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ORIGINAL ARTICLE

Recent employment trend of childhood cancer survivors in Japan: a cross-sectional survey

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Abstract
Background Previous research has shown that some adult childhood cancer survivors (CCSs) have experienced employment difficulties. However, the actual employment status of CCSs in Japan has not been studied.
Participants and methods The participants were selected from the membership directory of Heart Link mutual-aid health insurance and recruited by the Childhood Cancer Patients' Network. We conducted a cross-sectional survey (a self-rated questionnaire on employment) via postal mail or an email communication with a link to an Internet website. We explored the association between the characteristics of CCSs who require disability qualification and having experienced unemployment. The adjusted odds ratios (ORs) for the factors with an outcome of interest were estimated with logistic regression analysis.
Results In total, 44 CCSs indicated that they had a disability qualification. The significant independent factors related to needing a disability qualification were late effects [OR 12.3; 95 % confidence interval (CI) 3.37–45.2], brain tumors (OR 9.55; 95 % CI 1.90–48.0), and being a high school graduate (OR 9.86; CI 2.67–36.4). The unemployment rate was 15.9 % among CCSs, excluding homemakers and students. Approximately 70 % of unemployed CCSs had some late effects; independent factors related to unemployment were late effects (OR 6.22; 95 % CI 1.80–21.40), dropping out of school (OR 8.46; 95 % CI 1.66–43.10), and brain tumors (OR 2.73; 95 % CI 0.83–8.96). Most unemployed CCSs were likely to seek work, despite their health problems.
Conclusions The unemployment rate is not high in Japan, but some CCSs need extended disability qualification. The independent factors related to unemployment were late effects and dropping out of school.

Keywords Childhood cancer survivors · Employment · Unemployment · Occupation · Social outcome · Disability

Abbreviations

CCS	Childhood cancer survivors
CCSS	The Childhood Cancer Survivor Study
OR	Odds ratio
CI	Confidence interval

Introduction

Because of advances in treatment, 70–80 % of children diagnosed with cancer become long-term survivors. In Japan, the estimated number of childhood cancer survivors (CCSs) is greater than 50,000, and we expect that at least 30,000 survivors have already reached adulthood (20 years of age or older). Although there is an increased number of CCSs, many survivors experience various health problems later in life because of the cancer and its treatment [1, 2]. In addition, these various physical problems (termed "late effects") also seem to affect CCSs' social outcomes (e.g., marriage, education, and employment, etc.), both directly and indirectly [3].

Previous research has suggested that adult CCSs experience employment difficulties [4–7]. In the previous Childhood Cancer Survivor Study (CCSS), a greater percentage of survivors reported a lack of any employment in the past 12 months (9.3 %) than their siblings did (6.7 %) [8]. Elevated risk for never having been employed was associated with failing to complete high school, young age (<4 years) at diagnosis, cranial radiation therapy of 30 Gy, and being female [9]. CCSs from all diagnostic categories were less likely to have been employed during the past 12 months than members of the sibling group; the age- and sex-adjusted likelihood of being employed was lowest among brain and bone tumor survivors [9].

Despite these findings, the actual employment status of CCSs in Japan has not been studied. In the current study, we conducted a cross-sectional survey of CCSs in Japan in order to identify their employment outcomes.

Participants and methods

Study design

We performed a cross-sectional survey (a self-rated employment questionnaire) via postal mail or email with a link to an Internet website (see Supplemental Appendix 1). The study was conducted from July until September 2012.

Participants

The first sample group was selected from 631 applications to or the membership directory of Heart Link mutual-aid health insurance in Niigata [10]. The second sample group was recruited from the Childhood Cancer Patients' Network, including the Pediatric Brain Tumor Association in Japan [11].

Survey method

The first group was sent a brochure explaining the purpose and methods of the study, and asking them to return the questionnaire directly to the Heart Link mutual-aid health insurance office by postal mail anonymously within 1 month. The second group was sent an email explaining the purpose and methods of the study, and asking them to respond to the questionnaire via an Internet website link. Informed consent was assumed if the participant returned the questionnaire.

The questionnaire consisted of 32 items, with 9 items (questions Q1–8 and Q15) that asked about the participant's basic characteristics. Through the questionnaire, we evaluated regular, routine checkups (Q9), health status and the presence of late effects (Q10–Q11), disability qualification (Q12 and 14), employment (Q13), marriage (Q16–17), and present issues found worrisome (Q18). Through Q21–Q23, we assessed job satisfaction, influence of childhood cancer experience, and sharing about the cancer diagnosis with one's employer. Q24 through Q30 assessed unemployment-related issues: reasons for unemployment, employment difficulties, worries about unemployment, major living costs, and whether participants' and/or their parents want them to work. Q31 assessed worries of student CCSs about future employment.

Ethical issues

The study was performed in accordance with the Declaration of Helsinki and approved by the ethics committee of St. Luke's International Hospital, no. 12-R046.

Statistical analyses

We performed χ^2 tests (or Fisher's exact tests for cells with expected counts of more than five) within categorical predictors. A trend test was used to rank trends of health and economic status over CCSs with late effects. We explored the association between characteristics of the CCSs who required a disability qualification (limited to the CCSs who were 18 years or older to evaluate educational achievement) and those who had experienced unemployment (excluding housewives and students). The adjusted odds ratios (ORs) for factors with an outcome of interest were estimated with logistic regression analysis. Data were analyzed with SPSS software, v. 20.0 (IBM Japan, Tokyo, Japan).

Results

A total of 240 questionnaires (217 from the first sample group and 23 from the second sample group) were collected by November 2012. The response rate was 34.4 % (217 out of 631) for the first sample group. The response rate for the second sample group could not be calculated because we only informed the web-site homepage of this research to the Childhood Cancer Patients' Network and we couldn't know the number of the CCSs who have watched the homepage. One questionnaire was excluded because the CCS did not answer the questionnaire him/herself. There were 123 male and 116 female respondents.

Demographic data

The participants' demographic characteristics are listed in Table 1. The mean age was 24.3 years (median 24; range

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Table 1 Background of the participating childhood cancer survivors

	Male (n = 123)	Female (n = 116)	χ^2 (p value)
Age at survey (years)			
20 years or younger	39 (32 %)	33 (28 %)	0.226
21–24 years	26 (21 %)	30 (26 %)	
25–29 years	35 (29 %)	23 (20 %)	
30 years or older	22 (18 %)	30 (26 %)	
Diagnosis of cancer			
Leukemia	60 (50%)	66 (57 %)	0.681
Lymphoma	15 (13 %)	8 (7 %)	
Other solid cancers	18 (15 %)	19 (16 %)	
Bone/soft tissue sarcoma	7 (6 %)	6 (5 %)	
Brain tumor	20 (17 %)	17 (15 %)	
Age at diagnosis (years)			
3 years or younger	36 (29 %)	33 (28 %)	0.341
4–7 years	32 (26 %)	25 (22 %)	
8–12 years	27 (22 %)	37 (32 %)	
13 years or older	28 (23 %)	21 (18 %)	
Treatment			
Chemotherapy	108 (88 %)	106 (91 %)	0.367
Radiation	63 (51 %)	59 (51 %)	0.956
Surgery	47 (38 %)	42 (36 %)	0.749
Stem cell transplantation	29 (24 %)	19 (16 %)	0.165
Immunotherapy	6 (4 %)	3 (3 %)	0.501[a]
Others	11 (9 %)	6 (5 %)	0.257
Regular checkup (per year)			
None	37 (30 %)	30 (26 %)	0.327
Once per several years	2 (2 %)	7 (6 %)	
Once	40 (33 %)	43 (37 %)	
Twice	20 (16 %)	12 (10 %)	
Three times	7 (6 %)	9 (8 %)	
More than four times	17 (14 %)	15 (13 %)	
Living district			
Hokkaido/Tohoku	5 (4 %)	9 (8 %)	0.516
Kanto (excepting Niigata)	48 (39 %)	38 (33 %)	
Niigata	31 (25 %)	25 (22 %)	
Tokai/Hokuriku	13 (11 %)	10 (9 %)	
Kinki	13 (11 %)	14 (12 %)	
Chu-shikoku/Kyusyu	13 (11 %)	19 (17 %)	
Education			
Junior high school	10 (8 %)	8 (7 %)	0.263[a]
High school	35 (29 %)	26 (22 %)	
College or vocational school	16 (13 %)	25 (22 %)	
University or graduate school	53 (43 %)	53 (46 %)	
Dropout	9 (7 %)	4 (3 %)	

[a] Fisher's exact test

16–42 years). While female CCSs tended to be somewhat older, this difference was not significant. More than half of the CCSs (both male and female) had suffered from hematological cancers, and approximately 15 % had suffered from brain tumors and solid cancers, respectively. The mean age at cancer diagnosis was 7.5 years (median 7; range 0–19 years). The mean age at treatment completion was 10.4 years (median 10; range 0–27 years), and this survey was conducted approximately 14 years after treatment completion. Regarding primary cancer treatment, 90 % of CCSs received multiagent chemotherapy, 51 % received radiation, 37 % underwent surgery, and 20 % received hematopoietic stem cell transplantation. There were no statistical differences between males and females for all basic characteristics. Approximately 28 % of CCSs had not had a regular checkup at the time of this survey, but 33 % had regular checkups once per year, and another 33 % had two or more regular checkups per year. There was no statistical difference between the geographic locations of males and females; a majority of the participants lived in the Kanto area, including the Niigata prefecture.

CCS characteristics

Table 2 lists the current status of different CCS characteristics according to gender. Nearly half of the CCSs reported the presence of various late effects. The most predominant late effects were endocrinological problems and short stature, which was found in both males and females. The marriage rate of females was significantly higher than that of males in the 30 years or older group. There were 17 male and 16 female unemployed CCSs; 8 of the females were housewives. The unemployment rate was 15.9 % (25 of 157), excluding homemakers and students. More than half of CCSs were in good health, and approximately 10 % were in poor or bad health. Approximately 50 % reported good or fair economic status, but male CCSs reported poor or bad economic status significantly more often than females did.

Association between CCS characteristics and late effects

The prevalence of late effects was significantly associated with multiple CCS characteristics (see Table 3). The specific cancer diagnosis was associated with different proportions of reported late effects: CCSs who had been diagnosed with a brain tumor or bone/soft tissue sarcoma reported significantly more prevalence of late effects than those with other diagnoses (76 and 67 %, respectively). With respect to cancer treatment, radiation, surgery, and stem cell transplantation were associated with a higher prevalence of late effects than other treatments (66, 61, and 77 %, respectively). Approximately 70 % of unemployed CCSs experienced some late effects compared with 44 % of employed CCSs. Finally, CCSs who had better subjective health and economic status were significantly less likely to report late effects.

Table 2 Present status of the total childhood cancer survivors

	Male (n = 123)	Female (n = 115)	χ^2 (p value)
Late effects			
Yes	60 (49 %)	52 (45 %)	0.582
Endocrinological problems	22 (18 %)	26 (22 %)	0.383
Short stature	20 (16 %)	13 (11 %)	0.258
Neurocognitive problems	10 (8 %)	7 (6 %)	0.529
Skin/hair loss	9 (7 %)	6 (5 %)	0.494
Eye problems	5 (4 %)	6 (5 %)	0.683
Hearing imparement	5 (4 %)	4 (3 %)	0.999[a]
Bone/muscle problems	4 (3 %)	2 (2 %)	0.684[a]
Psychological problems	3 (2 %)	2 (2 %)	0.999[a]
Surgery-related problems	3 (2 %)	2 (2 %)	0.999[a]
Secondary cancer	0	2 (2 %)	0.235[a]
Marriage			
20 years or younger	0/39 (0 %)	0/33 (0 %)	N/A
21–24 years	1/25 (4 %)	1/30 (3 %)	0.718[a]
25–29 years	3/35 (9 %)	5/23 (22 %)	0.259[a]
30 years or older	7/22 (32 %)	15/30 (50 %)	0.040
Employment			
Yes	66 (54 %)	66 (57 %)	0.733
No at present	16 (13 %)	16[b] (14 %)	
Never	1 (1 %)	0	
Student	40 (33 %)	34 (29 %)	
Health status at present			
Good	61 (50 %)	67 (58 %)	0.418
Fair	23 (19 %)	19 (16 %)	
Moderate	28 (23 %)	17 (15 %)	
Poor	9 (8 %)	12 (10 %)	
Bad	2 (2 %)	1 (1 %)	
Economic status			
Good	12 (10 %)	23 (20 %)	0.043
Fair	42 (35 %)	48 (42 %)	
Poor	33 (28 %)	21 (18 %)	
Bad	14 (12 %)	6 (5 %)	
Unknown	19 (16 %)	16 (14 %)	

