Ford JS, Henderson TO, et al. Health behaviors, medical care, and interventions to promote healthy living in the Childhood Cancer Survivor Study cohort. *J Clin Oncol* 2009;27:2363–73.
8. Haupt R, Spinetta JJ, Ban I, et al. Long term survivors of childhood cancer: cure and care. The Erice statement. *Eur J Cancer* 2007;43:1778–80.
9. Oeffinger KC, Eshelman DA. Transition issues. In: Schwartz C, Hobbie W, Constine L, Ruccione K, editors. *Survivors of Childhood and Adolescent Cancer*. Berlin: Springer-Verlag 2005;333–43.
10. Henderson TO, Friedman DL, Meadows AT. Childhood cancer survivors: transition to adult-focused risk-based care. *Pediatrics* 2010;126:129–36.
11. Ginsberg JP, Hobbie WL, Carlson CA, Meadows AT. Delivering long-term follow-up care to pediatric cancer survivors: transitional care issues. *Pediatr Blood Cancer* 2006;46:169–73.
12. Oeffinger KC, Wallace WH. Barriers to follow-up care of survivors in the United States and the United Kingdom. *Pediatr Blood Cancer* 2006;46:135–42.
13. Kadan-Lottick NS, Robison LL, Gurney JG, et al. Childhood cancer survivors' knowledge about their past diagnosis and treatment: Childhood Cancer Survivor Study. *J Am Med Assoc* 2002;287:1832–9.
14. Parsons SK, Saiki-Craighill S, Mayer DK, et al. Telling children and adolescents about their cancer diagnosis: cross-cultural comparisons between pediatric oncologists in the US and Japan. *Psychooncology* 2007;16:60–8.
15. Ishida Y, Ozono S, Maeda N, et al. Medical visits of childhood cancer survivors in Japan: a cross-sectional survey. *Pediatr Int* 2011;53:291–9.
16. Henderson TO, Hlubocky FJ, Wroblewski KE, Diller L, Daugherty CK. Physician preferences and knowledge gaps regarding the care of childhood cancer survivors: a mailed survey of pediatric oncologists. *J Clin Oncol* 2010;28:878–83.
17. Mertens AC, Cotter KL, Foster BM, et al. Improving health care for adult survivors of childhood cancer: recommendations from a delphi panel of health policy experts. *Health Policy* 2004;69:169–78.
18. Zebrack BJ, Eshelman DA, Hudson MM, et al. Health care for childhood cancer survivors: insights and perspectives from a Delphi

panel of young adult survivors of childhood cancer. *Cancer* 2004;100:843–50.
19. *The homepage of Japanese leukemia/lymphoma study group (JPLSG)*, Nagoya, 2010.
20. Britto MT, DeVellis RF, Hornung RW, DeFriese GH, Atherton HD, Slap GB. Health care preferences and priorities of adolescents with chronic illnesses. *Pediatrics* 2004;114:1272–80.
21. Scal P, Ireland M. Addressing transition to adult health care for adolescents with special health care needs. *Pediatrics* 2005;115:1607–12.
22. Cohen SY, Wamboldt FS. The parent–physician relationship in pediatric asthma care. *J Pediatr Psychol* 2000;25:69–77.
23. Lotstein DS, Ghandour R, Cash A, McGuire E, Strickland B, Newacheck P. Planning for health care transitions: results from the 2005–2006 National Survey of Children With Special Health Care Needs. *Pediatrics* 2009;123:e145–52.
24. McDonagh JE. Growing up and moving on: transition from pediatric to adult care. *Pediatr Transplant* 2005;9:364–72.
25. Takahashi M. Collaboration between pediatricians and primary care physicians regarding long term follow-up of adult childhood cancer survivors—Interviews with Japanese pediatricians. Annual Report of Research project in the Ministry of Health, Labour and Welfare 'A comprehensive support for families having children with cancer', 2011;102–16.

PEDIATRICS INTERNATIONAL Official Journal of the Japan Pediatric Society
Pediatrics International (2011) **53**, 694–700 doi: 10.1111/j.1442-200X.2011.03355.x

Original Article

Intellectual development after treatment in children with acute leukemia and brain tumor

Shizuka Watanabe,[1,2,4] Yuriko Azami,[3] Miwa Ozawa,[1] Takahiro Kamiya,[1] Daisuke Hasegawa,[1] Chitose Ogawa,[1] Yasushi Ishida,[1] Ryota Hosoya,[1] Junko Kizu[4] and Atsushi Manabe[1]

Departments of [1]Pediatrics, [2]Pharmacy, and [3]Clinical Psychology, St Luke's International Hospital, and [4]Department of Practical Pharmacy, Faculty of Pharmacy, Keio University, Tokyo, Japan

Abstract ***Background***: The influence of central nervous system (CNS)-directed chemotherapy on intelligence remains controversial. In this study, we investigated the influence of treatment on intellectual development in acute lymphoblastic leukemia (ALL) and brain tumor patients undergoing CNS-directed treatments.

Methods: Among patients treated in the Department of Pediatrics, St Luke's International Hospital between April 2000 and March 2009, the subjects were 38 patients with ALL or brain tumors who underwent regular Wechsler intelligence tests.

Results: The subjects consisted of 26 patients with ALL and 12 with brain tumors. Prophylactic cranial irradiation was not performed in patients with ALL, whereas it was done for all those with brain tumor. In patients with ALL, the IQ 1 year later was not changed from the start of treatment. In those with brain tumors, the verbal IQ 1 year later was significantly lower than that at the start of treatment. In patients with ALL, intelligence tests were performed 3 years after the start of treatment and there were no marked changes between the two time-points ($n = 11$). In those with a brain tumor, intellectual functions further decreased after the completion of treatment to as late as 5 years after the initiation of treatment ($n = 7$).

Conclusions: There is no intellectual impairment in any patient with ALL at post-treatment follow-up 3 years after the start of treatment, while intelligence is serially reduced in brain tumor patients. An innovative intervention may be needed for this group of patients.

Key words acute lymphoblastic leukemia, brain tumor, children, late effects, neurocognitive impairment.

Recently, the cure rate of childhood cancer has improved. However, treatment- or primary-disease-related complications persisting over a long period and late complications appearing after a specific interval following the completion of treatment have been reported. As childhood cancer develops in the process of physical/mental development, not only the disease but also treatment may influence such development, differing from adult cancer. Furthermore, survival may be prolonged after the completion of treatment. Therefore, the prognosis and quality of life depend on the presence or absence of late complications after the completion of primary disease treatment. It is important to examine the influence of late complications related to childhood cancer treatment.

In the treatment of acute lymphoblastic leukemia (ALL), which is the most common malignancy in children, combination regimens with anticancer agents and their doses have changed with recent advances in treatment methods. In particular, the number of patients for whom cranial irradiation therapy (CRT) is indicated has markedly decreased. As ALL may invade the central nervous system (CNS), CRT was performed to prevent leukemia of the CNS and improved the cure rate of ALL.[1] However, late effects, such as disturbance of the CNS and growth disorders, appeared after irradiation, as well as the occurrence of brain tumor[2] and Moyamoya disease,[3] raising an issue.[4,5] Instead of this procedure, high-dose chemotherapy with methotrexate (MTX) or cytarabine (Ara-C) and the intrathecal administration of these agents were employed. Concerning the influence of high-dose chemotherapy, some studies indicated that chemotherapy alone reduced intelligence,[6,7] whereas others emphasized that chemotherapy alone did not have such an influence,[8,9] and no consensus has been reached.

In our hospital, intelligence tests for all patients with malignancy in the early phase of treatment have been conducted since 2000 to evaluate intellectual development. Since September 2006, post-treatment examination has also been performed in a prospective manner. In this study, we investigated the influence on intellectual development based on the results of intelligence tests at the start of treatment, 1 year after diagnosis, and on post-treatment follow up in patients with ALL. We previously examined the short-term influence on intelligence from the start until the completion of treatment in patients with ALL, and reported a significant increase in the intelligence level after treatment completion, suggesting that there is no influence of childhood cancer treatment on intelligence immediately after the completion of treatment.[10] On the other hand, CRT is still combined with chemotherapy in many patients with brain tumors, differing from those with ALL. In this study, we reviewed the influence on intellectual development based on test results from regular post-treatment follow up in ALL and brain tumor patients.

Correspondence: Atsushi Manabe, MD, Department of Pediatrics, St Luke's International Hospital, 9-1 Akashi-cho, Chuo-ku, Tokyo 104-8560, Japan. Email: manabe-luke@umin.ac.jp

Received 30 November 2010; revised 11 January 2011; accepted 7 February 2011.

Methods

Patients

Among patients treated in the Department of Pediatrics, St Luke's International Hospital between April 2000 and March 2009, the subjects were 38 patients with ALL or brain tumors who underwent intelligence tests.

The Wechsler Preschool and Primary Scale of Intelligence (WPPSI),[11] Wechsler Intelligence Scale for Children-Third Edition (WISC-III),[12] or Wechsler Adult Intelligence Scale-Revised (WAIS-R)[13] intelligence tests were employed in accordance with the subjects' growth and age. However, we excluded patients showing infiltration of the CNS at the initial consultation and those with Down syndrome.

Concerning treatment, 25 of the 26 patients with ALL had no irradiation, and received an intrathecal administration of MTX, Ara-C and steroids. In the remaining patient, total body irradiation (TBI) at 12 Gy instead of cranial irradiation was performed as pretreatment for transplantation. ALL patients were treated according to protocol L99-15 and L04-16 of the Tokyo Children's Cancer Study Group (TCCSG).[14] All brain tumor patients underwent irradiation at 24 to 50 Gy without high-dose chemotherapy with MTX or Ara-C. Chemotherapy for patients with germ cell tumor included ifosfamide, carboplatin and etoposide from three to eight cycles. Chemotherapy for patients with medulloblastoma included cyclophosphamide, cisplatin, etoposide, vincristine and intrathecal MTX, whereas chemotherapy for a child with pilocytic astrocytoma consisted of ifosfamide, etoposide, cisplatin and vincristine.

Collection of patient data

For the survey, we analyzed the sex, age, date of diagnosis, dates of intelligence tests at the start of treatment, at the completion of inpatient treatment, and on post-treatment follow up, intelligence test results, treatment regimens, and the presence or absence of CRT based on medical records.

The protocol of this study was approved by the Study Review Board of St Luke's International Hospital and the Ethics Review Board of Keio University.