N/A not applicable

[a] Fisher's exact test

[b] Eight out of 16 female CCSs were housewives

Disability qualification

Among the 239 participants, 29 CCSs (12 %) already had the disability qualification, and an additional 15 reported that they needed it (Fig. 1). The total number of CCSs who need the disability qualification is 44. Table 4 shows

Table 3 Association factors or status with late effects

Late effects	Yes (n = 112)	No (n = 123)	χ^2 (p value)
Age at survey (years)			
20 years or younger	32 (44 %)	40 (56 %)	0.914
21–24 years	26 (46 %)	30 (54 %)	
25–29 years	27 (47 %)	31 (53 %)	
30 years or older	26 (51 %)	25 (49 %)	
Diagnosis of cancer			
Leukemia	52 (41 %)	74 (59 %)	0.002
Lymphoma	9 (39 %)	14 (61 %)	
Other solid cancers	15 (41 %)	22 (59 %)	
Bone/soft tissue sarcoma	8 (67 %)	4 (33 %)	
Brain tumor	28 (76 %)	9 (24 %)	
Age at diagnosis (years)			
3 years or younger	32 (46 %)	37 (54 %)	0.854
4–7 years	27 (47 %)	30 (53 %)	
8–12 years	28 (44 %)	36 (56 %)	
13 years or older	25 (52 %)	23 (48 %)	
Treatment			
Chemotherapy	104 (49 %)	109 (51 %)	0.111
Radiation	80 (66 %)	42 (34 %)	<0.001
Surgery	54 (61 %)	35 (39 %)	0.001
Stem cell transplantation	37 (77 %)	11 (23 %)	<0.001
Immunotherapy	4 (44 %)	5 (56 %)	0.999[a]
Marriage			
Yes	14 (44 %)	19 (56 %)	0.687
Employment			
Yes	57 (44 %)	74 (56 %)	0.041
No at present	22 (69 %)	10 (31 %)	
Never	1 (100 %)	0	
Student	32 (43 %)	42 (57 %)	
Health status at present			
Good	35 (27 %)	93 (73 %)	<0.001
Fair	25 (60 %)	17 (40 %)	<0.001[b]
Moderate	30 (68 %)	14 (32 %)	
Poor	20 (95 %)	1 (5 %)	
Bad	2 (67 %)	1 (33 %)	
Economic status			
Good	11 (31 %)	24 (69 %)	0.04
Fair	40 (45 %)	49 (55 %)	0.005[b]
Poor	28 (52 %)	26 (48 %)	
Bad	14 (70 %)	5 (30 %)	

[a] Fisher's exact test

[b] Trend test

associations between CCS characteristics and the need for the disability qualification limited to survivors 18 years or older. Univariate analysis showed that the significantly

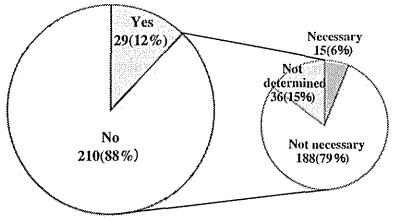

Fig. 1 Do you have or need the disability qualification?

related factors were education, primary cancer diagnosis, radiation, surgery, and late effects. Logistic regression analysis revealed that the significant independent related factors were late effects (OR 12.3; 95 % CI 3.37–45.2), brain tumors (OR 9.55; 95 % CI 1.90–48.0), lymphoma (OR 5.92; 95 % CI 1.07–32.7), and being a high school graduate (OR 9.86; CI 2.67–36.4). Gender and treatment contents were not associated with reporting a need for the disability qualification after adjustment of other factors.

Employment status

We classified the CCSs into three groups according to employment status: employed, unemployed, and students (see Table 5). More than half of the employed CCSs reported being satisfied with their current job, but approximately 40 % also reported that their work had been influenced by their childhood cancer experience. In addition, 61 % had told their employer and/or colleagues about their cancer diagnosis. There were no significant differences between males and females.

In contrast to employed CCSs, 60–80 % of unemployed CCSs reported having experienced some job

Table 4 Related factors of childhood cancer survivors who need the disability qualification (limited to survivors 18 years or older)

	Necessary ($n = 37$)	Not necessary ($n = 164$)	χ^2 (p value)	Logistic regression analysis	
				Odds ratio (95 % CI)	p value
Age at survey (years)					
20 years or younger	10 (25 %)	30 (75 %)	0.582	N/A	
21–24 years	8 (15 %)	45 (85 %)		N/A	
25–29 years	9 (15 %)	49 (85 %)		N/A	
30 years or older	10 (20 %)	40 (80 %)		N/A	
Gender					
Male	23 (22 %)	81 (78 %)	0.16	1.58 (0.57–4.36)	0.376
Education					
Dropout	2 (15 %)	11 (85 %)	0.005	0.79 (0.10–6.38)	0.826
Junior high school	4 (22 %)	14 (78 %)		2.28 (0.04–141)	0.695
High school	21 (35 %)	39 (65 %)		9.86 (2.67–36.4)	0.001
College or vocational school	5 (13 %)	34 (87 %)		1.26 (0.28–5.79)	0.766
University	2 (12 %)	90 (88 %)		Ref.	
Diagnosis of cancer					
Leukemia	8 (8 %)	97 (92 %)	<0.001	Ref.	
Lymphoma	7 (32 %)	15 (68 %)		5.92 (1.07–32.7)	0.002
Other solid cancers	2 (7 %)	28 (93 %)		0.67 (0.07–6.09)	0.720
Bone/soft tissue sarcoma	3 (25 %)	9 (75 %)		4.11 (0.52–32.3)	0.179
Brain tumor	17 (57 %)	13 (43 %)		9.55 (1.90–48.0)	0.006
Treatment					
Chemotherapy	33 (18 %)	148 (82 %)	0.846	1.11 (0.16–7.66)	0.917
Radiation	27 (25 %)	80 (75 %)	0.008	1.81 (0.52–6.32)	0.353
Surgery	25 (32 %)	53 (68 %)	<0.001	1.91 (0.52–6.99)	0.326
Stem cell transplantation	7 (17 %)	34 (83 %)	0.805	0.37 (0.10–1.39)	0.141
Late effects					
Yes	40 (37 %)	67 (63 %)	<0.001	12.3 (3.37–45.2)	<0.001

Hosmer–Lemeshow: $\chi^2 = 3.37$ ($p = 0.909$)

N/A not applicable

Table 5 Employed, unemployed and student childhood cancer survivors

Employed childhood cancer survivors ($n = 131$)	Male ($n = 65$)	Female ($n = 66$)	χ^2 (p value)
Job satisfaction			
Good	11 (18 %)	12 (18 %)	0.690
Fair	19 (31 %)	26 (39 %)	
Moderate	21 (34 %)	16 (24 %)	
Poor	8 (13 %)	7 (11 %)	
Bad (want to quit)	3 (5 %)	5 (8 %)	
Influence by childhood cancer experience			
Much	12 (19 %)	13 (20 %)	0.626
Fair	15 (23 %)	14 (21 %)	
Moderate	9 (14 %)	10 (15 %)	
Little	17 (26 %)	11 (17 %)	
Not at all	12 (26 %)	18 (27 %)	
Telling the cancer diagnosis to the company and/or colleagues			
Yes	40 (61 %)	34 (52 %)	0.288
No	25 (39 %)	31 (48 %)	
Un-employed childhood cancer survivors ($n = 31$)	**$n = 16$**	**$n = 15$**	**χ^2 (p value)**
Some difficulties in employment by childhood cancer experience			
Yes	13 (81 %)	9 (60 %)	0.193
No	3 (19 %)	6 (40 %)	
Please specify the reasons of unemployment			
Failure despite of job seeking	5 (31 %)	4 (27 %)	0.921
No job seeking	2 (12 %)	1 (7 %)	
Unable to get a job because of late effects	3 (19 %)	3 (20 %)	
Others	6 (38 %)	7 (47 %)	
Worry about un-employment			
Not at all	0	1 (6 %)	0.020
Little	2 (13 %)	1 (6 %)	
Moderate	0	3 (19 %)	
Some	0	5 (31 %)	
Much	12 (75 %)	4 (25 %)	
Others	2 (13 %)	1 (6 %)	
Your parent's wish			
Prefer you to work	13 (81 %)	8 (53 %)	0.271
Either will do	0	3 (20 %)	
Prefer not you to work	1 (6 %)	1 (7 %)	
Unknown	2 (12 %)	3 (20 %)	
Major living costs covered by			
Yourself	3 (19 %)	0	0.012
Parents	11 (69 %)	7 (44 %)	
Spouse	0	8 (50 %)	
Public help	1 (6 %)	1 (6 %)	
Do you want to work if they understand CCSs?			
Yes, much to work	7 (41 %)	7 (47 %)	0.755
Yes, if possible	5 (27 %)	4 (27 %)	
It depend on the job	2 (12 %)	3 (20 %)	
Others	2 (12 %)	1 (7 %)	

Table 5 continued

Un-employed childhood cancer survivors ($n = 31$)	$n = 16$	$n = 15$	χ^2 (p value)
Do you want the job-training place like the heart link working project?			
Yes	15 (94 %)	15 (100 %)	0.999[a]
No	1 (6 %)	0	
Students ($n = 69$)	**$n = 39$**	**$n = 30$**	**χ^2 (p value)**
Do you have some worries about your future employment?			
Yes	19 (49 %)	18 (60 %)	0.352
No	20 (51 %)	12 (40 %)	

[a] Fisher's exact test

Table 6 Related unemployment factors (excluding housewives and students)

	Unemployed ($n = 25$)	Employed ($n = 131$)	χ^2 (p value)	Logistic regression analysis	
				Odds ratio (95 % CI)	p value
Age at survey (years)					
20 years or younger	4 (29 %)	10 (71 %)	0.608	N/A	
21–24 years	6 (14 %)	37 (86 %)		N/A	
25–29 years	8 (15 %)	45 (85 %)		N/A	
30 years or older	7 (15 %)	39 (85 %)		N/A	
Gender					
Male	17 (21 %)		0.098	2.05 (0.71–5.90)	0.183
Education					
Dropout	5 (39 %)	8 (62 %)	0.110	8.46 (1.66–43.1)	0.010
Junior high school	1 (17 %)	5 (83 %)		1.66 (0.11–24.8)	0.713
High school	8 (21 %)	30 (79 %)		1.78 (0.52–6.12)	0.359
College or vocational school	4 (12%)	29 (88 %)		1.26 (0.29–5.54)	0.757
University	7 (10 %)	60 (90 %)		Ref.	
Diagnosis of cancer					
Leukemia	10 (12 %)	74 (88 %)	0.016	Ref.	
Lymphoma	4 (25 %)	12 (75 %)		1.55 (0.34–7.19)	0.575
Other solid cancers	1 (4 %)	23 (96 %)		0.22 (0.02–2.32)	0.210
Bone/soft tissue sarcoma	2 (18 %)	9 (82 %)		1.05 (0.14–7.92)	0.964
Brain tumor	8 (38 %)	13 (62 %)		2.73 (0.83–8.96)	0.098
Treatment					
Chemotherapy	24 (17 %)	118 (83 %)	0.303	N/A	
Radiation	16 (19 %)	70 (81 %)	0.312	N/A	
Surgery	12 (19 %)	50 (81 %)	0.426	N/A	
Stem cell transplantation	8 (23 %)	26 (77 %)	0.564	N/A	
Late effects					
Yes	21 (27 %)	57 (73 %)	<0.001	6.22 (1.80–21.4)	0.004

Hosmer–Lemeshow: $\chi^2 = 4.99$ ($p = 0.759$)

N/A not applicable

difficulties because of the childhood cancer experience. While only 10 % reported not having tried to find work, 30 % reported failure in job seeking, and 20 % reported the inability to obtain employment because of their late effects. A majority of the CCSs reported worry concerning their unemployment status, especially the males (75 %). Both males (81 %) and females (51 %) reported that their parents preferred they find employment. For the majority of the sample, living costs were being covered by parents or spouses (females only). Most unemployed CCSs reported wanting to work if their employers understood CCSs better.

Table 6 shows associations between CCS characteristics and employment status. Univariate analysis revealed significant associations between primary cancer diagnosis and late effects. Logistic regression analysis revealed the independent related factors for unemployment were late effects (OR 6.22; 95 % CI 1.80–21.40) and dropping out (OR 8.46; 95 % CI 1.66–43.1). Finally, brain tumors tended to be associated with a high unemployment rate (OR 2.73; 95 % CI 0.83–8.96).