Neuropsychological tests

For Wechsler's intelligence tests, including the WPPSI, WISC-III, and WAIS-*R* tests, intellectual functions were evaluated using the deviation IQ. This parameter reflects the relative position in each age group; in establishing this parameter, IQ scores in a population of the same age were standardized so that the mean and standard deviation were 100 and 15, respectively.

The verbal IQ (VIQ) to assess verbal knowledge/thinking power, performance IQ (PIQ) to assess the information-processing capacity, including visual cognition and motor performance, and full IQ (FIQ) were determined. The VIQ was calculated based on knowledge, similarities, calculation, word, and comprehension scores. The PIQ was calculated based on picture completion, digit symbol, picture arrangement, block design, and combination scores. The FIQ was calculated based on the results of these 10 downstream tests.

Table 1 Patient backgrounds

	All ($n = 26$)	Brain tumor ($n = 12$)
Sex (male/female)	12/14	7/5
Age at diagnosis (years)	7.3 (4.8–15.2)[†]	8.4 (5.1–19.2)
Total dose of HD-MTX (g/m^2)	6–20[‡]	NA
Total dose of HD-Ara-C (g/m^2)	16–124	NA
Frequency of intrathecal MTX chemotherapy (times)	10–17	2–5
Cranial irradiation therapy (Gy)	0[§]	24–50
Presence or absence of shunt (patients)	NA	1
Interval from diagnosis until the date of intelligence tests at the start of treatment (days)	42 (5–153)	87 (30–161)
Interval from diagnosis until the date of intelligence tests 1 year after diagnosis (days)	381 (216–427)	384 (146–489)
Interval from diagnosis until the date of first follow-up intelligence tests after the completion of treatment (days)	1125 (871–1839)	827 (514–1320)
Interval from diagnosis until the date of second follow-up intelligence tests after the completion of treatment (days)	NA	1276 (1127–1659)
Interval from diagnosis until the date of third follow-up intelligence tests after the completion of treatment (days)	NA	1934 (1528–2339)

[†]Median (range). [‡]Range. [§]One patient received 12 Gy of total body irradiation as a part of conditioning treatment before transplantation.
HD-Ara-C, high-dose chemotherapy with cytarabine; HD-MTX, high-dose chemotherapy with methotrexate; MTX, methotrexate; NA, not applicable.

Statistical analysis

For statistical analysis, Wilcoxon's signed-rank test and the Friedman test were performed. We employed SPSS 16.0 J for Windows Base System software (SPSS, Tokyo, Japan). $P < 0.05$ was regarded as significant.

Results

Study patients

The patient backgrounds are shown in Table 1. The subjects consisted of 26 with ALL and 12 with brain tumors (seven with germ cell tumors, four with medulloblastoma, and one with pilocytic astrocytoma). The median ages at diagnosis in the former and latter were 7.3 (range: 4.8–15.2 years) and 8.4 (range: 5.1–19.2 years) years, respectively. Because Wechsler's intelligence test is applicable only for older children, patients who were younger than 4.8 years were not included in this study.

Time-points of IQ examinations are shown in Table 1. In patients with ALL, it was performed twice in all the 26 patients and thrice in 11 patients whereas in those with brain tumor it was done twice in all 11, thrice in seven, four times in three, and five times in two.

Changes in intelligence from the start until the completion of treatment

We investigated the VIQ, PIQ, and FIQ at the start and completion of treatment in 26 patients with ALL and 12 with brain tumors using Wilcoxon's signed-rank test. No patient with ALL showed decrease in IQ at completion in comparison with the start of treatment. In all patients with ALL, the IQ values increased at the completion of treatment, although there were no significant differences (VIQ: $P = 0.445$; PIQ: $P = 0.073$; FIQ: $P = 0.087$, Fig. 1). In brain tumor patients, the VIQ at completion was significantly lower than at the start of treatment ($P = 0.033$). Both the PIQ and FIQ at completion were lower than at the start of treatment (PIQ: $P = 0.239$; FIQ: $P = 0.455$), although individual differences were more marked than those in the VIQ (Fig. 2).

Changes in intelligence from the start of treatment until post-treatment follow up

Next, we assessed the changes of IQ at three time-points using the Friedman test. In patients with ALL, the change was not significant in VIQ or PIQ (VIQ: $P = 0.32$; PIQ: $P = 0.695$), however, FIQ increased significantly ($P = 0.03$) (Fig. 3). In patients with brain tumor, we also analyzed at three time-points. The result was that there was no statistically significant change in VIQ, PIQ, or FIQ (VIQ: $P = 0.065$; PIQ: $P = 0.957$; FIQ: $P = 0.311$) (Fig. 4).

Prognosis for patients

All the patients with ALL are alive at a median of 4.2 years (0.5–8.7 years) after diagnosis. Two patients with germ cell tumor died: one patient died 4 years after diagnosis, probably due to adrenal insufficiency and the other patient died 4.5 years after diagnosis after she developed secondary brain tumor consisting of glioblastoma and astrocytoma.[15] It was possible that the decline of IQ was related with secondary brain tumor. The other 10 patients with brain tumor are alive at a median of 2.3 years (0.5–8.9 years) after diagnosis.

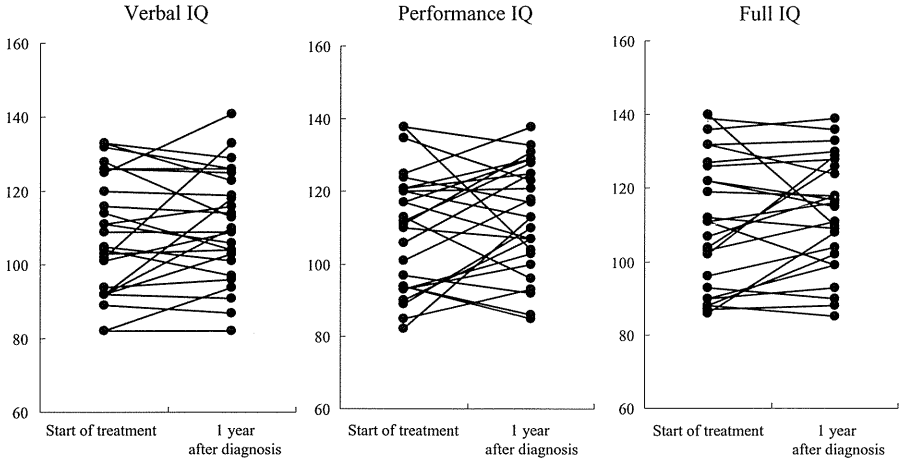

Fig. 1 Changes in acute lymphoblastic leukemia patients' intelligence from diagnosis until 1 year later.

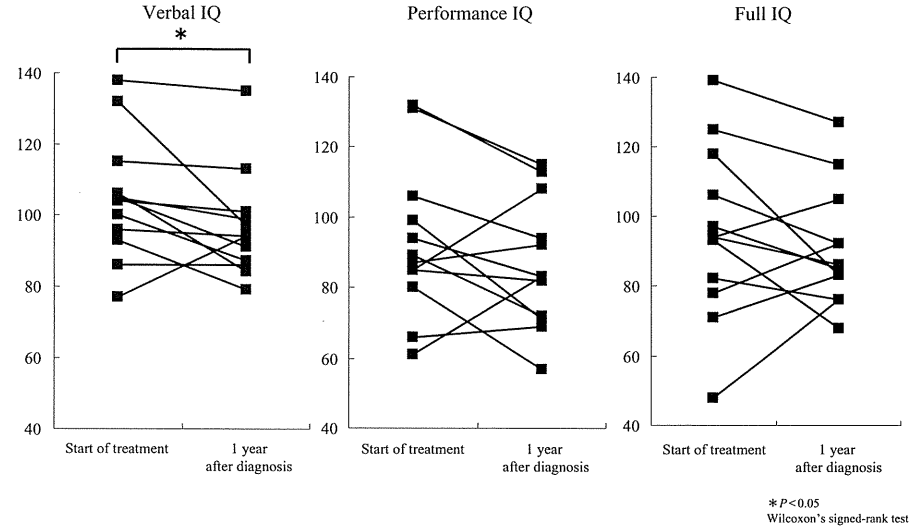

Fig. 2 Changes in brain tumor patients' intelligence from diagnosis until 1 year later.

Discussion

Previously, CRT was performed in all patients regardless of the risk of CNS involvement, but many studies have reported the influence of CRT on intelligence. CRT may be the most important factor involved in intellectual disturbance.[16] Based on this, CRT, as a strategy to prevent ALL involving the CNS, has been switched to chemotherapy. Currently, irradiation is indicated for high-risk patients alone. In fact, the recent protocol of a previous study at St Jude Children's Research Hospital was prepared so that no patient underwent irradiation.[17] However, the influence of chemotherapy on intelligence was not fully assessed. Several studies have indicated the reduction of intelligence in the absence of CRT.[6,7] Thus, the influence of chemotherapy remains controversial.

In this study, there was no reduction of intelligence from the start until 1 year later in any patient with ALL. This was similar to the results regarding IQ 1 year after diagnosis published by Copeland *et al.*[8] However, several studies have reported that intellectual disturbance serially became more marked after onset.[18–20] Therefore, we also serially examined intelligence on follow up after the completion of treatment. The results suggest that ALL treatment does not influence intelligence, even 3 years after the start of treatment; however, a longer follow up is needed to confirm this result.

Harila *et al.*[20] compared intelligence among ALL patients undergoing CRT, those receiving chemotherapy alone, and controls. In the CRT group, the VIQ and PIQ were lower than in the control group. The comprehension score was significantly lower than the control group. In the chemotherapy group, the VIQ was lower than the control group. In particular, the information, digit symbol, and similarity scores were significantly lower than in the control group. In our survey, there was no significant decrease in any parameters. The reason for discrepancy between Harila's study and ours is unclear. It should be noted that the first time-point of Harila's study was the completion of therapy, whereas that of our study was soon after diagnosis.

Our analysis of data using the Friedman test showed increase in FIQ ($P = 0.03$) in patients with ALL. This increase was difficult to explain. At present, we interpret it as that decrease in FIQ was not observed, rather than increase in FIQ was observed. A longer follow up will clarify this point.