Discussion

We found that the unemployment rate was 15.9 % among the CCSs, excluding homemakers and students, and that 40 % of all employed CCSs reported that their work had been influenced by their childhood cancer experience. Approximately 70 % of unemployed CCSs reported having some late effects. The independent related factors for unemployment were late effects (OR 6.22), dropping out of school (OR 8.46), and brain tumors (OR 2.73). Most unemployed CCSs were likely to seek work despite their health problems and the presence of late effects.

The prevalence of late effects in this study was similar to that in previous studies [12], including other Japanese populations [2]. Frequently reported late effects included endocrine dysfunction, short stature, and neurocognitive problems (that latter is frequently observed in brain tumor survivors). The high prevalence of neurocognitive problems can be explained by the high percentage of brain tumor survivors (15 %) in this study. The finding that the presence of late effects is inversely associated with employment, health, and economic status (see Table 3) is consistent with previous research [13].

A total of 44 CCSs reported that the disability qualification is necessary. The most significant related independent factors were late effects (OR 20.1), brain tumors (OR 9.29), and lower academic achievement (OR 6.3 for junior high school). The Japanese government proposed the new Cancer Control Act in 2012, which explores the employment needs and work-related problems of cancer survivors, promotes employer understanding and an employer-sponsored consultation system, and establishes a society in which cancer survivors can work and live in trust. In the US, the Americans with Disabilities Act of 1990 states that a covered entity shall not discriminate against a qualified individual with a disability, including cancer patients. This applies to job application procedures, hiring, advancement and discharge of employees, workers' compensation, job training, and other terms, conditions, and privileges of employment. In Japan, cancer survivors are not included in the disability qualification. They discussed which types of cancer survivors could be included in the current disability qualification.

In this study, the unemployment rate was 15.9 % among the CCSs, excluding homemakers and students. This rate was similar to the rate of 11 % in the CCSS study [6] and the rate of 16 % in Sweden [14], but relatively lower than the rate of 37 % in Turkey [15]. Independent factors related to unemployment were late effects (OR 6.22), dropping out of school (OR 8.46), and brain tumors (OR 2.73). de Boer et al. [16] reported a meta-analysis on adult CCSs and unemployment. CCSs were nearly twice as likely to be unemployed as healthy controls (OR 1.85, 95 % CI 1.27–2.69). Brain tumor survivors were nearly five times more likely to be unemployed (OR 4.74; 95 % CI 1.21–18.65), whereas the risks for blood or bone cancer survivors were elevated but not statistically significant (OR 1.42; 95 % CI 0.79–2.55; OR 1.97; 95 % CI 0.88–4.40, respectively). Apart from type of diagnosis, predictors of unemployment were a younger age, lower education, being female, late effects, and radiotherapy. Our results are primarily consistent with these findings [14, 16–18].

We have the unpublished data that most CCSs are highly motivated to become helpful to others (a survey by the Children's Cancer Association of Japan). In this study, many unemployed CCSs were likely to seek work despite their health problems and late effects [19]. They require social understanding regarding their specific difficulties including late effects, and we as a society need to make advocacy on their behalf a priority [20].

Our study has two key strengths. First, this is the first nationwide survey in Japan that has focused on CCSs' employment problems. Second, we included a large enough sample to conduct a multivariate analysis on the factors with two outcomes of interest. There are, however, some limitations to the study. First, this is a cross-sectional study, so it cannot determine causal relationships. Second, we did not include a comparison group (such as siblings of CCSs). Finally, the response rate was fairly low (34.4 %) for the first sample group and unknown for the second sample group. The results may be subject to response bias (i.e., those with a stronger interest in the topic may have been more likely to respond to the survey). These disadvantages must be considered given the logistic difficulty of obtaining information from some isolated CCSs. Our ongoing research focuses on seeking out these isolated, unemployed CCSs and individually interviewing them.

In conclusion, our study suggests that the unemployment rate of CCS in Japan is not high, but that some CCSs need

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.

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

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Original Article

Factors influencing timing of neonatal discharge in Japan: Retrospective study

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Abstract ***Background***: The aim of this study was to evaluate the birth and discharge dates of neonates and analyze their distribution over days of the week and the old lunar calendar.

Methods: A retrospective study of the neonates discharged in the years 1990, 2000, 2005, and 2010 was conducted in a general hospital in Tokyo, Japan. Data are represented as odds ratios (OR) of the total number of discharges per day divided by the expected number of days per year, for each day of the week as well as each 6 day cycle of the lunar calendar.

Results: The timing of discharge has an uneven distribution across the days of the week, with weekday discharge rates significantly lower than weekend discharge rates. This uneven distribution is particularly significant in the preterm subgroup. In contrast, there is a minor uneven distribution of births across the days of the week and that of discharges across the 6 day cycle of the lunar calendar. Logistic regression analysis for 2005 and 2010 identified admission fee paid by insurance and prematurity as significant factors associated with weekend/holiday discharge (OR, 1.84; 95% confidence interval [CI]: 1.23–2.75; OR, 1.71; 95%CI: 1.15–2.55, respectively). The average length of stay of neonates discharged on the weekend was longer than that for those discharged on a weekday, in both term and preterm infants.

Conclusions: Japanese parents prefer the convenience of weekends over old superstitions about using the lunar calendar to determine the discharge date.

Key words neonatal discharge, superstition, timing, weekends.

The time of discharge of a neonate from a hospital depends on a number of factors to ensure a smooth transfer to life at home. Such factors include the neonate's medical status, adequate home environment, readiness for discharge (parents' mastery of the essential knowledge and skills), medical costs for both parents and hospital, and, occasionally, superstitions.[1,2] Several previous reports have focused on the timing of discharge from a nursery, or a neonatal intensive care unit in both high-risk neonates,[3,4] as well as mature babies.[5–8] Recent changes in health-care costs have placed additional importance on the earlier discharge of neonates.[9–11] Optimal timing of discharge, however, should be based on neonatal criteria and family convenience, rather than on hospital-related issues.[1,4,5,12]

In Japan, the belief of Rokuyo (the 6 day cycle of the lunar calendar) has been commonly used to determine the date of various social events such as weddings, or funerals. Hira *et al.* previously reported that a significantly higher proportion of Japanese adult patients were discharged on lucky days (Taian), and fewer on unlucky days (Butsumetsu), according to the old lunar calendar.[13] Many parents and grandparents used to select their newborn babies' discharge day by this old superstition.

We hypothesized that neonates are admitted for delivery in a random manner with no specific preference for any day of the week,[6] or of the lunar calendar.[13] The appropriate timing of discharge should therefore be independent of the day of the week[6] and the lunar calendar if the Taian/Butsumetsu belief[13] is not used to determine neonatal discharge day. Given that the distribution of discharge day is skewed, we investigated the factors that determine discharge day. To evaluate this, we assessed the neonatal birth and discharge timing in a general hospital setting.

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Methods

This was a retrospective study of newborns delivered at St Luke's International Hospital (an urban general hospital in Tokyo, Japan) in the years 1990, 2000, 2005, and 2010 who were then discharged home. We selected the information in the years 2005 and 2010 for multiple logistic regression analysis using admission fee paid by insurance as a covariant factor. We excluded neonates with life-threatening disease and those who were transferred to other hospitals for further examination or treatment.

Data collection

Dates of birth and discharge were assigned to the corresponding days of the week. Data are represented as odds ratios (OR) of total discharges per day divided by the real number of days of the week per year. We also calculated the mean number of patients discharged in the 6 day cycle of the lunar calendar individually (Taian, Shakku, Sensho, Tomobiki, Senpu, and Butsumetsu)[13] and evaluated the OR of the total discharges per day divided by the actual expected number of days. Neonates were divided into full-term and preterm groups. Term gestation was defined as completion of 37 weeks of gestation at delivery. Covariate factors include the age of the mother at delivery, gender of the neonates, delivery type (vaginal delivery, vacuum extraction, or cesarean section), mother's complications, birthweight, gestational period, and Apgar score at 1 min, which have previously been reported as influential factors.[3–8] Using the normal approximation of the multinomial distribution, we tested the OR for proportional differences in discharge for each day of the week and for the day assigned to the lunar calendar. Data were validated by two independent pediatricians (M.N and Y.N.) for accuracy by review of the patients' hospital charts. Comparison of the length of stay and discharge was performed for each day of the week and the lunar calendar.

Ethics

Ethics approval was obtained from the Research Ethics Committee of St Luke's International Hospital, Japan.

Statistical analysis

We performed chi-squared tests or Fisher's exact test (for cells with expected counts <5) within categorical predictors. For cross-table comparisons, adjusted standardized residuals were used

Table 1 Subject characteristics

Year	1990	2000	2005	2010	*P*
	n (%) or mean ± SD	*n* (%) or mean ± SD	*n* (%) or mean ± SD	*n* (%) or mean ± SD	
No. neonates	957	1010	1020	1166	N/A
Male	490 (51.3)	541 (53.6)	508 (49.8)	624 (53.5)	0.231
Gestational age (weeks)	39.0 ± 1.58	39.0 ± 1.90	38.8 ± 2.05	38.8 ± 1.97	0.003
Preterm	38 (4.0)	59 (5.9)	94 (9.2)	91 (7.8)	<0.001
Birthweight (g)	3084 ± 419	3039 ± 445	2968 ± 500	2971 ± 453	<0.001
<2500	69 (7.2)	91 (9.0)	133 (13.1)	137 (11.7)	<0.001
<1500	5 (0.5)	5 (0.5)	16 (1.6)	10 (0.9)	0.032
<1000	0	0	9 (0.9)	6 (0.5)	<0.001[†]
Apgar score < 7 at 1 min	29 (3.0)	27 (2.7)	19 (1.9)	53 (4.5)	0.003
First delivery	645 (68.3)	656 (65.3)	699 (68.5)	551 (64.7)	<0.001
Cesarean section	130 (13.7)	191 (18.9)	288 (28.2)	346 (29.7)	<0.001
Vacuum extraction	68 (7.1)	82 (8.2)	19 (1.9)	15 (1.3)	<0.001
Meconium staining in amniotic fluid	26 (2.7)	95 (9.4)	157 (15.5)	215 (18.7)	<0.001
Mother's age (years)	30.2 ± 4.52	32.1 ± 4.38	33.6 ± 4.53	34.5 ± 4.26	<0.001
Any complications in the mother	34 (3.6)	75 (7.5)	182 (17.9)	219 (18.8)	<0.001
Japanese mother and father (%)	917 (95.9)	947 (93.9)	979 (96.0)	1118 (95.9)	0.048
Residence area					
Chuo-ku or Koto-ku	338 (35.4)	331 (32.7)	445 (43.7)	699 (60.1)	<0.001
Other Tokyo	370 (38.7)	470 (46.4)	413 (40.5)	331 (28.4)	
Kanto district excluding Tokyo	214 (22.4)	183 (18.1)	135 (13.2)	123 (10.6)	
Not Kanto	34 (3.6)	29 (2.9)	26 (2.7)	11 (0.9)	
Length of stay (days)	7.41 ± 7.25	7.44 ± 7.10	9.9 ± 20.4	8.15 ± 9.62	<0.001

[†]Fisher exact test. N/A, not available.

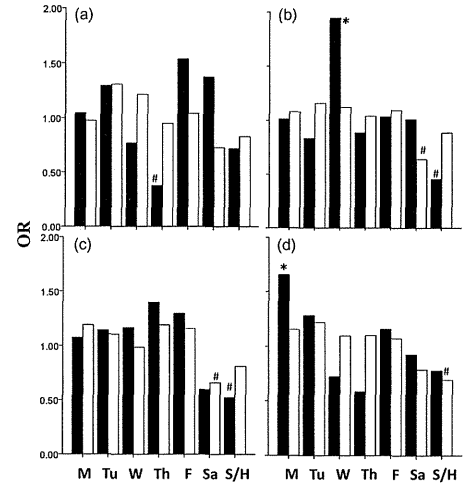

Fig. 1 Odds ratios (OR) of each day of the week/expected day vs day of birth for (□) term and (■) preterm neonates. (a) 1990; (b) 2000; (c) 2005; (d) 2010. There is a lower likelihood of births occurring on weekends, that is, either on Saturday or Sunday (#decrease, $P < 0.05$). S/H, Sunday or holiday. *Increase, $P < 0.01$.

to evaluate the difference between the observed and expected values; columns that yielded adjusted standardized residual >1.96 were considered significant. The adjusted OR for weekend discharge were estimated on logistic regression analysis for 2005 and 2010 because additional information such as admission fee payment was able to be obtained. As adjusted variables, we selected covariate factors for which P was <0.20 on univariate analysis in addition to the presumed associated factors such as gender, Apgar score and residence area. The length of stay for each day of the week and the lunar calendar was compared using analysis of variance, and significant differences were determined on Tukey test (Kruskal–Wallis test). Data were analyzed using SPSS version 20.0 (IBM Japan, Tokyo, Japan).

Results

The basic characteristics of the 4160 neonates are listed in Table 1. During the past 20 years, several changes have occurred. The mean gestational period had little change, but the percentage of preterm and low birthweight neonates has increased significantly. Additionally, the average age of the mother and the proportion of cesarean sections have increased in recent years. The number of cases involving complications in the mother and the staining of the amniotic fluid with meconium has increased, while the proportion of vacuum extraction use has decreased. The proportion of foreign fathers or mothers has not changed during the period under evaluation, but parental residential areas have changed significantly.

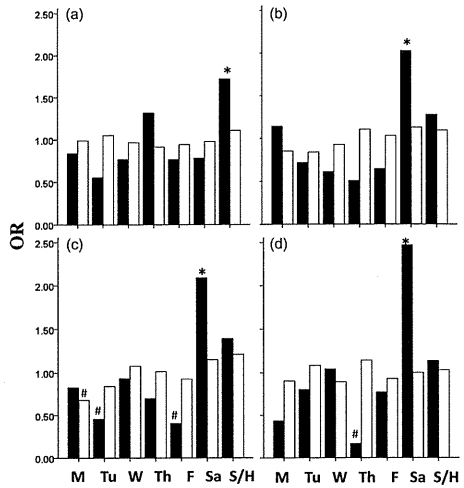

Fig. 2 Odds ratio OR of each day of the week/expected day vs day of discharge for (□) term and (■) preterm neonates. (a) 1990; (b) 2000; (c) 2005; (d) 2010. There is a significantly lower likelihood of discharges occurring only on Mondays in 2005, but weekend discharges tend to occur slightly more frequently than weekday discharges from 1990 to 2010. These discharges are more likely to occur on a weekend than on a weekday. The most frequent discharge days are S/H (Sunday/holiday) only in 1990 compared to Saturday in 2000, 2005, and 2010. *Increase, $P < 0.05$; #decrease, $P < 0.05$.

Day of the week

The relative frequency of birth and the discharge days for all term and preterm neonates are shown in Figures 1,2, respectively. As shown in Figure 1, weekday births are more common than weekend ones in both preterm and term neonates. Exceptions include Thursday in 1990, Wednesday in 2000, and Monday in 2010. The infrequent birth days that are significant include Saturday in 2000, and 2005, and Sunday/holiday in 2010.

Figure 2 shows an almost equal distribution of discharge days among the term neonates, with weekend discharges occurring at a slightly higher frequency than weekday discharges. There were fewer preterm neonates being discharged on weekdays than on weekends ($P < 0.05$). The most frequent discharge days in the preterm group are Saturday in 2000, 2005, and 2010, and Sunday/holiday in 1990. We found an unequal distribution of birth and discharge days in the preterm neonatal group compared to the term group.

Day of the lunar calendar (Taian belief)

The OR of the discharge days for both term and preterm neonates are shown in Figure 3. There is an almost equal distribution of discharges across all days, with Taian (lucky day) discharges occurring slightly more frequently than others in the 2000 and 2005 preterm groups. We were unable to detect significant associations between Taian belief and day of discharge.

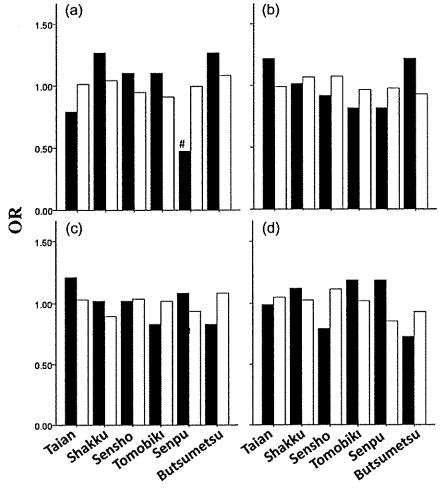

Fig. 3 Odds ratios (OR) of each day of the week/expected day vs Rokuyo day of discharge for (□) term and (■) preterm neonates. (a) 1990; (b) 2000; (c) 2005; (d) 2010. According to the Rokuyo, the 6 day cycle of the lunar calendar is classified as Taian (lucky day), Shakku, Sensho, Tomobiki, Senpu, and Butsumetsu (unlucky day).

Table 2 Factors in discharge day of the week (univariate analysis)

Factors	Weekday(Mon–Fri) *n* (%)	Weekend or holiday *n* (%)	*P*-value
No. neonates	2649 (63.7)	1510 (36.3)	N/A
Year			
1990	633 (66.2)	323 (33.8)	**0.020**
2000	645 (63.7)	368 (36.3)	
2005	611 (59.9)	409 (40.1)	
2010	758 (65.0)	408 (35.0)	
Gender			
Male	1389 (64.2)	775 (35.8)	0.474
Female	1256 (63.1)	733 (36.9)	
Gestational age			
Term (≥37 weeks)	2505 (64.9)	1354 (35.1)	**<0.001**
Preterm (≤36 weeks)	133 (47.2)	149 (52.8)	
Birthweight			
Not low birthweight (≥2500 g)	2407 (64.7)	1314 (35.3)	**<0.001**
Low birthweight (<2500 g)	238 (55.1)	194 (44.9)	
Apgar score at 1 min			
7–10	2562 (63.9)	1447 (36.1%)	**0.033**
0–6	70 (54.7)	58 (45.3)	
Maternal characteristics			
Age <35 years	1549 (64.1)	868 (35.9)	0.553
Any complication	242 (61.4)	152 (38.6)	0.324
Japanese mother and father	2518 (63.6)	1443 (36.4)	0.442
Delivery			
Cesarean section	572 (59.9)	383 (40.1)	**0.006**
First delivery	1624 (63.7)	927 (36.3)	0.509
Vacuum extraction	123 (66.8)	61 (33.2)	0.356
Meconium staining in amniotic fluid	329 (66.7)	164 (33.0)	**0.142**
Residence area			
Chuo-ku or Koto-ku	1144 (63.1)	66.9 (36.9)	0.666
Other Tokyo	1012 (63.9)	572 (36.1)	
Kanto district excluding Tokyo	420 (64.1)	235 (35.9)	
Not Kanto	69 (69.0)	31 (31.0)	

N/A, not available.

Factors associated with weekend birth and discharge

Table 2 lists the factors associated with discharge day of the week on univariate analysis. A significant difference exists between the proportions discharged on a weekday compared to the weekend/holiday. Factors associated with weekend/holiday discharge include the year 2005, preterm and low-birthweight neonates, neonates with low Apgar score, and neonates delivered by cesarean section. We collected information on payment of admission fee in 2005 and 2010. In Table 3, logistic regression analysis identified admission fee paid by insurance, prematurity and the year 2005 to be the three independent factors associated with weekend/holiday discharge ($P < 0.05$), with OR of 1.84, 1.71 and 1.22, respectively.

There are a few significant differences between the weekday and weekend/holiday birth proportions (Table 4). Cesarean section is the only factor associated with weekend/holiday birth. Logistic regression analysis identified cesarean section and prematurity as significant independent factors associated with weekend/holiday birth ($P < 0.05$), with OR of 0.32, and 1.51, respectively (data not shown). We also found no significant differences between proportions of Taian discharge and others (Table S1).

Length of stay

The mean length of stay was compared by discharge day of the week, and an overall longer length of stay for term neonates discharged on Saturdays compared to those discharged on weekdays was found ($P < 0.001$). As shown in Table 5, the mean length of stay for preterm neonates discharged on weekends/holidays tended to be longer than that of those discharged on weekdays.

There were no significant differences in the mean length of stay for term neonates according to the lunar calendar discharge days. Although the mean length of stay for preterm neonates discharged on a Taian day tends to be longer than that of other days, the difference is not significant.

Discussion

In this study, we evaluated the patterns of neonatal birth and discharge in four different years. In a scenario where babies are born in a random manner and their discharge is optimized,

Table 3 Factors in weekend day discharges (multivariate analysis for 2005 and 2010)

Factors	Discharge day		P (χ^2)	Logistic regression analysis†	
	Weekdays (n = 1374)	Weekends/holydays (n = 820)		Adjusted OR (95%CI)	P
Gender (Male)	718	654	0.539	0.96 (0.80–1.15)	0.642
2005	611	409	**0.013**	**1.22 (1.02–1.46)**	**0.031**
2010	761	409		Reference	
Preterm ≤36 weeks	83	103	**<0.001**	**1.71 (1.15–2.55)**	**0.008**
Term ≥ 37 weeks	1271	717		Reference	
Low birthweight < 2500g	142	129	**<0.001**	0.83 (0.56–1.23)	0.362
Not low birthweight ≥ 2500 g	1229	689		Reference	
Cesarean section	376	258	**0.039**	0.95 (0.77–1.18)	0.648
Meconium staining	249	123	0.067	0.85 (0.67–1.08)	0.184
Payment: Paid by themselves	1167	643	<0.001	Reference	
Mixed	49	26		0.98 (0.60–1.60)	0.920
Paid by insurance	136	149		**1.84 (1.23–2.75)**	**0.003**
Apgar score: 0–6 at 1 min	43	32	0.338	1.07 (0.64–1.80)	0.787
7–10 at 1 min	1329	788		Reference	
Residence area: Chuo-ku or Koto-ku	722	426	0.630	Reference	
Other Tokyo	470	274		0.91 (0.75–1.11)	0.369
Kanto district excluding Tokyo	153	105		1.08 (0.82–1.44)	0.583
Not Kanto	25	12		0.64 (0.31–1.32)	0.228

†Hosmer-Lemeshow test: $\chi^2 = 3.14$ ($P = 0.925$). OR, odds ratio.

Table 4 Factors in birth day of the week (univariate analysis)

Year	Weekday (Mon–Fri) n (%)	Weekend or holiday n (%)	P
No. neonates	3134 (75.4)	1021 (24.6)	N/A
Year			
1990	715 (74.8)	241 (25.2)	0.795
2000	757 (74.7)	256 (25.3)	
2005	779 (76.4)	241 (23.6)	
2010	883 (75.7)	283 (24.3)	
Gender			
Male	1628 (75.35)	535 (24.7)	0.823
Female	1503 (75.6)	486 (24.4)	
Weeks in delivery			
Term (≥37 weeks)	2912 (75.5)	947 (24.5)	0.768
Preterm (≤36 weeks)	215 (76.2)	67 (23.8)	
Birthweight			
Not low birthweight (≥2500 g)	2795 (75.2)	924 (24.8)	0.209
Low birthweight (<2500 g)	335 (77.9)	95 (22.1)	
Apgar score at 1 min			
7–10	3027 (75.5)	982 (24.5)	0.896
0–6	96 (75.0)	32 (25.0)	
Maternal characteristics			
Age <35 years	1816 (75.1)	601 (24.9)	0.581
Any complication	313 (79.4)	81 (20.6)	0.058
Japanese mother and father	2981 (75.3)	980 (24.7)	0.187
Delivery			
Cesarean section	836 (87.5)	119 (12.5)	**<0.001**
First delivery	1924 (75.4)	627 (24.6)	0.753
Vacuum extraction	145 (78.8)	39 (21.2)	0.277
Meconium staining in amniotic fluid	361 (73.2)	132 (26.8)	0.253
Residence area			
Chuo-ku or Koto-ku	1375 (75.8)	438 (24.2)	0.736
Other Tokyo	1189 (75.1)	395 (24.9)	
Kanto district excluding Tokyo	488 (74.5)	167 (25.5)	
Not Kanto	79 (79.0)	21 (21.0)	

N/A: not available.

neonates would be born evenly across all days of the week.[6] Furthermore, if neonates returned home in a non-random manner based on parental convenience or belief, it is likely that there would be a higher weekend or Taian (lucky day) discharge rate in Japan.[13] We found that the discharge of term neonates is almost equally distributed across all the days, with a slightly higher frequency of weekend discharge. In contrast, for preterm neonates, there are fewer discharges on weekdays compared to weekends (the most frequent discharge days include Saturday in 2000, 2005, and 2010 and Sunday/holiday in 1990).

These results contradict the findings of a previous report by Touch *et al.* in the USA.[6] They found that the timing of nursery discharge was unevenly distributed across the days of the week, with significantly lower weekend (Saturday and Sunday) discharge rates compared to weekday discharge rates. In Japan, the 5 day work week system was introduced in the 1980s, but it was adopted by public servants and all public schools in 1992 and 2002, respectively.[14] As shown in Figure 2, the most frequent discharge days are Sunday/holiday in 1990, compared to Saturday in 2000, 2005, and 2010. This difference can be explained by the fact that in 1990, most parents worked on Saturdays.