Patients with a brain tumor showed a significant decrease in the VIQ as early as 1 year after the start of treatment, that is,

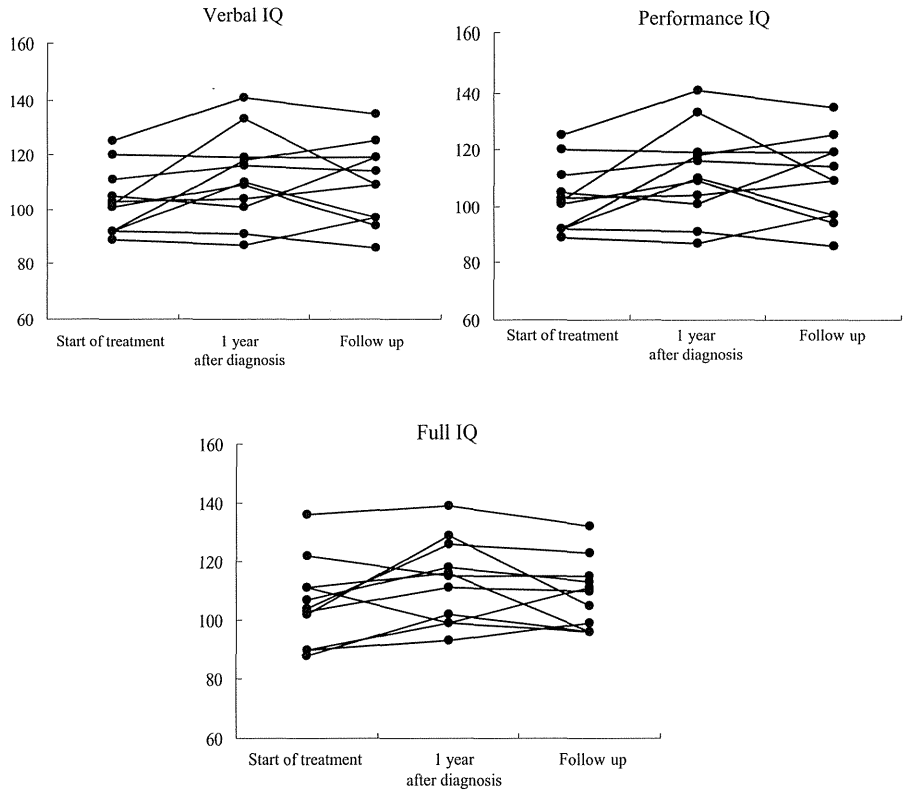

Fig. 3 Changes in acute lymphoblastic leukemia patients' intelligence until post-treatment follow up.

completion of treatment. Post-treatment follow up revealed a further decrease in IQ. Palmer *et al.*[21] also indicated a decrease in IQ within 1 year after diagnosis. Mulhern *et al.*[22] reviewed the literature and indicated that irradiation of the brain adversely affected neurocognitive function in children with brain tumor, especially at a younger age.

Rutkowski *et al.*[23] conducted a clinical trial using chemotherapy alone with intensive intraventricular methotrexate for children with medulloblastoma and found that it resulted in an excellent survival rate without serious impairment of IQ. Although the long-term effect of innovative modality needs to be confirmed, it should encourage a long trial.

In conclusion, our study employing regular intelligence testing indicates that patients with ALL who are treated without cranial irradiation may not experience a decrease in IQ. It also suggests that treatment without irradiation for children with a brain tumor is urgently needed.

Acknowledgments

We wish to thank all the pediatricians and nurses who participated in the treatment and follow up of the patients in this study. This study was supported in part by a grant from the Ministry of Health, Labour and Welfare.

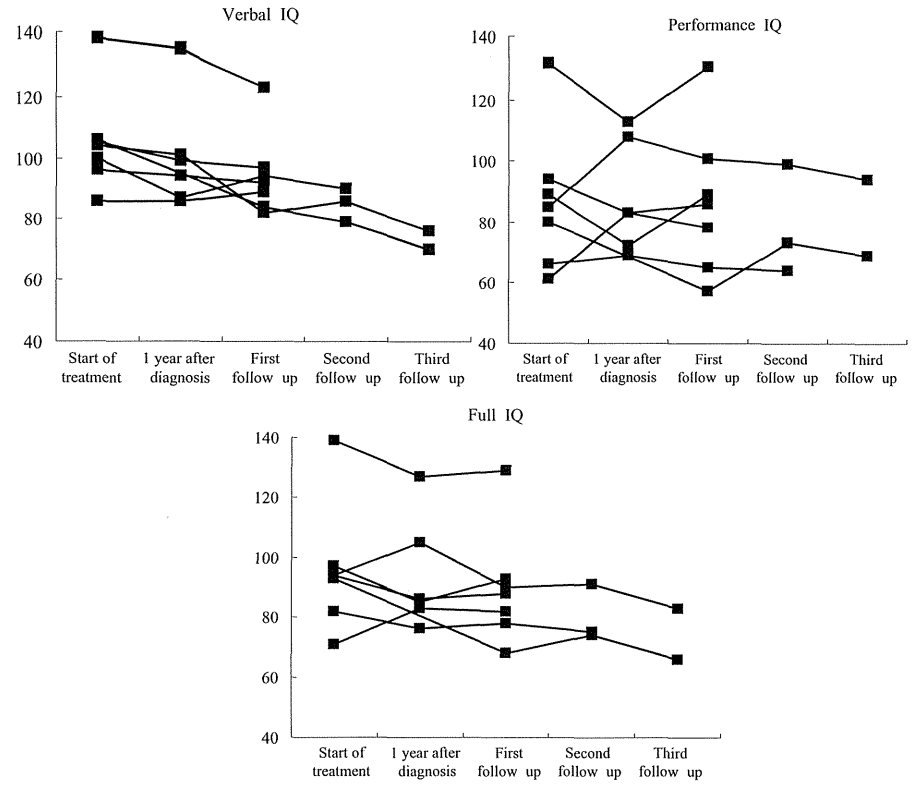

Fig. 4 Changes in brain tumor patients' intelligence until post-treatment follow up.

References

1 Pui CH, Robison L, Look AT. Acute lymphoblastic leukaemia. *Lancet* 2008; **371**: 1030–43.
2 Oeffinger KC, Mertens AC, Skalar CA *et al.* Chronic health conditions in adult survivors of childhood caner. *N. Engl. J. Med.* 2006; **355**: 1572–82.
3 Kikuchi A, Maeda M, Hanada R *et al.* Moyamoya syndrome following childhood acute lymphoblastic leukemia. *Pediatr. Blood Cancer.* 2007; **48**: 268–72.
4 Campbell LK, Scaduco M, Sharp W *et al.* A meta-analysis of the neurocognitive sequelae of treatment for childhood acute lymphocytic leukemia. *Pediatr. Blood Cancer* 2007; **49**: 65–73.
5 Gaynon PS, Trigg ME, Heerema NA *et al.* Children's Cancer Group trials in childhood acute lymphoblastic leukemia: 1983–1995. *Leukemia* 2000; **14**: 2223–33.
6 Ochs J, Mulhern R, Fairclough D *et al.* Comparison of neuropsychologic functioning and clinical indicators of neurotoxicity in long-term survivors of childhood leukemia given cranial radiation or parenteral methotrexate: A prospective study. *J. Clin. Oncol.* 1991; **9**: 145–51.
7 Mulhern RK, Fairclough D, Ochs J. A prospective comparison of neuropsychologic performance of children surviving leukemia who received 18-Gy, 24-Gy, or no cranial irradiation. *J. Clin. Oncol.* 1991; **9**: 1348–56.
8 Copeland DR, Dowell RE Jr, Fletcher JM *et al.* Neuropsychological test performance of pediatric cancer patients at diagnosis and one year later. *J. Pediatr. Psychol.* 1988; **13**: 183–96.
9 Copeland DR, Moore BD 3rd, Francis DJ, Jaffe N, Culbert SJ. Neuropsychologic effects of chemotherapy on children with cancer: A longitudinal study. *J. Clin. Oncol.* 1996; **14**: 2826–35.
10 Watanabe S, Azami Y, Manabe A *et al.* Neuropsychologic effects of the treatment of the children with cancer. *Jpn. J. Pediatr. Oncol.* 2008; **45**: 143–9 (in Japanese).

11 Wechsler D. *Wechsler Preschool and Primary Intelligence Scales for Children, Revised.* The Psychological Corporation, New York, NY, 1974.
12 Wechsler D. *Wechsler Intelligence Scale for Children, III. Revised.* The Psychological Corporation, New York, NY, 1991.
13 Wechsler D. *Wechsler Adult Intelligence Scales, Revised.* The Psychological Corporation, New York, NY, 1981.
14 Manabe A, Ohara A, Hasegawa D *et al.* Significance of the complete clearance of peripheral blast after 7 days of prednisolone treatment in children with acute lymphoblastic leukemia: The Tokyo Children's Cancer Study Group Study L99-15. *Haematologica* 2008; **93**: 1155–60.
15 Makidono A, Kobayashi N, Saida Y, Manabe A, Kawamori J, Suzuki K. Metachronous gliomas following cranial irradiation for mixed germ cell tumors. *Childs Nerv. Syst.* 2009; **25**: 713–8.
16 Meadows AT, Gordon J, Massari DJ, Littman P, Fergusson J, Moss K. Declines in IQ scores and cognitive dysfunctions in children with acute lymphoblastic leukemia treated with cranial irradiation. *Lancet* 1981; **2**: 1015–8.
17 Pui CH, Campana D, Pei D *et al.* Treating childhood acute lymphoblastic leukemia without cranial irradiation. *N. Engl. J. Med.* 2009; **360**: 2730–41.
18 Jankovic M, Brouwers P, Valsecchi MG *et al.* Association of 1800cGy cranial irradiation with intellectual function in children with acute lymphoblastic leukemia. *Lancet* 1994; **344**: 224–7.
19 Kato M, Azuma E, Ido M *et al.* Ten-year survey of the intellectual deficits in children with acute lymphoblastic leukemia receiving chemotherapy. *Med. Pediatr. Oncol.* 1993; **21**: 435–40.
20 Harila MJ, Winqvist S, Lanning M, Bloigu R, Harila-Saari AH. Progressive neurocognitive impairment in young adult survivors of childhood acute lymphoblastic leukemia. *Pediatr. Blood Cancer* 2009; **53**: 156–61.
21 Palmer SL, Gajjar A, Reddick WE *et al.* Predicting intellectual outcome among children treated with 35-40 Gy craniospinal irradiation for medulloblastoma. *Neuropsychology* 2003; **17**: 548–55.
22 Mulhern RK, Merchant TE, Gajjar A, Reddick WE, Kuu LE. Late neurocognitive sequelae in survivors of brain tumors in childhood. *Lancet Oncol.* 2004; **5**: 399–408.
23 Rutkowski S, Bode U, Deinlein F *et al.* Treatment of early childhood medulloblastoma by postoperative chemotherapy alone. *N. Engl. J. Med.* 2005; **352**: 978–86.

小児がん経験者の晩期合併症の予測は可能か

—聖路加国際病院小児科の経験—

石田也寸志*，渡辺　静，小澤　美和，米川　聡子，小川千登世，長谷川大輔，細谷　要介，
吉原　宏樹，真部　淳，森本　克，西村　鼎三，細谷　亮太

聖路加国際病院小児科

Can we predict the late effects of childhood cancer survivors?—St. Luke's experience

Yasushi Ishida, Shizuka Watanabe, Miwa Ozawa, Satoko Yonekawa, Chitose Ogawa, Daisuke Hasegawa, Yosuke Hosoya, Hiroki Yoshihara, Atsushi Manabe, Tsuyoshi Morimoto, Kozo Nishimura, Ryota Hosoya

St. Luke's International Hospital, Department of Pediatrics

Abstract

We evaluated whether the five-level follow-up (FU) classification proposed by the Japanese Pediatric Leukemia and Lymphoma Study Group (JPLSG) long-term FU committee can predict the incidence of late effects in the childhood cancer survivors. <Methods> Using a retrospective cohort design, all childhood cancer survivors in the pediatric department of St. Luke's International Hospital between 1972 and 2011 were retrospectively assigned an FU level intensity at the end of treatment. We evaluated the odds ratios (ORs) for late effects at the last observation using uni-variate and logistic regression analyses. <Results> We analyzed 300 cases from 388 survival cases up unitl March 31, 2011, excluding 88 cases because an FU level judgment was impossible. As for hematological cancers: level 3=41%, 4=37%, brain tumors: level 4=100%, solid tumors: level 2=25%, level 3=44%, LCH: level 1=62%, bone and soft tissue tumors were level 3=36%, 4=25%, 5=40%. The cumulated incidence of late effects: level 1 survivors were 0%, level 2 was 15%, level 3 was 37%, level 4 was 72%, level 5 was 100%, respectively. The logistic regression analysis showed that a brain tumor (OR: 65.4), a solid tumor (OR: 3.45), a bone or soft tissue tumor (OR: 10.4), age 26 years or older at the last observation (OR: 6.75), CPM>5 g/m^2 (OR: 5.64), and an allogeneic hematopoietic stem cell transplantation (OR: 10.9) were independent risk factors for late effects. <Conclusion> The JPLSG 5-FU level classification at the end of treatment are useful in the prediction for late effects, and FU plan can be made on a risk by utilizing this classification.

Key words: ???

要　旨

JPLSG長期フォローアップ（FU）委員会の5段階のFUレベルが，晩期合併症発症の予想に役立つかどうか検証した．【対象と方法】研究デザインはレトロスペクティブコホート研究で，対象は1972年から2011年に当院小児科で診療した小児がん症例で治療を終了しているものである．治療終了時FUレベルと最終観察日の晩期合併症について単変量とロジスティック解析を行いオッズ比（OR）を求めた．【結果】2011年3月31日の時生存388例で，FUレベル判定不能88例を除き，残り300例を解析した．血液がんではレベル3=41%，4=37%，脳腫瘍はレベル4=100%，固形腫瘍はレベル2=25%，レベル3=44%，LCHはレベル1=62%，骨軟部腫瘍はレベル3=36%，4=25%，5=40%であった．晩期合併症は，レベル1：0%，レベル2：15%，レベル3：37%，レベル4：72%，レベル5：100%で，ロジスティク解析では，脳腫瘍（OR: 65.4），固形腫瘍（OR: 3.45），骨軟部腫瘍（OR: 10.4），最終観察年齢26歳以上（OR: 6.75），CPM>5 g/m^2（OR: 5.64），同種造血細胞移植（OR: 10.9）が晩期合併症の独立したリスク因子であった．【結語】治療終了時の5段階のFUレベル評価は晩期合併症の予測に有用であり，この分類を活用することによりリスクに基づいたFU計画が可能である．

キーワード：小児がん経験者，晩期合併症，予測，フォローアップレベル，リスク

I　はじめに

小児がんの治療成績の進歩は顕著であり，現在では小児がん患児の70%以上が治癒するようになったが，成人がんとは違い身体的・精神的に成長途上に発病するため，疾患のみの影響だけではなく治療の影響を強く受けると考えられている[1]．北米CCSS（Childhood Cancer Survivor Study）研究では，経時的な身体的な晩期合併症の累積割合が分析された[2]．それによると身体的な晩期合併症のうち，少なくとも1つの軽度以上の障害は62.3%，医療行為を必要とする重症な障害は27.5%の小児がん経験者でみられ，2つ以上複数の晩期合併症は37.6%でみられた．身体的晩期合併症の30年の累積発症率は軽度以上の障害で73.4%，重症な障害では42.4%にも達し観察期間でプラトーになることはなかった．このことから治療終了後5年経過した時点で晩期合併症がない場合であっても長期フォローアップ（FU）は必須であることが裏付けられた[2]．

著者らは，これまでに青年期から成人期を迎えた本邦の小児がん経験者の晩期合併症とQOLの実態を調査した[3,4]．診断時年齢は経験者では約8歳で，調査時年齢は約23歳であった．原疾患では，造血器腫瘍が129例を占め，固形腫瘍では，神経芽腫11例，脳腫瘍と骨腫瘍が10例ずつであった．治療としては，化学療法98%，放射線60%，手術38%，造血幹細胞移植25%であった[3]．医師記載情報による何らかの晩期合併症は女性50%，男性64%で認められ，内分泌障害，低身長，骨筋肉系，肝機能障害，皮膚・脱毛などが多く認められた[4]．

以上のように，本邦でも欧米の報告[2,5]同様に晩期合併症はまれではないことが知られるようになってきた[6]が，晩期合併症は小児がん経験者すべてに均一なリスクがあるわけではない[7]．リスクに応じてFUの強度を工夫することが，小児がん経験者や家族の心身の負担を減らし，医療経済的にも重要と考えられる．JPLSG長期フォローアップ委員会では，晩期合併症発症のリスクを評価するために表1のような5段階のフォローアップレベルを提案している[8]．

本研究では，この提案されたFUレベルが，過去のコホート症例において晩期合併症をアウトカムとして評価したリスク予想に妥当性を持つかどうか検証するために，FUレベルとアウトカム頻度の相関，個人特性（診断時年齢や性別）とアウトカムとの関連，アウトカムに影響が強い治療因子を検討した．

2011年7月15日受付，2011年9月1日受理
* 別刷請求先：〒104-8560 東京都中央区明石町9-1
聖路加国際病院小児科　石田也寸志
E-mail: yaishida@luke.or.jp

表1　JPLSG提案のフォローアップレベル

レベル	分類	対象者	ケアプロバイダー	コンタクト頻度
1	一般的健康管理群	外科手術のみ（頭頚部，胸腹部，四肢）	健康診断医	1/年*
2	経過観察群	低リスクの化学療法を受けた患者 DOX 250 mg/m^{2}未満，かつ CPM 5 g/m^{2}未満，かつ CDDP 300 mg/m^{2}未満，かつ IFO 45 g/m^{2}未満，かつ DEX使用歴なし	家庭医，または長期フォローアップ外来	1/年*
3	標準的FU群	高リスクの化学療法を受けた患者 250 mg/m^{2}以上，あるいは CPM 5 g/m^{2}以上，あるいは CDDP 300 mg/m^{2}以上，あるいは IFO 45 g/m^{2}以上，あるいは DEX使用歴ありを受けた患者 20 Gy未満頭蓋照射患者 自家移植併用大量化学療法（放射線放射線含まない） 頭蓋以外の放射線照射患者	長期フォローアップ外来	1/年*
4	強化FU群	20 Gy以上頭蓋放射線照射患者 同種造血細胞移植を受けた患者 再発治療を受けた患者 遺伝性腫瘍症候群のある患者 脳腫瘍患者 自家血液細胞移植併用大量化学療法（放射線照射を含む）を受けた患者	長期フォローアップ外来	1/年*
5A	要介入群（重篤な病態・全身的問題）	臓器機能障害による社会参加不能患者 臓器機能低下に伴う要生活制限患者 晩期合併症の症状のある患者 晩期合併症に対して治療が必要な患者	長期フォローアップ外来	1/3–6ヶ月
5B	要介入群（疾患特異的な問題）	臓器特異的な外科的治療後のフォローが必要な患者 （例；骨肉腫後の人工関節，網膜芽細胞腫後の義眼）	専門診療科外来	必要時

DOX: Doxorubicin, CPM: Cyclophosphamide, CDDP: Cisplatin, IFO: Ifosfamidem, DEX: Dexamethasone
*；年1回の受診では，受診日を誕生月にするなどの工夫が望まれる．
**；乳児期にanthracyclineの投与を受けた経験者については，強い心機能低下を合併することが知られており，特に注意を要する．

II　対象と方法

研究デザインは，1病院のレトロスペクティブコホート研究である．

1. 研究対象

発症時年齢が20歳未満で，1972年から2011年に当院小児科に診療録のある小児がん患者のうち，以下の基準を満たすものとした．

1）当院で診断・治療を行ったものまたは長期フォロー

アップ目的で当科に紹介されたもの，2）2011年3月31日までに治療を終了しているもの，除外基準としては，1）セカンドオピニオンのみで受診した症例，

2）2011年3月31日までに死亡が確認されたもの，3）日常生活・合併症に影響する原病と関係のない基礎疾患を有するもの，とした．

2. 検討した項目

1）個人特性：診断時年齢，性別，基礎疾患，2）診断名，病期，再発（有無），3）治療：プロトコール名，手術（有無），放射線（頭蓋照射，それ以外，線量），化学療法（Doxorubicine: DOX, Cyclophospamide: CPM, Cis-platin: CDDP, Ifospamide: IFO, Dexamethasone: DEX—3分割カテゴリカルデータ），造血細胞移植（有無，種類），4）転帰（無病生存，有病生存，死亡），5）カルテで確認された最終観察日．

各項目について，表1に示したJPLSG長期FU委員会提案のFUレベル分類に従い，治療終了時のFUレベルを判定した．

3. アウトカム

FUレベルを調査した担当者とは別に外来担当主治医がアウトカムを判断し分類した．治療終了の時点でのアウトカムとしては，1）晩期合併症は，①特になし，②何らかの症状あり（軽度の臨床症状があるか臨床検査所見の異常のみで治療を要さないもの），③治療の必要あり（何らかの治療・薬物補充を必要とするもの），④不明の4分類で，前記②と③を晩期合併症ありと判定した．2）日常生活については，①特に問題なし，②社会参加困難（日常生活に支障はないが社会生活上何らかの問題を有するもの），③要生活制限（身の回りの日常生活に支障があるもの），④不明の4分類である．また晩期合併症があったものについては，その種類を調査した．