Unexpectedly, the Japanese belief in Taian/Butsumetsu did not influence the determination of neonatal discharge day. In a previous study, Hira *et al.* found that a significantly higher number of adult patients were discharged on Taian and fewer on Butsumetsu; additionally, older women frequently tended to get discharged on Taian than on Butsumetsu.[13] The present data suggest that for preterm neonates, Taian discharges occurred slightly more frequently in the years 2000 and 2005; the difference, however, was not significant owing to the small number of preterm neonates.

With respect to the distribution of the birth days, the present results are consistent with those of a previous report.[6] This study showed that cesarean section and prematurity are independent factors significantly associated with weekend/holiday birth. The predominant distribution of both preterm and term births on weekdays can be explained by a reluctance to perform elective induction and cesarean delivery on the weekends. In addition, the decision to deliver a fetus in a marginally abnormal uterine environment, may be postponed to a weekday due to issues with staffing.

Despite the predominance of weekday birth, one would still expect a generally random distribution of discharges throughout the week. Unlike issues with the day of delivery, a predominance of weekend discharge for both the term and preterm groups most likely represents an unnecessary delay in discharge and prolonged hospitalization for the neonates.[15] The comparison of the length of stay of neonates discharged on weekdays and weekend/

Table 5 Day of the week and lunar calendar day vs length of stay

Term neonates	n	Length of stay (days) Mean ± SDs	95%CI (length of stay)	ANOVA
Monday	424	6.23 ± 2.41	6.00–6.48	$P < 0.001$
Tuesday	519	6.43 ± 2.62	6.21–6.66	Significant difference
Wednesday	512	6.64 ± 2.58	6.41–6.86	between:
Thursday	548	6.96 ± 3.17	6.70–7.23	Mon/Tue/Wed/Fri/Sun
Friday	502	6.69 ± 2.08	6.50–6.87	vs Sat
Saturday	**568**	**7.20 ± 3.97**	**6.87–7.53**	Mon/Tue vs Thu
Sunday/holiday	786	6.54 ± 2.55	6.36–6.71	Kruskal–Wallis test:
				$P < 0.001$
Preterm neonates				ANOVA
Monday	28	23.5 ± 29.0	12.3–34.8	$P = 0.870$
Tuesday	25	23.1 ± 16.6	16.2–29.9	Kruskal–Wallis test:
Wednesday	34	28.0 ± 42.2	13.3–42.7	$P = 0.328$
Thursday	22	24.1 ± 27.6	11.9–36.3	
Friday	24	34.9 ± 44.2	16.3–53.6	
Saturday	80	32.4 ± 37.2	24.1–40.7	
Sunday/holiday	69	30.8 ± 55.4	17.4–44.1	
Term neonates				ANOVA
Taian	658	6.94 ± 4.28	6.61–7.27	$P = 0.323$
Shakku	650	6.54 ± 2.86	6.32–6.76	Kruskal–Wallis test:
Sensho	673	6.69 ± 2.70	6.49–6.90	$P = 0.355$
Tomobiki	631	6.66 ± 2.38	6.47–6.84	
Senpu	603	6.95 ± 6.05	6.47–7.43	
Butsumetsu	648	6.76 ± 3.45	6.49–7.02	
Preterm neonates:				ANOVA
Taian	51	**40.1 ± 64.8**	21.9–58.4	$P = 0.298$
Shakku	51	22.8 ± 16.8	18.1–27.6	Kruskal–Wallis test:
Sensho	44	27.8 ± 32.9	17.8–37.8	$P = 0.368$
Tomobiki	46	32.4 ± 40.9	20.2–44.5	
Senpu	46	28.8 ± 39.4	17.1–40.5	
Butsumetsu	44	23.3 ± 32.8	13.3–33.2	

CI, confidence interval.

holiday indicates a significantly longer length of stay for the former. Especially in preterm neonates, discharge on weekend days seems to contribute to longer hospital stay because the mean length of stay on weekend discharge was longer than on weekday discharge. Logistic regression analysis showed that non-insured payment and prematurity were significantly associated with the tendency towards weekday discharge. Insured cover including prolonged stay in the hospital seemed to enable the parents to select more convenient discharge days. Fox and Kanarek, and Margolis *et al.* previously reported that insurance status might be one of the most influential factors on early discharge for newborns.[16,17] We hypothesize that additional variability in discharge day might occur within different regions, but there was no difference in parental living regions even after multivariate analysis.

This study has a number of important strengths. First, we could evaluate changes from 1990 to 2010. There have been no changes in the neonatal discharge principles at St Luke's International Hospital, Tokyo, during these 20 years. Second, there were sufficient numbers of neonates to allow statistical analysis. Third, the neonatal nursing ward at the hospital has sufficient capacity to hold the necessary number of deliveries; there is usually no need to decline admission for delivery or facilitate early neonatal discharge because of the presence of a full nursing ward. There are, however, certain limitations in the present study. First, this study was conducted only at one general hospital in Japan. We are not certain to what extent the present findings can be generalized to other Japanese hospitals. Second, we did not collect all the information pertaining to the reasons underlying the parents' choice of discharge day. Third, the current study did not have sufficient statistical power detect a minor increase of preference to Taian, especially in the preterm subgroup.[13]

Taken together, the present results suggest that Japanese parents prefer the convenience of weekends over superstitious belief in the lunar calendar when determining discharge dates in preterm infants. If parent-related issues of delayed discharge were to be considered, improving the availability of necessary services, and reconsidering staffing issues on weekends may be indispensable to conducting effective parental education at the time of discharge. We conclude that a re-shuffling of the staff during weekends would enable an effective multidisciplinary case management approach and planning of discharge of neonates from the nursery or neonatal intensive care unit. This might be beneficial to the neonates and their families discharged on weekends.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 Factors associated with Taian discharge day (univariate analysis)

日本小児科学会雑誌　118巻1号　65～74（2014年）

論　策

小児がん経験者に対する社会的偏見の実態調査

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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]．

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

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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

表3　小児がん経験者回答者の背景

特性	合計（割合）	男性	女性	t-test（P値）
対象人数	n＝90	n＝51	n＝39	
回答時の年齢：平均±標準偏差（中央値）	24.0±4.0（24）	24.1±4.1（24）	24.0±3.9（24）	0.933
原疾患				Fisher（P値）
急性リンパ芽球性白血病	30（33%）	14	16	
急性骨髄性白血病	12（13%）	5	7	
慢性骨髄性白血病	3（ 3%）	2	1	
白血病とのみ記載	7（ 8%）	5	2	
リンパ腫	13（14%）	9	4	0.665
神経芽腫	10（11%）	7	3	
ウイルムス腫瘍	3（ 3%）	2	1	
その他固形腫瘍	8（ 8%）	5	3	
無回答	4（ 4%）	2	2	
生活環境				
一人暮らし	34（38%）	22	12	
両親と同居中	34（39%）	19	16	
兄弟/友人と同居中	3（ 3%）	1	2	0.686
結婚して相手と同居中（同棲中含む）	15（17%）	8	7	
その他	3（ 3%）	1	2	
最終学歴				
高卒	23（26%）	13	10	
高専・専門学校卒	27（30%）	10	17	0.039
短大卒	4（ 4%）	2	2	
大学/大学院卒・大学在学	36（40%）	26	10	
職業				
学生	30（37%）	20	10	
会社員（ホワイトカラー）	15（17%）	12	3	
製造・販売（ブルーカラー）	8（ 9%）	6	2	
医療関係（看護師，介護士，薬剤師）	7（ 8%）	0	7	0.003
フリーター	1（ 1%）	1	0	
専業主婦	2（ 1%）	0	2	
無回答	27（28%）	12	15	
就職状況				
学生	30（34%）	20	10	
常勤勤務	46（52%）	25	21	
パートタイム・アルバイト	8（ 9%）	5	3	0.345
家事手伝い・就職準備中	3（ 3%）	1	2	
専業主婦	2（ 2%）	0	2	
無回答	1（ 1%）	0	1	
結婚歴				
未婚	75（83%）	44	31	
結婚	14（16%）	7	7	0.431
再婚	1（ 1%）	0	1	
社会適応について				
全く困ったことはない	45（50%）	25	20	
少しあるが対応できている	40（44%）	23	17	
かなり困っている	1（ 1%）	1	0	
非常に困っている	0	0	0	1.000
その他	3（ 3%）	2	1	
無回答	1（ 1%）	0	1	

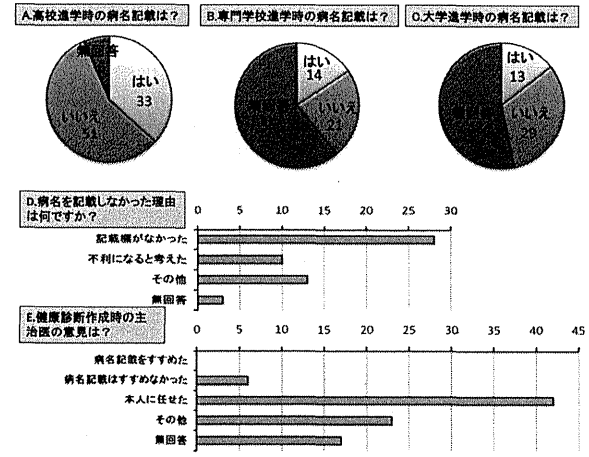

図1　進学時の病名記載に関して（全て人数）
病名記載に関して，A：高校進学時，B：専門学校進学時，C：大学進学時，D：病名記載で「いいえ」とした理由は？E：健康診断作成での主治医の意見は？

していなかった人に理由を尋ねたところ，病名告知により断られた人が7人(17%),「はじめから加入できないと思ってあきらめていた」が約半数を占めた．ハートリンク共済の認知度は約8割と高く，特に女性では認知度が有意に高かった（p＝0.016）．

考　察

現在では小児がんは医学的に約80%が治癒する疾患となっているが，今回の結果をみると学校（高校・大学）の半数以上，一般企業の4分の3はそのことを知らないと答えており，未だ社会的には十分認知されていないことがあきらかにされた．その理由としては，成人がんが年間約60万人発生しているのに対し，小児がんは年間2,000名程度とまれであること，厚労省のがん対策はこれまで5大がんをはじめとする成人がんに集中しており小児がんはほとんど取り上げられなかったこと，以前は小児がん闘病のことは家族・経験者本人が心情的にもオープンにしにくい経験であったことなどが関係していると考えられた．ただ本研究の結果では学校も一般企業も社会的偏見を受けている可能性が高いと考えていたのは約1割であり，7～8割の人が偏見はないと答えていたこと，別の厚労省研究班の調査では成人期の小児がん経験者の8割以上に病名告知が進んでいる状況を考えると，今後はこの点に関して積極的な社会的啓発が必要であると考えられた．

本研究の結果から，進学や就職の際に，小児がんの既往歴を約6～7割は記載しなかったと答えたが，理由としては記載欄がなかった以外には，病名の記載が不利になると危惧している小児がん経験者及び主治医が多い傾向があった．その中で専門学校進学時と就職時に女性では半数以上が病名を記載しており，男女差が大きいことが注目された．女性に病名記載者が多かった理由は明らかではないが，一般に女性小児がん経験者の方が活発でオープンな傾向が見られること，以前のがんの子供を守る会の調査でも日本では男性の方が経済的自立や就労の切実さが高く就職に不利にならないようにという配慮が大きいことが関係しているのかもしれない．

一方学校側と企業側は小児がんという既往病名記載だけのため書類審査で不合格とすると回答したものが1.8～5.4% いたことに注意が必要である．

進学に関しては，平成15年6月5日付けの文部科学省高等教育局長通知[9]に，「入学者選抜に際して健康診断により不合格の判定を行うについては，疾病など心身の異常のため志望学部・学科等の教育の目的に即した履修に耐えないことが，入学後の保健指導等を考慮してもなお明白な場合に限定し，真に教育上やむを得ない場合のほかは，これらの制限を廃止あるいは大幅に緩和する方向で引き続きその見直しを行うことが望ましい．」と書かれており，小児がんの既往歴のみで不合格にすることが適切ではないことは明白である．就職に関しても，厚生労働省は平成5年5月10日付事務

表4　性別による回答の違い

特性	回答	男性	女性	P値
病名記載について				
高校進学時	はい	20	13	0.606
	いいえ	28	23	
専門学校進学時	はい	3	11	0.019
	いいえ	13	8	
大学進学時	はい	9	4	0.651
	いいえ	22	7	
就職時	はい	5	15	0.001
	いいえ	33	15	
就職時に病名記載「はい」の方				
面接官の反応	好意的	1	6	0.777
	懐疑的	1	1	
	触れない	3	8	
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				
話した	はい	7	16	0.003
	いいえ	25	11	
異性との交際経験はありますか				
交際経験	はい	30	31	0.036
	いいえ	21	8	
相手に既往を話したか	はい	22	26	0.315
	いいえ	8	5	
生命保険について				
加入しているか	はい	26	18	0.614
	いいえ	22	19	
加入している場合				
告知して加入		17	10	0.824
告知せず加入		8	4	
加入していない場合				
既往のため加入できず		3	3	0.973
できないと思ってあきらめた		11	9	
興味がない		5	4	
ハートリンク共済について				
知っているか	はい	37	36	0.018
	いいえ	14	3	