4. 統計学的な方法

性別，現在の年齢，初発時年齢，原疾患（診断病名），化学療法の内容・放射線療法の種類と線量・造血細胞移植の種類（自家・同種）・再発について，晩期合併症をアウトカムとしてオッズ比を算出した．それらのうち，$p<0.2$ のものを説明変数としたロジスティク回帰分析を行い，ステップワイズ変数減少法を用いて独立したリスク因子を解析した．すべての統計解析は，SPSS Statistics Ver. 19 日本語版（日本IBM社，東京）を用いた．

III 結　果

図1に対象症例から解析症例を選択した過程を示した．

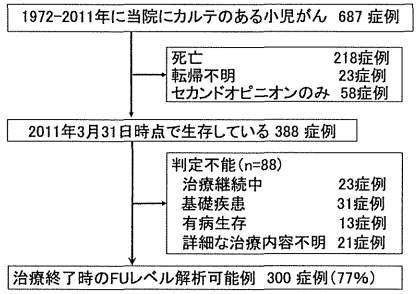

図1　解析症例の選択プロセス

1972–2011年に当院にカルテのある小児がんは687症例であり，死亡例・転帰不明例，セカンドオピニオンのみで受診した症例を除き，2011年3月31日の時点で生存が確認された症例は388例であった．FUレベルが判定不能とした症例は88例であった．その中で判定不能とした基礎疾患としてはダウン症候群12症例，診断時から内分泌障害が存在した3症例，診断時に認められた広汎性発達障害11症例，診断時に認められた内部障害4症例（内訳は心室中隔欠損，QT延長，てんかん，WAGR症候群），その他低出生体重児のため発達遅延を認めた1症例であった．最終的に今回は，300症例（生存例の77%）を対象として以下の解析を行った．

表2に男女別に解析対象疾患の背景を示した．診断時平均年齢は，男女とも約6歳で，解析時の平均年齢は約18歳であった．原疾患の診断名は，急性リンパ芽球性白血病（ALL）が153例で約半数を占め，血液がんが合計で215例（72%）を占めた．脳腫瘍は15例（5%），固形腫瘍は合計48例（16%），ランゲルハンス細胞組織球症（LCH）が13例（4%），骨軟部組織肉腫が20例（7%）であった．病期はIII期あるいは高危険群が約40%を占め，31例（10%）に再発を認めた．治療としては，94例（32%）で手術が行われ，頭蓋照射は59例（23%），頭蓋以外への照射は39例（15%）で施行されていた．化学療法としては，DOXは184/252（73%），CPMは173/248（70%），CDDPは32/253（13%），IFOは23/255（9%），DEXは71/230（31%）で使用されていた．造血細胞移植としては，自家移植が14例（5%），同種移植が34例（11%）施行されていた．疾患や治療の背景に大きな性差はなかった．

表3に原疾患別の治療終了時のFUレベル分類を示した．血液がんでは，レベル3=41%，4=37%，脳腫瘍はレベル4=100%，固形腫瘍はレベル2=25%，レベル3=44%，LCHはレベル1=62%，骨軟部腫瘍はレベル3=36%，4=25%，5=40%であった．図2に治療終了時のFUレベル別に晩期

表2　解析対象症例の背景

	男性（n=164）	女性（n=137）	合計（n=300）
診断時の年齢（平均±標準偏差（中央値））	5.9±4.8（5.0）	6.2±5.1（4.5）	6.0±5.0（5.0）
解析時の年齢#（平均±標準偏差（中央値））	17.5±8.7（17.0）	18.2±9.3（18.0）	17.8±9.0（18.0）
診断名			
急性リンパ芽球性白血病（ALL）	87	66	153
急性骨髄性白血病（AML）	14	10	24
骨髄異形成症候群（MDS）	3	2	5
慢性骨髄性白血病（CML）	2	2	5
非ホジキンリンパ腫（NHL）	10	8	18
脳腫瘍	10	5	15
神経芽腫	10	12	22
網膜芽細胞腫	1	1	2
肝芽腫	0	2	2
Wilms腫瘍	4	6	10
胚細胞腫瘍	4	2	6
その他固形腫瘍	0	6	6
ランゲルハンス細胞組織球症（LCH）	5	8	13
骨肉腫	7	1	8
Ewing肉腫	3	3	5
横紋筋肉腫	4	3	7
病期			
I期あるいは標準危険群	42	40	82
II期あるいは中間危険群	15	23	38
III期あるいは高危険群	67	50	117
IV期あるいは超危険群（HEX）	40	23	63
再発あり *	39	2	31
手術あり *	49/160	45/134	94/294
頭蓋照射なし *	106/140	96/122	202/262
照射線量<20 Gy	16	17	33
照射線量≧20 Gy	18	9	27
頭蓋以外への照射なし *	118/140	108/125	226/265
照射あり	22	17	39
化学療法 *			
Doxorubicin < 250 mg/m^2	74/129	64/123	138/252
≧250 mg/m^2	24/129	22/123	46/252
Cyclophosphamide < 5 g/m^2	57/125	53/123	110/248
≧5 g/m^2	37/125	26/123	63/248
Cisplatin < 300 mg/m^2	3/131	5/122	8/253
≧300 mg/m^2	15/131	9/122	24/253
Ifosfamide < 45 g/m^2	012/131	6/255	18/255
≧45 g/m^2	5/131	0/124	5/255
Dexamethasone使用あり	36/121	35/109	71/230
造血細胞移植なし *	130	119	249/297
自家移植	10	4	14
同種移植	23	11	34

2011年3月31日現在　* に関しては全例調査ができていない項目である（分母に調査症例数を示した）

合併症の有無（症状ありと治療が必要）と社会生活上の問題の有無（生活制限ありと社会参加困難）の割合を示した．レベル1では，晩期合併症は0%であり，レベル2では晩期合併症15%（症状あり13%，治療必要2%），レベル3では晩期合併症37%（症状あり22%，治療必要16%），レベル4では晩期合併症72%（症状あり31%，治療必要41%），レベル5では晩期合併症100%（症状あり55%，治療必要45%）であった．社会生活上の問題に関しては，レベル1と2では0%，レベル3では問題11%（生活制限あり5%，社会生活困難6%），レベル4では問題36%（生活制限あり

表3　原疾患別のフォローアップレベル

	フォローアップレベル				
	1	2	3	4	5
血液がん合計	2（1%）	39（19%）	85（41%）	76（37%）	3（1%）
急性リンパ芽球性白血病（ALL）	0	34（22%）	67（44%）	49（32%）	3（2%）
急性骨髄性白血病（AML）	0	3（12%）	10（42%）	11（46%）	0
骨髄異形成症候群（MDS）	1	1（20%）	0	4（80%）	0
慢性骨髄性白血病（CML）	0	0	0	4（100%）	0
非ホジキンリンパ腫（NHL）	1（6%）	1（6%）	8（44%）	8（44%）	0
脳腫瘍	0	0	0	15（100）	0
固形腫瘍合計	9（19%）	12（25%）	21（44%）	6（13%）	0
神経芽腫	4（18%）	7（32%）	8（36%）	3（14%）	0
網膜芽細胞腫	0	1（50%）	0	1（50%）	0
肝芽腫	0	1（50%）	1（50%）	0	0
Wilms 腫瘍	0	3（30%）	6（60%）	1（10%）	0
胚細胞腫瘍	2（33%）	0	3（50%）	1（17%）	0
その他固形腫瘍	3（50%）	0	3（50%）	0	0
ランゲルハンス細胞組織球症（LCH）	8（62%）	3（23%）	2（15%）	0	0
骨軟部組織腫瘍計	0	1（5%）	6（30%）	5（25%）	8（40%）
骨肉腫	0	0	2（25%）	2（25%）	4（50%）
Ewing 肉腫	0	1（20%）	1（20%）	1（20%）	2（40%）
横紋筋肉腫	0	0	3（43%）	2（29%）	2（29%）
合　計	18（6%）	55（18%）	114（38%）	102（34%）	11（4%）

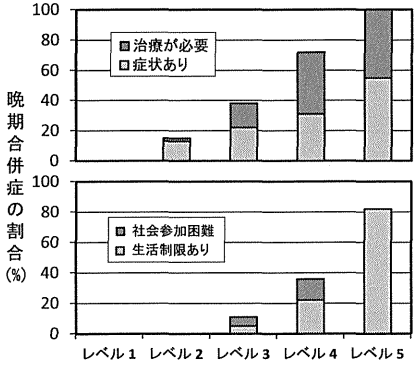

図2　治療終了時 FU レベルと晩期合併症

22%，社会生活困難 14%），レベル 5 では問題 82%（生活制限あり 82%）であった．

表 4 に晩期合併症（症状ありまたは治療必要）に対する各々のリスク因子について単変量解析でオッズ比（OR）を示した．有意のリスク因子は，診断時 12 歳以上（OR: 2.95），最終観察年齢 26 歳以上（OR: 3.46），治療した年が最近のもの（OR: 0.36 と 0.43），原発疾患としては脳腫瘍（OR: 20.2），骨軟部腫瘍（OR: 7.79），病期 II 期（OR: 2.50），III 期（OR: 7.78），IV 期（OR: 7.40），CPM 5 g/m² 以上（OR: 3.80），CDDP 300 mg/m² 以上（OR: 5.66），IFO 使用（OR: 5.75），頭蓋照射 20 Gy 以上（OR: 3.23），頭蓋以外の照射あり（OR: 9.12），造血細胞移植：自家（OR: 5.09）同種（OR: 3.71），外科手術（OR: 2.34），再発あり（OR: 3.44）であった．

晩期合併症に影響の強い独立したリスク因子を探索するため，ロジッスティク回帰分析を行った結果を表 5 に示した．最終的なモデルで有意のリスク因子と考えられたのは，脳腫瘍（OR: 65.4），固形腫瘍（OR: 3.45），骨軟部腫瘍（OR: 10.4），最終観察年齢 26 歳以上（OR: 6.75），CPM>5 g/m²（OR: 5.64），同種造血細胞移植（OR: 10.9）であった．