連絡で，「雇用時の健康診断は採用選考時に同規則（労働安全衛生規則第43条）を根拠として採用可否決定のための健康診断を実施することは適切さを欠くものである」としている[6]．

このことを考慮すると，小児がんという既往病名記載だけのため書類審査で不合格とする判定は少数であったとはいえ不適切といわざるを得ない．以上のような法律的な裏付けもあることから，小児がんの治療成績の向上に関する社会的認知を高めつつ，小児がん経験者の正当な権利を主張し，学校や企業での実績を積み上げることで，小児がん経験者の社会的偏見が少なくなることが期待される．

異性との交際に関しては，約7割の経験者があると答えたが，2005年度の内閣府の調査では，一般20歳代男性23.9%，女性7.8%，30歳代男性8.7%，女性3.0%が異性との交際経験もないと答えているのと比べ今回の結果は多少低い傾向が見られるものの男女差を含めて大きな差ではなかった[7]．実際に結婚まで至った15人は，全員恋愛結婚で，相手に病名を話しており特に結婚上のトラブルは生じていなかった．ただし今回の調査では該当者が見られなかったため見合い結婚後の問題に関しては不明であった[8]．

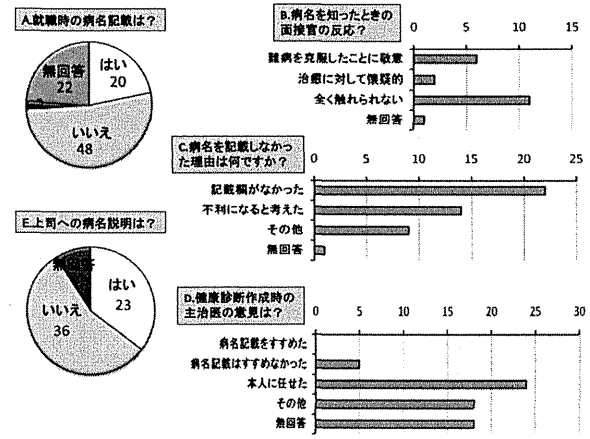

図2　就職時に病名記載に関して（全て人数）
A：就職時の病名記載は？ B：病名を知ったときの面接官の反応は？ C：病名記載で「いいえ」とした理由は？ D：健康診断作成での主治医の意見は？ E：定期健診を受けるため，上司に小児がんであったことを話しましたか？

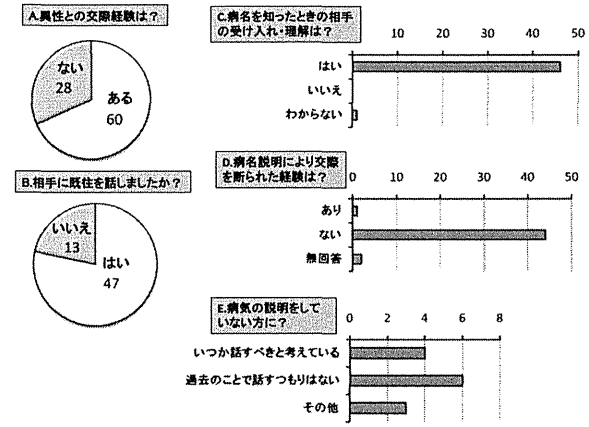

図3　異性との交際経験に関して（全て人数）
A：異性との交際経験はありますか？ B：交際相手に既往を話しましたか？ C：相手は既往の病気のことを受け入れ，理解されましたか？ D：病名説明により，交際を断られた経験はありますか，E：病気の既往を話していない方に

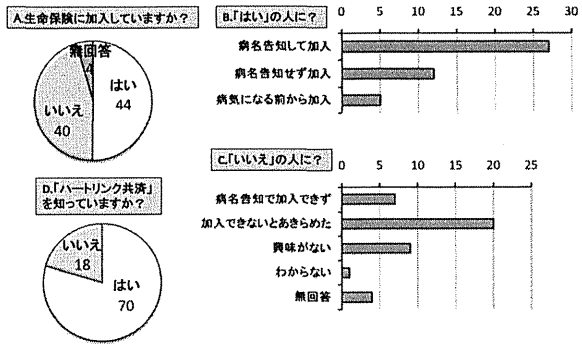

図4　生命保険に関して（全て人数）
A：生命保険に加入していますか？ B：「はい」の方に，C：「いいえ」の方に，D：ハートリンク共済をご存知ですか？

生命保険に関しては，病名を告知せず加入している者，病気になる前から加入しており小児がんの告知が不十分と考えられる者がおり，このような場合には将来の保険の支払い履行に関して疑問が残った．また加入していない人の大多数は，加入できないとあきらめているものや興味がないとするものも多く，今後経験者自身もこのことを社会的問題として認知していく必要がある．本調査ではハートリンク共済（主に小児がんを対象とした共済による保障制度 http://hartlink.net/）の認知率は高かったが，特に女性で高いのが注目された．その理由として，本研究の小児がん経験者は新潟がんセンターで治療を受けた患児であって，同共済は新潟に本部があるためと考えられ，この認知度の高さが日本全体を代表しているとは考えにくい．

本研究の短所は，横断的な比較的少数例の研究であり，解析対象が小児がん経験者に関しては新潟地区に限られたために選択バイアスがあり，結果の一般化が困難なことである．また社会適応や就職率も他の小児がん経験者の報告[9]より良好な集団であることを考慮する必要がある．またサンプル数が学校・企業とも200と比較的少数であり，特に企業の回収率は37％と不良であったため，十分な統計解析は困難であった．今後企業に関しては，全国規模のより多数施設を対象とした調査を施行し，統計的に分析可能な研究を実施する予定である[10]．

結　語

学校・企業・小児がん経験者の各視点から社会的偏見に関する実態調査の結果をまとめた．

1）「小児がんは現在では約80％が治癒する疾患となっている」事は未だ社会的に認知されていない．

2）進学時には小児がん既往は特に問題とならない．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ある．

3）就職時も既往歴は問題にならない傾向である．しかし，一部には不採用とする企業もあり，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．

4）恋愛結婚であれば特にトラブルは生じていない．

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日本小児科学会の定める利益相反に関する開示事項はありません．

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緩和医療薬学

編集 日本緩和医療薬学会

南江堂

A 疼痛マネジメント

1 がん疼痛マネジメント

がん疼痛とは，広義にはがん患者に生じた疼痛のすべてを指し，がん自体（腫瘍の浸潤や増大，転移）が原因となった痛みと，がんに関連した痛み（筋の攣縮，リンパ浮腫，便秘，褥瘡などによる痛み），がん治療に起因する痛み（術後痛や，化学療法に起因した末梢神経障害や口内炎による痛みなど），がん患者に併発したがん以外の疾患による痛み（変形性脊椎症，骨関節炎などの痛み）の4種類に分類される．日常の臨床では，がん自体により引き起こされた疼痛のみを指すこともあるが，腫瘍以外の疼痛も治療の対象として認識されるべきである．原因によって治療法は異なるが，腫瘍自体による痛み（狭義のがん疼痛）はWHO方式がん疼痛治療法に従った薬物療法が基本となる．

がん疼痛は，がんの診断時に20～50％の患者に存在し，進行がん患者全体では75％にのぼる．痛みがあるがん患者の8割は，身体の2ヵ所以上に痛みがあり，6割の患者の痛みの原因は複数である．これらの状況は病状の進行によって変化していくため，繰り返し評価を継続していく必要がある．がん疼痛治療は，多くのがん患者が経験する症状であるが，適切な評価と治療によって治療が可能な症状でもある．

わが国のがん疼痛の治療成績を示す直接的なデータはないが，がん疼痛に使用されているモルヒネ，オキシコドン，フェンタニルの3種類のオピオイド鎮痛薬の人口あたりの消費量は先進国中で最も少ない．これを受けて，平成24年に改訂されたがん対策推進基本計画においても「日本では，欧米先進諸国に比べ，がん性疼痛の緩和等に用いられる医療用麻薬の消費量は少なく，がん性疼痛の緩和が十分でないと推測される」と述べられており，わが国の現状においては，オピオイド鎮痛薬が中等度以上のがん疼痛に対して，日常生活に使用が再鎮痛レベルを目標に処方あるいは増量されることが必要である．

がん疼痛マネジメントにおける薬剤師の果たすべき役割は，がん疼痛治療にかかわっている医療チームへの専門的な知識の提供と，明確なプレゼンス（参加）の確立である．ここでいう医療チームとは，いわゆる“緩和ケアチーム”ばかりでなく，診療所や訪問看護ステーションと協働する保険薬局から参加する薬剤師を含んでいる．

薬剤師のがん疼痛マネジメントへの参加は，がん疼痛治療の治療薬であるオピオイドがモルヒネ製剤のみであった1990年代までと異なり，2000年以降は，フェンタニル経皮吸収型製剤（貼付剤），オキシコドン徐放錠が相次いで臨床現場で使用可能になり，剤型も極めて多彩となっている．

病棟や外来（薬局）などでの服薬指導などの基本的な業務に加え，特に最近話題となってきた制吐薬による錐体外路症状などの副作用対策の問題や，臓器機能低下などに伴う鎮痛薬や鎮痛補助薬などの薬物動態学的影響，オピオイドと併用薬剤による薬物相互作用の問題などはがん疼痛マネジメントを担うチーム内において薬剤師が担うべき専門分野である．

2 外来疼痛マネジメント

a) 理解しておくこと

患者は

①痛みを我慢している．

②鎮痛薬を使用することに抵抗がある．

③身体的苦痛に対してどうしたらよいのかわからない．

日本人は痛みを我慢することが美徳とされていた．「これくらいの痛みは我慢しなさい」といわれて育った人間が，痛みを上手に表現できることはまれと思ったほうがよい．がん患者にとって痛みを表現することは，病状が進行していることを自ら認めることにもつながる．特に主治医に痛みを訴えることは，主治医の処方や治療方針に疑問を訴えるくらい勇気が必要なのである．

また，鎮痛薬は胃に負担をかけるので，身体によくないからできるだけ服用しないことが望ましいと考えている患者も少なくない．しかし，身体的苦痛は我慢してもよくならないことを自覚しているが，どうしたらよいのかわからないのも事実である．

b) 医療者が行うこと

①痛みを包括的に評価する．

②適切な鎮痛薬を処方する．

③副作用対策を十分に行う．

④原因治療を並行して行う．

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Original Article

Clinical Guideline for Pharmacological Management of Cancer Pain: The Japanese Society of Palliative Medicine Recommendations

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Pain is the most frequent and distressing symptom in cancer patients. As part of a worldwide effort to improve the quality of pain control, several clinical guidelines for the management of cancer pain have been published and revised in the last decade. The Japanese Society of Palliative Medicine first published a Japanese clinical guideline for the management of cancer pain in 2000. Since then, many clinical studies concerning cancer pain management have been conducted, new drugs have become available in Japan and the methodology of developing a guideline has been refined. Therefore, we decided to develop a novel clinical guideline. This review paper summarizes the recommendations and the rationales of this new clinical guideline for the pharmacological management of cancer pain. In addition, a short summary of the clinical guideline development process is provided. This new Japanese Society of Palliative Medicine guideline highlights the importance of conducting well-designed studies to identify the best practices in cancer pain management.

Key words: cancer pain – opioid analgesics – nonopioid analgesics – guideline

INTRODUCTION

Pain is the most distressing symptom in cancer patients, and it affects 70–80% of patients with advanced disease (1). Current evidence from countries including Japan suggests that many cancer patients suffer from pain and do not receive adequate pain relief (2–7). As part of a worldwide effort to improve the quality of pain control, several clinical guidelines for the management of cancer pain have been published and revised in the last decade (8–13). As one of such efforts, the Japanese Society of Palliative Medicine (JSPM) first published a Japanese clinical guideline for the management of cancer pain in 2000 (14). Although a formal systematic review was conducted, recommendations of the JSPM guideline in 2000 were the same as the existing guidelines and the grading system of recommendations was anecdotal. Since then, many clinical studies concerning cancer pain management have been conducted, and new drugs have become available in Japan. In addition, the methodology of developing a guideline has been refined (15,16). A novel clinical guideline to integrate new findings using the validated methodology is warranted.

This review paper summarizes the recommendations and the rationales for this new clinical guideline for the pharmacological management of cancer pain. In addition, a short summary of the development process for this guideline is provided.

SHORT SUMMARY OF THE DEVELOPMENT PROCESS

The objective of developing the guideline was to establish the standard pharmacological management of cancer pain. The target population includes all cancer patients who experience pain, whereas the primary users of this guideline are all medical personnel who care for cancer patients, including palliative care physicians, oncologists, nurses and pharmacists.

Task Force

The committee of JSPM nominated the task force members from a pool of specialists with adequate clinical experience to cover multidisciplinary areas, and the JSPM Board gave the final approval. The task force comprised 56 physicians (31 palliative care physicians, 15 anesthesiologists, 5 oncologists and 5 home care physicians), 25 pharmacists, 23 nurses, 1 epidemiologist and 7 other professionals (Appendix).

Systematic Literature Review

First, the task force gathered clinical questions by administering a questionnaire to all members of the task force. These items were then restructured into 65 questions. Next, the task force performed a systematic literature review of each clinical question using the electronic search function in the PubMed database; a manual search of all articles published in the *Journal of Pain and Symptom Management* and *Palliative Medicine* from January 2000 to July 2008, a search of the PaPaS (Pain, Palliative and Supportive Care) category of the Cochrane database and a review of reference literature of relevant guidelines (8–13) and textbooks (17–22). This review process included only studies that evaluated drugs available in Japan. The abstracts of all identified literature references were read, and the full text of all relevant literature was reviewed.

Drafting Recommendations and Delphi Methods

Each member in charge of a clinical question drafted the recommendations and general background descriptions. The Delphi method was then performed to examine the validity of each statement. The Delphi method is a standardized method used to reach consensus; we used the modified Delphi method (23). All statements in the clinical guideline were separated into >150 meaningful units, and the task force members were requested to rate the validity of all statements on a nine-point Likert-type scale from one (inappropriate) to nine (appropriate). After three Delphi rounds and an external review by 12 external reviewers (5 palliative care physicians, 2 radiation oncologists, 1 anesthesiologist, 1 home care physician, 1 nurse, 1 pharmacist and 1 epidemiologist), the final version was established.

Evidence and Recommendation Levels

The task force decided to use an original recommendation table for this clinical guideline, following the concepts from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to articulate the levels of evidence and the strengths of each recommendation (Table 1) (15). We decided to use 'should' for expressing recommendation strength 1 and 'may' for recommendation strength 2 in this paper.

RECOMMENDATIONS

We created 65 recommendations: 24 for the general management of cancer pain, 24 for the management of pain from specific etiologies, 15 for the management of opioid-induced adverse effects and 2 for patient education. This guideline also included chapters on general background descriptions, flow charts to visualize the recommendations, a complete reference list followed by the search strategy and a summary of other related international guidelines that have previously been published.

Table 2 demonstrates all the recommendations listed in the guideline, and Fig. 1 shows an overview and the main algorithm for using those recommendations.

The key recommendations and their rationales are described below.

Table 1. Recommendation table

Strength of recommendation	
1 (strong)	Recommended treatment is certainly of benefit to the patient, and the benefit exceeds the harm or burden. In the statement, 'should' is used.
2 (week)	Recommended treatment may be of benefit to the patient. Or the benefit competes with the harm or burden from the recommended treatment. In the statement, 'may' is used.
Level of evidence	
A (high)	The evidence from the results of studies is established. The result will not change, even if further study is performed, e.g. multiple high-quality randomized controlled trials with concordant results, or a meta-analysis of randomized controlled trials
B (low)	Although some studies support the result, evidence is not enough. Further study may change the result, e.g. randomized, controlled trials with inconsistent results, low-quality randomized controlled trials, small number of randomized controlled trials, non-randomized controlled trials or multiple observational trials with consistent results
C (very low)	There is insufficient evidence for the result, e.g. small number of observational trials, case reports and expert opinions

Table 2. Recommendations in the guideline of the Japanese Society of Palliative Medicine

1. Management of cancer pain
   - *1.1 Assessment*
     - 1.1.1 Comprehensive assessment of pain should be carried out.
   - *1.2 Patients with mild pain*
     - 1.2.1 Acetaminophen should be administered to cancer patients with mild pain [1A].
     - 1.2.2 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) should be administered to cancer patients with mild pain [1B].
     - 1.2.3 The type of non-opioid analgesic should be chosen in accordance with the effectiveness and tolerability of an individual patient [1A].
     - 1.2.4 Prostaglandin E1 analogs, proton pump inhibitors or H2 receptor blockers should be used for the prevention of peptic ulcer in patients who are treated with an NSAID [1A].
   - *1.3 Patients with moderate-to-severe pain or inadequately controlled pain despite treatment with nonopioid analgesics*
     - 1.3.1 Opioids should be administered to cancer patients with moderate-to-severe pain or inadequately controlled pain despite treatment with nonopioid analgesics [1B].
     - 1.3.2 The type of opioid should be chosen individually according to the patient's condition [1B].
     - 1.3.3 In cancer patients with stable and mild-to-moderate pain, either sustained-release or immediate-release opioids may be used. In cancer patients with severe or unstable pain, immediate-release opioids or parenteral opioids may be used [2B].
     - 1.3.4 Patients should be carefully assessed and observed for nausea/vomiting during opioid therapy, and antiemetics should be readily available whenever nausea/vomiting occurs [1C].
     - 1.3.5 Patients should be carefully assessed and observed for constipation during opioid therapy; moreover, they should be provided with instructions regarding adequate fluid intake, diet and laxatives for the prevention of constipation [1C].
     - 1.3.6 Nonopioid analgesics may be continued when opioids are introduced in patients with inadequate pain control by nonopioid analgesics [2B].
   - *1.4 Patients with inadequately controlled pain despite initial opioid use*
     - 1.4.1 Non-opioid analgesics should be used concurrently with opioids in patients who experience continuous pain with regular opioid use [1A].
     - 1.4.2 The dose of regular opioid should be increased in patients who experience continuous pain with regular opioid use [1B].
     - 1.4.3 Type of opioid should be switched in patients with inadequately controlled pain under a certain type of opioids [1B].
     - 1.4.4 Another type of opioid may be added in patients with inadequate pain control by a certain type of opioid [2C].
     - 1.4.5 The administration route may be changed to intravenous or subcutaneous infusion in patients with inadequate pain control with an oral or a transdermal preparation of opioid analgesics [2C].
     - 1.4.6 Ketamine may be used in combination with opioids in patients with inadequately controlled pain after a sufficient increase in opioid dose [2B].
     - 1.4.7 Corticosteroids may be used in combination with opioids only for particular pain etiologies, paying careful attention to the risk of adverse reactions in patients who experience pain after a sufficient increase in opioid dose [2C].
   - *1.5 Patients with breakthrough pain*
     - 1.5.1 The rescue dose of opioids should be used in patients with breakthrough pain [1B].
     - 1.5.2 The rescue dose may be increased if adverse events are acceptable and the initial rescue dose provides inadequate analgesic effects [2C].
     - 1.5.3 For patients with end-of-dose failure, the dose of regular opioids should be increased or interval of regular opioids should be shortened [1B].
2. Treatment of pain from specific etiology
   - *2.1 Neuropathic cancer pain*
     - 2.1.1 Any of the adjuvant analgesics (anticonvulsants, antidepressants, antiarrhythmics, ketamines or corticosteroids) may be used in cancer patients with neuropathic pain [2B].
     - 2.1.2 Another type of adjuvant analgesics may be added in patients with inadequate control of neuropathic pain after increasing the dose of a certain adjuvant analgesic sufficiently, in consultation with an expert [2C].
   - *2.2 Bone metastatic pain*
     - 2.2.1 Bisphosphonate may be used in patients with pain from bone metastasis, in consideration of expected prognosis [2B].
   - *2.3 Epigastric pain due to pancreatic cancer*
     - 2.3.1 Celiac plexus block may be performed in patients with epigastric pain due to pancreas cancer [2A].
   - *2.4 Pain in the thoracic area*
     - 2.4.1 Nerve block (such as epidural block, intercostals nerve block, nerve root block or intrathecal phenol block) may be performed in patients with pain in the thoracic area [2C].

Continued

Table 2. *Continued*

   - *2.5 Perineal pain*
     - 2.5.1 Saddle block or superior hypogastric plexus block may be performed in patients with perineal pain [2C].
   - *2.6 Pain from malignant psoas syndrome*
     - 2.6.1 Muscle relaxants may be used in patients with malignant psoas syndrome [2C].
     - 2.6.2 Nerve block (such as epidural block or nerve root block) may be performed in patients with malignant psoas syndrome [2C].
   - *2.7 Pain from malignant bowel obstruction*
     - 2.7.1 Octreotide or scopolamine butylbromide may be used in patients with pain from malignant bowel obstruction [2B].
     - 2.7.2 Corticosteroids may be used in patients with pain from malignant bowel obstruction [2B].
3. Treatment of adverse events of opioids
   - *3.1 Nausea/vomiting*
     - 3.1.1 Etiology of nausea/vomiting should be assessed, and any reversible etiology should be treated.
     - 3.1.2 Anti-emetics should be used in patients developing nausea/vomiting on opioids. Type of anti-emetics should be chosen from anti-dopaminegics, prokinetics, or antihistaminics [1C].
     - 3.1.3 Type of opioids should be switched to another in patients developing nausea/vomiting on a certain opioid [1B].
     - 3.1.4 Administration route may be changed to intravenous or subcutaneous infusion in patients developing nausea/vomiting on oral opioids [2C].
   - *3.2 Constipation*
     - 3.2.1 Etiology of constipation should be assessed, and any reversible etiology, especially fecal impaction or bowel obstruction, should be treated.
     - 3.2.2 Laxatives should be used in patients developing constipation on opioids [1B].
     - 3.2.3 Type of opioids should be switched to fentanyl in patients on morphine or oxycodone with refractory constipation after laxatives [1B].
   - *3.3 Drowsiness*
     - 3.3.1 Etiology of drowsiness should be assessed, and any reversible etiology should be treated. The possibility of opioid overdose should also be assessed.
     - 3.3.2 Psycho-stimulants may be used in patients developing drowsiness on opioids, in consultation with an expert [2C].
     - 3.3.3 Type of opioids should be switched to another in patients with drowsiness on a certain opioid [1B].
     - 3.3.4 Administration route may be changed to intravenous or subcutaneous infusion in patients developing drowsiness on oral opioids [2C].
   - *3.4 Delirium*
     - 3.4.1 Etiology of delirium should be assessed, and any reversible etiology should be treated.
     - 3.4.2 Anti-psychotics may be used in patients developing delirium on opioids [2B].
     - 3.4.3 Type of opioids should be switched to another in patients with delirium on a certain opioid [1B].
     - 3.4.4 Administration route may be changed to intravenous or subcutaneous infusion in patients developing delirium on oral opioids [2C].
4. Patient education in cancer pain management
   - 4.1.1 Patients should be given education about cancer pain management [1A].

JSPM, Japanese Society of Palliative Medicine

Assessment of Cancer Pain

(i) A comprehensive assessment of the pain should be performed. A comprehensive assessment includes an assessment of the etiology of the pain and that of the pain itself.

The influence of the pain on daily life; the pattern, intensity, location and quality of pain; and the exacerbating/relieving factors should be evaluated. In addition, the response to current treatment and the effectiveness of a rescue dose should be evaluated.

For assessing the etiology of cancer-related pain, it is important to evaluate whether it is directly related to the cancer itself and/or to its treatment. In addition, it is important to evaluate whether the pain is a sign of an oncological emergency and identify its etiology (e.g. neuropathic pain, bone pain and perineal pain). This assessment includes history, physical examinations and imaging studies, and it must lead to a therapeutic approach.

Patients with Mild Pain

(i) Acetaminophen should be administered to cancer patients with mild pain. [1A]

A randomized controlled trial of patients with advanced cancer demonstrated that acetaminophen decreased pain intensity to a significantly greater extent than placebo (24). A Cochrane review also concluded that acetaminophen is more effective than placebo in improving cancer pain (25).