IV　考　察

今回のレトロスペクティブな聖路加国際病院小児科症例の解析において，JPLSG の提唱した FU レベルに従って対象症例を 5 段階に分類した．FU レベル分類別の全体症例分布は，表 3 に見られたようにレベル 1: 6%，レベル 2: 18%，レベル 3: 38%，レベル 4: 34%，レベル 5: 4% と正規分布に近い分布を示し，理想的と考えられた．また最も重要な知見は，図 2 に示したように晩期合併症や社会生活の問題点を有する割合と極めて良い相関が認められ，この治療終了時 FU レベル分類が，治療終了後の晩期合併症や社会生活

表4　晩期合併症のリスクに関する単変量解析

リスク候補因子	カテゴリー	症例数	晩期合併症割合	オッズ比（95%CI）	p 値
診断時年齢	< 1 歳	36	50%	1.71（0.80–3.65）	0.162
	1–5 歳	114	37%	1	
	6–11 歳	69	39%	1.10（0.60–2.04）	0.757
	12 歳以降	49	63%	2.95（1.47–5.91）	0.002
性別	男性	144	47%	1	
	女性	124	41%	0.80（0.49–1.30）	0.375
最終観察年齢	15 歳以下	111	34%	1	
	16–25 歳	100	44%	1.51（0.87–2.63）	0.147
	26 歳以上	56	64%	3.46（1.77–6.78）	< 0.001
治療年	1990 年以前	53	62%	1	
	1990–99 年	94	37%	0.36（0.18–0.72）	0.004
	2000 年以降	121	41%	0.43（0.22–0.83）	0.012
原発腫瘍	血液がん	179	39%	1	
	脳腫瘍	14	93%	20.2（12.59–158）	0.004
	固形腫瘍	44	43%	1.18（0.61–2.31）	0.621
	LCH	13	8%	0.13（0.02–1.02）	0.052
	骨軟部腫瘍	18	83%	7.79（2.20–27.9）	0.002
病期・リスク	I 期・標準危険	75	16%	1	0.065
	II 期・中間危険	31	32%	2.50（0.94–6.62）	< 0.001
	III 期・高危険	109	60%	7.76（3.75–16.0）	< 0.001
	IV 期・超危険	53	59%	7.40（3.24–16.9）	< 0.001
Cyclophospamide	なし	68	32%	1	
	< 5 g/m²	101	31%	0.93（0.48–1.79）	0.820
	≧ 5 g/m²	62	65%	3.80（1.84–7.87）	< 0.001
Doxorubicin	なし	66	42%	1	
	< 250 mg/m²	125	43%	0.81（0.44–1.50）	0.506
	≧ 250 mg/m²	45	56%	1.51（0.70–3.24）	0.290
Cisplatin	なし	205	35%	1	
	< 300 mg/m²	7	71%	4.72（0.89–24.9）	0.068
	≧ 300 mg/m²	24	75%	5.66（2.15–14.9）	< 0.001
Ifosphamide	なし	216	36%	1	
	< 45 g/m²	17	77%	5.75（1.81–18.2）	0.003
	≧ 45 g/m²	5	100%	N/A	
Dexamethason	なし	175	41%	1	
	あり	73	42%	1.03（0.57–1.85）	0.924
頭蓋照射	なし	183	38%	1	
	< 20 Gy	31	42%	1.17（0.54–2.53）	0.697
	≧ 20 Gy	24	67%	3.23（1.31–7.94）	0.011
他部位照射	なし	209	35%	1	
	あり	36	83%	9.12（3.63–22.9）	< 0.001
	不明	19	58%	2.51（0.97–6.51）	0.059
造血細胞移植	なし	230	40%	1	
	自家移植	13	77%	5.09（1.36–19.0）	0.015
	同種移植	24	71%	3.71（1.48–9.30）	0.005
外科手術	なし	177	37%	1	
	あり	86	58%	2.34（1.38–3.95）	0.002
再発	なし	244	41%	1	
	あり	24	71%	3.44（1.38–8.60）	0.008

N/A: not available

表5　晩期合併症のリスクに関する多変量解析（ロジスティック回帰）

リスク因子	カテゴリー	n	多変量オッズ比（95%CI）	p値
原発腫瘍	血液がん	153	Reference	
	脳腫瘍	12	65.4（6.78–631）	<0.001
	固形腫瘍	40	3.45（1.22–9.74）	0.019
	LCH	12	0.70（0.07–6.86）	0.757
	骨軟部腫瘍	14	10.4（2.34–46.5）	0.002
最終観察年齢	15歳以下	99	Reference	
	16–25歳	87	2.18（0.99–4.83）	0.054
	26歳以上	45	6.75（2.70–17.1）	<0.001
CPM	なし	68	Reference	
	<5 g/m	101	1.77（0.69–4.54）	0.234
	≧5 g/m	62	5.64（2.00–15.9）	0.001
造血細胞移植	なし	207	Reference	
	自家移植	9	1.92（0.31–12.0）	0.438
	同種移植	15	10.9（2.44–48.9）	0.002
再発	なし	221	Reference	
	あり	10	4.63（0.83–25.8）	0.080

* Hosmer-Lemeshow（χ^2乗値=2.701，p=0.952）

の問題の予測に役立つことが示されたことである．

多変量解析で最終モデルに独立したリスク因子として残ったのは，ORの高い順に，脳腫瘍（65.4），同種造血細胞移植（10.9），骨軟部腫瘍（10.4），最終観察年齢26歳以上（6.75），CPM>5 g/m^2（5.64），固形腫瘍（3.45）であった．興味深かったのは，単変量解析では自家移植の方が同種移植よりもオッズ比が高かったものの，多変量解析では自家移植は有意のリスク因子ではなくなり，同種移植のみがリスク因子として残ったこと，CDDPやIFOなどの抗がん剤，放射線照射や手術，病期・リスク分類，再発などが，最終モデルでは有意なリスク因子としては残らなかったことである．今後はこの結果を参考にして，レベル分けの基準を見直し，もう少しレベル分けをシンプルにすることも可能になるかもしれない．

これまで報告されている小児がん経験者のFUレベル評価としては，表6に示したイギリスのもの[9,10]が最も有名である．Eiserらは，198人の小児がん経験者を分類し，レベル1が8人，レベル2が97人，レベル3は93人であり，7人で分類の不一致症例が認められたと報告している[10]．またEdgarらは2009年のEuropean Symposium on Late Complications after Childhood Cancer（ESLCCC）で575人の分類を試み，レベル1が94人（16%），レベル2が257人（45%），レベル3は224人（39%）であり，平均11.5年後の晩期合併症の累積割合は，レベル1で3%，レベル2で51%，レベル3で93%と報告した[11]．この割合は本研究のJPLSGのレベル分けの結果と類似した結果ではあるが，イギリスの3-レベル分類は内容がシンプルすぎて（しかし逆に評価者の一致率が高いというメリットもある），ほとんどがレベル2か3であり晩期合併症の推定に関してきめ細やかな対応が困難であることが問題と考えられる．またフィラデルフィア小児病院が提唱しているthe intensity of treatment rating scale 2.0（ITR-2）[12]は，原疾患と病期で主に分類しており，分類方法の評価者による一致率などを検討しているが，著者らの調べた限りでまだその晩期合併症予測の有用性を検討した報告は見られず，アウトカムとの関連に関しては妥当性に問題が残る．また本研究の結果では前述したように，多変量解析の結果で病期・リスク分類の有意性が消失し，原疾患の種類と実際に受けた治療内容の方が重要なリスク因子になる可能性が示唆され，原疾患と病期の組み合わせによるITR-2分類よりもJPLSGのレベル分けの方が予測に役立つ可能性が高いと考えられた．

本研究の一番の限界は，解析対象が1施設の現在無病生存している比較的少数例の研究であり，ALLが50%を占め固形腫瘍が少なかったことなど選択バイアスがありえるため結果の一般化が可能かどうか不明な点である．次にレトロスペクティブなコホート研究であり，23例の転帰不明例，21例の詳細な治療内容が不明の症例が存在したことである．またプロスペクティブに計画された研究ではなかったため，Common Terminology Criteria for Adverse Events（CTCAE）を用いて詳細な晩期合併症のgrade分類ができなかった．最後に，解析対象年齢の中央値が17.8歳（診断後約12年）と観察期間が比較的短かったため，今回のJPLSGレベル分けで診断後20年30年経過後の長期の晩期合併症の予測が可能かどうかが不明な点である．

本研究には以上の様な限界はあるものの，長期フォローアップ委員会提案の治療終了時5段階FUレベル評価の妥当性を初めて検証し，この分類が晩期合併症発症の予測に有用であり，これを活用することによりリスクに基づいたFU計画が可能なことが示唆された意義は大きいと考えている．今後多施設共同研究を行い，結果の妥当性と一般化可能性を検証していく予定である．

表6　既報告のフォローアップレベル分け

	3-Level（英国）	ITR-2（フィラデルフィア）	JPLSG
レベル1	外科手術のみ 低リスク化学療法 例）Wilms腫瘍のStage 1/2 LCH（SS型） 胚細胞腫（手術のみ）	外科手術のみ（脳腫瘍除く） 例）Wilms腫瘍のStage 1/2 LCH（SS型） 胚細胞腫（手術のみ） 神経芽腫（手術のみ） 網膜芽細胞腫（眼球摘出）	外科手術のみ（頭頚部，胸腹部，四肢）
レベル2	通常の化学療法 24 Gy以下の頭蓋照射 例）多くの小児がん 第一寛解期のALL	ALL（標準危険群） CML（非移植例） 脳腫瘍（単独治療法） 胚細胞腫（化学療法/放射線） 肝芽腫（非転移症例） HL（Stage 1～3，非bulk腫瘍） 神経芽腫（Stage 1/2/4S） NHL（Stage 1～3） 網膜芽細胞腫（化学療法併用） 横紋筋肉腫（Stage 1/2）	低リスク化学療法を受けた患者 DOX 250 mg/m^{2}未満，かつ CPM 5 g/m^{2}未満，かつ CDDP 300 mg/m^{2}未満，かつ IFO 45 g/m^{2}未満，かつ DEX使用歴なし
レベル3	放射線照射（24 Gy以下の頭蓋照射以外） 大量療法 例）脳腫瘍 造血細胞移植後 Stage IVの小児がん	再発プロトコール（HLとWilmsの初回再発のみ） ALL（高危険・超危険群） APL 脳腫瘍 Ewing肉腫 肝芽腫（転移症例） HL（Stage 3B/4B/高危険群） JMML（非移植例） 神経芽腫（Stage 3/4，非移植例） NHL（Group C/Stage 4） 骨肉腫 横紋筋肉腫（Stage 3/4） Wilms腫瘍（Stage 3/4）	高リスク化学療法 250 mg/m^{2}以上，あるいは CPM 5 g/m^{2}以上，あるいは CDDP 300 mg/m^{2}以上，あるいは IFO 45 g/m^{2}以上，あるいは DEX使用歴あり 20 Gy未満頭蓋照射 自家移植併用大量化学療法（放射線放射線照射患者 頭蓋以外の放射線照射患者
レベル4	—	再発プロトコール（HLとWilmsの初回再発を除く） 造血細胞移植 AML JMML—移植症例	20 Gy以上頭蓋放射線照射患者 同種造血細胞移植を受けた患者 再発治療を受けた患者 遺伝性腫瘍症候群のある患者 脳腫瘍患者 自家血液細胞移植併用大量化学療法（放射線照射を含む）を受けた患者
レベル5A	—	—	社会参加不能患者 要生活制限患者 晩期合併症の症状のある患者 晩期合併症に対して治療が必要
レベル5B	—	—	臓器特異的な外科的治療後のフォローが必要な患者（例；骨肉腫後の人工関節，網膜芽細胞腫後の義眼）
設定根拠	使われた治療法	原疾患と病期	詳細な治療内容 一部原疾患を活用

LCH: Langerhans cell histiocytosis, ALL: acute lymphoblastic leukemia, CML: chronic myeloid leukemia, HL: Hodgkin lymphoma, NHL: non-Hodgkin lymphoma, APL: acute promyelocytic leukemia, JMML: juvenile myelomonocytic leukemia, DOX: Doxorubicin, CPM: Cyclophosphamide, CDDP: Cisplatin, IFO: Ifosfamide, DEX: Dexamethasone

本研究は，平成23・24年度厚生労働科学研究費補助金（がん臨床研究事業）「小児がんの罹患数把握および晩期合併症・二次がんの実態把握のための長期フォローアップセンター構築に関する研究」（研究代表者：黒田達夫）および平成24年度厚生労働科学研究費補助金（がん臨床研究事業）「小児造血器腫瘍に対する標準治療・診断確立のための研究」（研究代表者：堀部敬三）の補助を受けた．

謝　辞

本研究のデータ収集に際して協力をいただいた聖路加国際病院小児医療センターの下平友紀恵さんと井上真紀子さんに深謝します．英文抄録の校閲に関しては，聖ルカ・ライフサイエンス研究所臨床疫学センター客員研究員のDeshpande GA先生に深謝します．

文　献

1) JPLSG 長期フォローアップ委員会監訳：小児がん経験者の長期フォローアップ．日本医学館，東京，2008.
2) Oeffinger KC, Mertens AC, Sklar CA, et al: Chronic health conditions in adult survivors of childhood cancer. N Engl J Med, 355: 1572–1582, 2006.
3) 石田也寸志，本田美里，上別府圭子，他：小児がん経験者の晩期合併症およびQOLの実態に関する横断的調査研究　第1報．日本小児科学会雑誌，114: 665–675, 2010.
4) 石田也寸志，大園秀一，本田美里，他：小児がん経験者の晩期合併症およびQOLの実態に関する横断的調査研究　第2報．日本小児科学会雑誌，114: 676–686, 2010.
5) Geenen MM, Cardous-Ubbink MC, Kremer LC, et al: Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. JAMA, 297: 2705–2715, 2007.
6) Miyoshi Y, Ohta H, Hashii Y, et al: Endocrinological analysis of 122 Japanese childhood cancer survivors in a single hospital. Endocr J, 55: 1055–1063, 2008.
7) Hudson MM, Mulrooney DA, Bowers DC, et al: High-risk populations identified in Childhood Cancer Survivor Study investigations: implications for risk-based surveillance. J Clin Oncol, 27: 2405–2414, 2009.
8) 石田也寸志：小児がん経験者の長期フォローアップ，堀部敬三（編）：小児がん診療ハンドブック　医薬ジャーナル社．大阪，2011, 46–56.
9) Wallace WH, Blacklay A, Eiser C, et al: Developing strategies for long term follow up of survivors of childhood cancer. BMJ, 323: 271–274, 2001.
10) Eiser C, Absolom K, Greenfield D, et al: Follow-up after childhood cancer: evaluation of a three-level model. Eur J Cancer, 42: 3186–3190, 2006.
11) Edgar AB, Harrison S, Kelly S-L, et al: Intensity of Long Term Follow Up for Survivors of Childhood Cancer can be Safely Determined by Therapy-based Risk-stratification, ESLCCC09. Edinburgh 2009, pp. 65.
12) Werba BE, Hobbie W, Kazak AE, et al: Classifying the intensity of pediatric cancer treatment protocols: the intensity of treatment rating scale 2.0 (ITR-2). Pediatr Blood Cancer, 48: 673–677, 2007.

論　策

小児がん経験者に対する社会的偏見の実態調査

聖路加国際病院小児科[1]，新潟県立新潟がんセンター小児科[2]
石田也寸志[1]　浅見　恵子[2]

要　旨

本邦において小児がん経験者に対する進学・就職時の学校や企業側の意向と小児がん経験者自身の経験の実態を探り，問題点を明確にすることを目的に調査を実施した．

無作為抽出した全国の高校/大学計200校，企業計200社，1975年4月～2007年3月までに新潟県立がんセンターで治療を終了し，病名告知を受けている18歳以上で同意を得られた小児がん経験者138名へアンケートを郵送して回答を回収した．回収率は，それぞれ54.5%，37%，65.2%であった．

その結果「小児がんは現在では約80%が治癒する疾患である事」は未だ学校の半数および企業の4分の3は認知していなかった．進学時には小児がん既往は特に問題とならないが，むしろ小児がん経験者及び主治医が，この事実を知らず「不利になる」と思い込んでいる可能性が高いこと，就職時も全体的には既往歴は問題にならない傾向であったが，1.8%の学校と5%の企業で不合格とすると答えたものがあり，既往歴と現病歴の違いを広く社会に啓発する必要があると考えられた．病名記載率や上司への説明率，異性との交際経験割合やハートリンク共済の認知度に関して女性の方が有意に高く，経験者本人の調査では恋愛結婚で病気のことを話していれば，特にトラブルは生じていなかった．

キーワード：小児がん，小児がん経験者，社会的偏見，進学，就労

はじめに

小児がん治療の飛躍的進歩により，治癒率はめざましく向上し，約80%が治癒し，成人となる長期生存者が年々増加し，現在では数万人に達している[1]．小児がんは身体的・精神的に成長途上に発病するため，成人のがんとは違い疾患のみの影響だけではなく治療の影響を強く受けることが予想される[2]．また治療終了後にも数十年にわたる長期の生命予後が期待され，進学・就労・結婚・出産などを含めた数多くのイベントを迎えるため自立支援を含めた長期経過観察の重要性が高まっている[3]．

しかし，このような本邦の成人に達した小児がん経験者が社会生活（学校進学，職業，結婚など）において，どのような偏見と立ち向かっているかは明らかではない．また本邦において小児がん経験者に対する進学時の学校側の姿勢や就職に関しての雇用者側の意向がどのようなものであるかに関する報告はこれまでみられない[4]．

（平成25年8月6日受付）（平成25年10月16日受理）
別刷請求先：（〒790-0024）松山市春日町83
愛媛県立中央病院小児医療センター
石田也寸志
E-mail: yaishida2009@yahoo.co.jp

今回，学校や企業側の意向と小児がん経験者自身の経験からこの点についての実態を知り，現状を把握し，問題点を明確にすることを目的にアンケート調査を実施した．

対象と方法

1）対象

学校については，全国学校協会に登録されている国公立大学177校より50校，私立大学711校より50校，国公私立高校5,395校より100校を無作為抽出した．企業に関しては，全国企業として東京証券取引場一部上場銘柄1,668社の中から業種に偏りなく100社無作為抽出し，中小企業として新潟県の資本金1,000万円以上の大中小企業でホームページを作成している企業より100社を無作為抽出した．小児がん経験者については，1977年4月～2007年3月（30年間）に新潟県立がんセンター小児科に入院し，治療を終了しかつ病名告知を受けている18歳以上の小児がん経験者138名を抽出した．

2）方法

研究方法は横断的アンケート調査で，学校は各入試課，企業は各本社総務人事課宛に，厚労省がん研究助成金研究班名でアンケート調査票を送付し，無記名で回答を依頼した．小児がん経験者に対しては，共著者の主治医から該当者にアンケートを送付し，調査研究の趣旨を説明し協力を依頼した．

3）調査内容

①学校と企業に対して：現在小児がんは約80%が治癒する病気である事を認知しているか，小児がん経験者は社会的偏見を受けている可能性はどうか，入学/入社試験健康診断書に既往歴として，小児がんの病名が記載されていたらどのように対応するか，小児がん経験者の入学/入社に対する意見をたずねた．また企業に対しては上記に加えて，入社後小児がん経験者であることが判明した場合にはどう取り扱うかをたずねた．

②小児がん経験者に対して：調査内容は表1にまとめて示した．

4）倫理的配慮

本研究は新潟県立がんセンターの倫理委員会で，平成19年10月に承認を受けた（平成19年度受付番号第33号）．アンケートは無記名とし，回答の任意性を担保し，調査用紙の返送をもって同意とみなした．

5）統計学的な方法

各項目について，アンケート集計を行い，各質問事項に対して学校と企業の比較をχ^2乗検定またはFisher検定（期待値が5未満のマスがみられた時）で有意差検定を行った．すべての統計解析は，SPSS Statistics Ver.19日本語版（日本IBM社，東京）を用いた．

結　果

（1）アンケート回収率

①学校200校中109校で54.5%，②企業200社中74社で37.0%，③小児がん経験者138名中88名で65.2%であった．

（2）学校と企業との比較（表2）

「小児がんは医学的に現在では約80%が治癒する疾患となっている」に関しては，学校（高校・大学）の38%，企業の22%が「はい」と答えていたが，有意に企業の認知度が低かった（p＝0.001）．社会的偏見を受けていると思うかどうかに関しては，いずれも70%以上が「いいえ」と答えており両者には差はなかった．

既往歴として，小児がんという病名が記載されていた時の対応としては，「既往歴は合否に関係ない」が一番多かったが，企業では「面接官や管理者の判断による」とする割合が有意に多かった．「書類審査で不合格とする」と答えた学校が2施設（1.8%），企業が4施設（5.4%）見られた．

企業側の入社後「小児がん経験者」ということが判明した時の対応に関しては，「有給休暇を認める」「敬意を表する」など肯定的・支持的な意見が多かったが，「多忙な部署」「エリートコースから外す」「同僚から特別視されることもあり得る」などの意見も見られた．

（3）小児がん経験者の背景因子（表3）

回答時の年齢は18歳から34歳（中央値24歳）で，原疾患は白血病が多く，一人暮らし，両親と同居がほぼ同数，結婚同居が15%で男女差は見られなかった．学歴は大卒・大学在学が40%，常勤勤務が50%で，病気のため就職不能は0人であったが，男性で大卒以上の割合が多かった．常勤勤務が52%を占めていたが，職業では男性で会社員や製造販売，女性で医療関係者が多かった．未婚が83%で，社会適応に困っている症例はほとんどなく，この点についても男女差は見られなかった．

A．進学時の病名記載に関して（図1と表4）

高校進学時は74人中33人（45%），専門学校進学時35人中14人（40%），大学進学時42人中13人（31%）と大きな差はなく，3～4割が病名を記載していた．表4に示したように全体には男女差はあまり見られなかったが，専門学校進学時には女性で病名記載をした割合が有意に多かった（p＝0.019）．病名を記載した人で，面接時に嫌な思いをしたと答えたのは40人中3人，合否に不利であったと考えていたのは40人中1人であった．病名記載で「いいえ」とした理由としては，「記載欄がなかった」とするものが55%と最も多かったが，「不利になると考えた」者も20%いた．その他（自由記載）としては，告知の前だったため4人，書く必要が無いと考えたため3人，完治したから，治療終了後10年以上経っているから各1人，覚えていない1人などであった．健康診断作成での主治医の意見としては，「本人にまかせた」が約半数で，記載をすすめたものはなかった．以上に関して男女差は見られなかった（データ省略）．

B．就職時に病名記載に関して（図2と表4）

病名を記載したと答えたのは29%で進学時より少なかったが，男性（13%）に比べて女性では半数が病名を記載していた（p＝0.001）．病名を記載したことで，面接時に嫌な思いをしたと答えたのは21人中2人，合否に不利であったと考えていたのは20人中3人であった．病名を知ったときの面接官の反応に関しては，「難病を克服したことに好意的」だったものが6人（30%），「治癒に対して懐疑的」が2人（10%）であったが，「全くふれられなかった」者が11人と半数以上を占めた（男女差なし）．

病名記載で「いいえ」とした理由としては，「記載欄がなかった」とするものが48%と最も多かったが，「不利になると考えた」者も30%おり進学時よりも高率であった．健康診断作成に際しての主治医の意見としては，「本人にまかせた」が44%で，記載をすすめたものはなかった．定期健診を受ける必要があることを理解

表1　小児がん経験者への質問事項

問1　回答者の背景
ア）性別　1. 男性, 2. 女性
イ）年齢　（　　）歳
ウ）診断名　（　　）
エ）生活環境　1. 一人暮らし, 2. 両親と同居中, 3. 兄弟と同居中, 4. 同棲中, 5. 結婚して相手と同居中, 6. 別居中, 7. その他
オ）結婚歴　1. 未婚, 2. 結婚, 3. 離婚, 4. 再婚
カ）最終学歴　1. 中学校卒, 2. 高校中退, 3. 高校卒, 4. 専門学校卒, 5. 短大卒, 6. 大学在学中, 7. 大学中退, 8. 大学卒, 9. 大学院卒, 10. その他
キ）職業　（　　）
ク）就職状況　1. 常勤で就職, 2. パートタイムで就職, 3. アルバイトのみ, 4. 家事手伝い, 5. 就職準備中, 6. 学生, 7. 病気のため就職不能, 8. 専業主婦, 9. その他
ケ）社会適応について　1. 全く困ったことはない, 2. 少しあるが対応できている, 3. かなり困っている, 4. 非常に困っている, 5. その他

問2　社会的偏見に関係ある事柄について
A. 進学時の病名記載
高校進学時　1. はい, 2. いいえ, 3. 無回答
専門学校進学時　1. はい, 2. いいえ, 3. 無回答
大学進学時　1. はい, 2. いいえ, 3. 無回答
(1) 病名記載で「はい」の方に
①面接で嫌な思いをされましたか？　1. はい, 2. いいえ, 3. 無回答
②合否に不利であったか？　1. はい, 2. いいえ, 3. 無回答
(2) 病名記載で「いいえ」とした理由は？
1. 記載欄がなかった, 2. 不利になると考えた, 3. その他（自由記載）
(3) 健康診断作成での主治医の意見
①病名記載をすすめた, ②病名記載はすすめなかった, ③本人にまかせた, ④その他, ⑤無回答
B. 就職時に病名記載をしましたか　1. はい, 2. いいえ, 3. 無回答
(1) 病名記載で「はい」の方に
Ⅰ　面接時に嫌な思いをされましたか？　1. はい, 2. いいえ, 3. 面接はまだ, 4. 無回答
Ⅱ　面接官の反応
①難病を克服したことに好意的, ②治癒に対して懐疑的, ③全くふれられなかった, ④無回答
Ⅲ　合否に不利であったか？　1. はい, 2. いいえ, 3. 無回答
(2) 病名記載で「いいえ」の方に
1. 記載欄がなかった, 2. 不利になると考えた, 3. その他（自由記載）
(3) 健康診断作成での主治医の意見
①病名記載をすすめた, ②病名記載はすすめなかった, ③本人にまかせた, ④その他, ⑤無回答
(4) 定期健診を受けるため，上司に小児がんであったことを話したか
1. はい, 2. いいえ, 3. 無回答
C　異性との交際経験はありますか？　1. はい, 2. いいえ, 3. 無回答
(1) 相手に既往を話しましたか？　1. はい, 2. いいえ, 3. 無回答
(2) (1) で「はい」の方に
Ⅰ　相手の方は事実を受け入れ，理解されたか　1. はい, 2. いいえ, 3. わからない
Ⅱ　病名説明により，交際を断られた経験はありますか　1. はい, 2. いいえ, 3. 無回答
(3) (1) で「いいえ」の方に　①いつか話すべきと考えている, ②過去のことなので話すつもりはない, ③その他（自由記載）
D　結婚されている方に
(1) 結婚にいたった経緯　1. 恋愛結婚　2. 見合い結婚　3. 知人の紹介. 4. その他
(2) 相手に既往を話したか 1. はい, 2. いいえ, 3. 無回答
(3) (2) で「はい」の方に（複数回答可）　1. 結婚前に話した, 2. 結婚後に話した　3. 相手の両親にも話した, 4. 相手のご家族も知っている, 5. 自分だけで話した, 6. 主治医に説明してもらった, 7. 現在，相手は何か言いますか
(4) (2) で「いいえ」の方に　1. 今後も話さない, 2. 折をみて話す, 3. 相手にのみ話す
(5) 過去の病気の説明で破談になった経験は　1. はい, 2. いいえ, 3. 無回答
E　生命保険に加入しているか？　1. はい, 2. いいえ, 3. 無回答
(1)「はい」の方に　1. 病名告知して加入, 2. 病名告知せずに加入, 3. 病気になる前から加入
(2)「いいえ」の方に　1. 病名告知により加入できなかった, 2. はじめから加入できないと思っていた, 3. 興味がない, 4. わからない, 5. 無回答
(3) ハートリンク共済をご存知ですか？　1. はい, 2. いいえ, 3. 無回答

表2　学校と企業の結果比較

	学校（n＝109）	企業（n＝74）	χ^2 または Fisher＊（p 値）
問1. 小児がんは約 80% が治癒する病気である事を知っていますか？			
1. はい	41（37.6%）	16（21.6%）	0.001
2. いいえ	58（53.2%）	58（78.4%）	
3. 無回答	10（ 9.1%）	0	
問2. 小児がん克服者は社会的偏見を受けている可能性が高いと考えられますか？			
1. はい	15（13.7%）	8（10.8%）	0.496
2. いいえ	77（70.6%）	58（78.3%）	
3. 無回答	17（15.6%）	8（10.8%）	
問3. 試験時の健康診断書に既往歴として，小児がんの病名が記載されていたらどのように対応されますか？（1つ選ぶ）			
1. 既往歴は関係なし	76（69.7%）	35（47.3%）	＜0.001
2. 面接官・管理者による	15（13.7%）	21（28.3%）	
3. 希望部署による	0	11（14.8%）	
4. 書類審査で不合格	2（ 1.8%）＊	4（ 5.4%）	
5. 健康診断書不要	12（11.0%）	0	
6. その他	4（ 3.6%）	3（ 4.0%）	
問4. 入社後，小児がん克服者であることが判明した場合にあてはまるもの全てを選んで下さい.（複数回答）			
1. がん治療という苦境を乗り越えた事に敬意を表する扱いをする		23（31.1%）	
2. 定期健診を有給休暇で認める		43（58.2%）	
3. 関係なし		6（ 8.1%）	
4. 病気の再燃が心配で多忙な部署よりはずす		13（17.6%）	
5. エリートコースより外れる事は仕方がないと考える		3（ 4.1%）	
6. 同僚より特別視される事もありうる環境である		8（10.8%）	
7. 無回答		7（ 9.5%）	

＊長期欠席者は理由によらず不合格となる

してもらうために上司に小児がんであったことを話した人は 65 名中 23 名（35%）で，女性では男性に比べ有意に多くの人が上司に話していた（p＝0.003）.

C　異性との交際経験に関して（図3と表4）

60 人（68%）の経験者が異性交際の経験を持ち，その中で相手に既往病名のことを話したのは 47 人（78%）であった．男性では 6 割，女性では 8 割が異性との交際経験があった（p＝0.036）．わからないと答えた 1 人を除いて，ほとんどが「相手の方は事実を受け入れ理解された」と答えた．しかし「病名説明により，交際を断られた経験はない」と答えたのは 44 人（94%）であった．病気の説明を相手にしていない 13 人のうち，6 人は「過去のことなので話すつもりはない」と答えていた．

D　結婚している経験者について

15 人の回答が寄せられ，全員恋愛結婚であり，全員相手に病名を話しており，14 人は結婚前に話したと答えたが，結婚後に話した人も 1 人いた．12 人は相手の両親にも話しており，8 人は相手の家族も知っていると答えた．病気の説明は自分だけで話した人が 7 人，主治医に説明してもらった人が 5 人であった．過去の病気の説明で破談になった経験があると答えた人はいなかった．なおこれらの項目において男女差は見られなかった（データ省略）.

E　生命保険に関して（図4と表4）

生命保険に加入していたのは，44 人（50%）であったが，「病名告知して加入」した人は 27 人（61%）で，「病名告知せずに加入」している人，「病気になる前から加入」している人もいた．調査時点で生命保険に加入