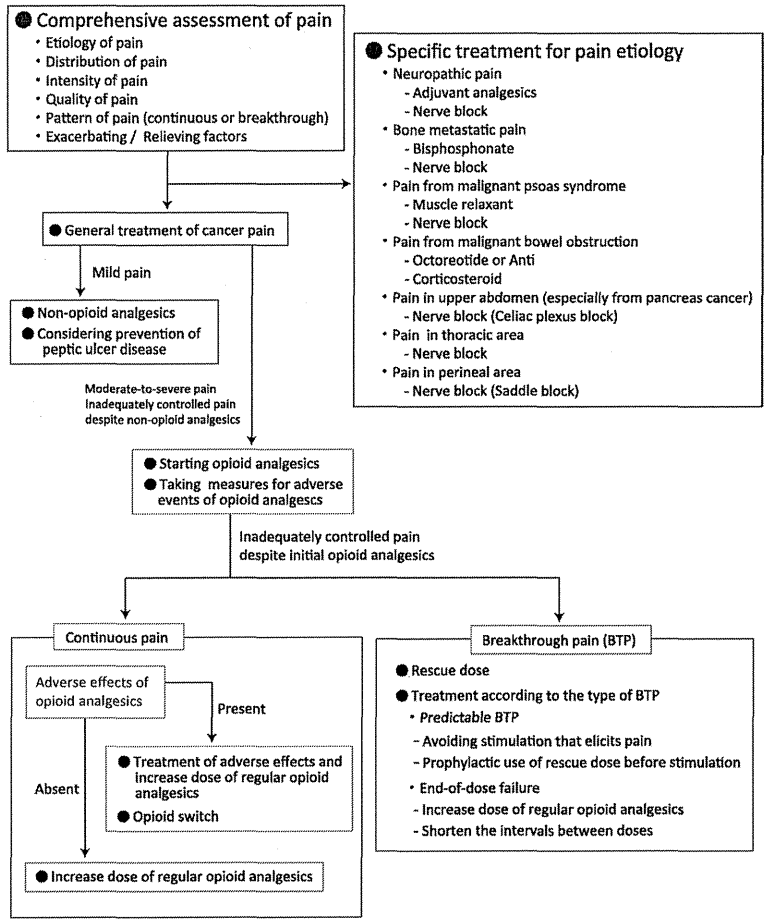

Figure 1. Overview of recommendations.

Because the available evidence shows that acetaminophen decreases pain in cancer patients who are not prescribed any analgesics, the panel has agreed that acetaminophen should be administered to cancer patients with mild pain.

(ii) Non-steroidal anti-inflammatory drugs should be administered to cancer patients with mild pain. [1B]

Several small, randomized controlled trials demonstrated that non-steroidal anti-inflammatory drugs (NSAIDs) decreased pain intensity in cancer patients to a significantly greater extent than placebo (26–28). A recent systematic review, including seven randomized controlled trials, concluded that NSAIDs are more effective than placebo in improving cancer pain (25).

Because the available evidence demonstrates that NSAIDs decrease pain in cancer patients who are not prescribed any analgesics, the panel has agreed that NSAIDs should be administered to cancer patients with mild pain.

(iii) The nonopioid analgesic type should be chosen in accordance with the effectiveness and tolerability of an individual patient. [1A]

Several small studies comparing different nonopioid analgesics demonstrated no significant difference in the effectiveness in treating cancer pain and the incidence of adverse events (29–32). A systematic review concluded that there is no evidence of the superiority of certain nonopioid analgesics over others (25).

Because the available evidence shows no superiority of certain nonopioid analgesics over others in terms of either efficacy or adverse event profile, the panel has agreed that the type of nonopioid analgesic should be chosen in accordance with the effectiveness and tolerability of an individual patient (e.g. renal function, risk of peptic ulcer, and bleeding tendency).

(iv) Prostaglandin E1 analogs, proton pump inhibitors, or H2 receptor blockers should be used for the prevention of peptic ulcer in patients who are treated with an NSAID. [1A]

According to the Evidence-Based Guideline for Gastric Ulcer in Japan (33), the efficacy of prostaglandin E1 analogs, proton pump inhibitors and high-dose H2 receptor blockers for the prophylaxis of NSAID-induced peptic ulcer has been demonstrated in several randomized controlled trials and systematic reviews.

Therefore, prostaglandin E1 analogs, proton pump inhibitors, or H2 receptor blockers should be used for the prevention of peptic ulcer in patients who are treated with an NSAID.

Patients with Moderate-to-severe Pain or Inadequately Controlled Pain Despite Treatment with Nonopioid Analgesics

(i) Opioids should be administered to cancer patients with moderate-to-severe pain or inadequately controlled pain despite treatment with nonopioid analgesics. [1B]

For patients with moderate-to-severe pain or inadequate pain control with a nonopioid analgesic, the World Health Organization (WHO) guideline recommends the use of Step 2 opioids first, and switching to Step 3 opioids (3-step strategy) afterward. Several observational studies have revealed the efficacy of this WHO analgesic ladder (34,35). Therefore, using the three-step strategy is likely to be safe and effective.

On the other hand, two randomized controlled trials demonstrated that using a Step 3 opioid first (two-step strategy) is significantly more effective than using the three-step strategy, in improving cancer pain (36,37). However, some adverse events such as nausea or constipation tended to be more frequent in the two-step strategy group in these studies.

Available evidence suggests that the three-step strategy is effective without troublesome adverse events, and the two-step strategy is more effective than the three-step strategy, but with more adverse events. Therefore, opioids should be administered to cancer patients with moderate-to-severe pain or inadequately controlled pain despite treatment with nonopioid analgesics, using both the three-step and two-step strategies.

(ii) The type of opioid should be chosen individually according to the patient's condition (i.e. availability of administration route, medical complications, coexisting symptoms and pain intensity). [1B]

A Cochrane review including 54 randomized controlled trials concluded that morphine is effective in improving cancer pain (38).

The efficacy of using oxycodone was evaluated in an observational trial including 390 cancer patients with moderate-to-severe pain (39). In this trial, the intensity of pain was significantly decreased after the administration of oxycodone, and there were no serious adverse events. A systematic review of four studies comparing oxycodone and morphine concluded that oxycodone is as effective as morphine in improving cancer pain (40). Also, a recent, small, randomized, controlled trial comparing the effectiveness of sustained-release oxycodone with that of sustained-release morphine in improving cancer pain demonstrated that these two preparations exerted an approximately equivalent analgesic effect (41).

Four randomized controlled trials comparing the efficacy of morphine with that of transdermal or intravenous fentanyl demonstrated no significant difference in analgesic effect between the groups (42–45). Two of these four studies demonstrated that the incidence of constipation was significantly lower in the fentanyl group than in the morphine group. Among the empirical studies using transdermal fentanyl as the initial opioid, two observational studies demonstrated that the intensity of pain decreased in a majority of patients, without the presence of serious adverse events (46,47). A randomized controlled trial comparing the efficacy of transdermal fentanyl with that of sustained-release morphine as the initial opioid in patients with mild-to-moderate pain demonstrated no significant difference in analgesic effect between the groups in the transdermal fentanyl group (48).

Available evidence showed no significant differences between morphine, oxycodone and fentanyl, regarding the efficacy. Therefore, the type of opioids should be chosen individually according to the patient's condition.

The administration route chosen should be the one most convenient and preferable to the patient. In general, the oral route is preferred. In case of difficulty in using the oral route, continuous parenteral infusion or transdermal or rectal routes can be chosen according to patient's preference.

Regarding complications, morphine is best avoided in patients with renal insufficiency because accumulation of active metabolites can lead to adverse events (49). Regarding coexisting symptoms, fentanyl causes constipation less frequently than other opioids (44,45,48); therefore, fentanyl is preferable in patients with severe constipation or those who need to avoid a decrease in bowel movements. Morphine has

been demonstrated to be effective in alleviating dyspnea in cancer patients (50); therefore, morphine is preferable in patients with dyspnea.

Regarding pain intensity, adjusting the dose of transdermal fentanyl within short time intervals is difficult because of its long half-life. Therefore, transdermal fentanyl should not be used as the initial opioid in patients with severe or unstable pain.

(iii) In cancer patients with stable and mild-to-moderate pain, either sustained-release or immediate-release opioids may be used. In cancer patients with severe or unstable pain, immediate-release opioids or parenteral opioids may be used. [2B]

A Cochrane review analyzed 15 randomized controlled trials that compared the efficacy of immediate-release and sustained-release morphine, and concluded that these two formulations are equivalent in terms of analgesic effect and incidence of adverse events, when used as around-the-clock opioids (38). The same result has been demonstrated in a double-blind, randomized controlled trial comparing immediate- and sustained-release oxycodone (51).

Although available evidence suggests that either immediate-release or sustained-release opioids can be used as around-the-clock opioids, patients with severe or unstable pain were excluded from these studies. The panel has agreed that either immediate-release or sustained-release opioids may be used as around-the-clock opioids in patients with mild-to-moderate stable pain, and a rapid titration with immediate-release opioids or parenteral opioids is desirable in patients with severe or unstable pain.

(iv) Patients should be carefully assessed and observed for nausea/vomiting during opioid therapy and antiemetics should be readily available whenever nausea/vomiting occurs. [1C]

Because there are, to date, no clinical trials evaluating the efficacy of prophylactic antiemetics against opioid-induced nausea/vomiting, current evidence of prophylactic antiemetic use remains insufficient.

On the basis of panel consensus, this guideline recommends that patients should be observed carefully for the development of nausea/vomiting during opioid therapy, and that antiemetics should be prescribed as required when nausea/vomiting occurs. Once opioid-induced nausea/vomiting develops, antiemetics should be continued for 1 to 2 weeks because tolerance to opioid-induced nausea/vomiting may develop within 1 to 2 weeks after initiating opioid therapy.

The type of antiemetic can be chosen from dopamine antagonists (e.g. haloperidol, prochlorperazine), gastrointestinal prokinetic agents (e.g. metoclopramide) or antihistamine drugs.

(v) Patients should be carefully assessed and observed for constipation during opioid therapy; moreover, they should be provided with instructions regarding adequate fluid intake, diet and laxatives for the prevention of constipation. [1C]

To date, there have been no clinical trials evaluating the efficacy of prophylactic laxative use for opioid-induced constipation. Despite insufficient evidence, on the basis of the panel consensus, this guideline recommends that patients should be carefully assessed and observed for constipation during opioid therapy, and that they should be provided with instructions regarding adequate fluid intake, diet, and laxatives as preventive measures against constipation, considering its high prevalence with chronic opioid therapy.

(vi) Nonopioid analgesics may be continued when opioids are introduced in patients with inadequate pain control by nonopioid analgesics. [2B]

A double-blind, randomized controlled trial demonstrated that the addition of ibuprofen to oxycodone/acetaminophen therapy provided significantly better analgesic effects compared with placebo in cancer patients with pain from bone metastasis (52). In addition, another small, double-blind, crossover, randomized controlled trial demonstrated that the addition of a diclofenac suppository to regular parenteral morphine therapy provided significantly better analgesic effects than placebo in cancer patients (53). Furthermore, another open-label, randomized controlled trial demonstrated that the addition of oral ketorolac to regular morphine therapy showed an insignificant but better analgesic effect compared with morphine only (54). In this trial, dose escalation of morphine was significantly slower, whereas the maximum morphine dose was significantly lower in the ketorolac group. Ketorolac use tended to decrease opioid-related constipation but increased gastric discomfort. Another small, randomized controlled trial demonstrated that compared with the addition of placebo, the addition of acetaminophen showed a small but significantly better analgesic effect in cancer patients administered opioids (55).

Available evidence suggests that the use of a nonopioid analgesic combined with an opioid is more effective than using an opioid alone, despite the possibility of increasing incidence of gastric discomfort. We have therefore concluded that in patients with inadequately controlled pain despite treatment with nonopioid analgesics, nonopioid analgesics may be continued when opioids are introduced.

Patients with Inadequately Controlled Pain Despite Initial Opioid Use

(i) Nonopioid analgesics should be used concurrently with opioids in patients who experience continuous pain with regular opioid use. [1A]

As previously mentioned, four randomized controlled trials comparing the combined use of nonopioid analgesics and opioids with the use of opioids alone demonstrated the superiority of the combination in producing an analgesic effect (52–55).

Available evidence shows that the addition of a nonopioid analgesic decreases residual continuous pain in patients receiving only a regular opioid. However, because the analgesic effect of nonopioid analgesics is at most moderate and their long-term use may result in several adverse events, the decision of adding nonopioid analgesics to regular opioid therapy should be made after carefully weighing the benefits of the analgesic effect against the risk of adverse events.

(ii) The dose of regular opioids should be increased in patients who experience continuous pain with regular opioid use. [1B]

Although to date, no clinical trials have compared the amount of increase in regular opioid dose and the interval between increments, several observational studies have demonstrated that the increase strategy based on the WHO method for cancer pain relief provided adequate pain relief (34,35).

Therefore, available evidence suggests that increasing the dose of regular opioids provides pain relief in patients with residual continuous pain despite regular opioid use. When increasing the dose of regular opioids, an increase of 30–50% of the regular daily dose is recommended. However, the total amount of rescue medication required on the previous day must be considered. With regard to the interval between doses, an interval of 24 h for immediate-release opioids or parenteral opioids, 48 h for sustained-release opioids and 72 h for transdermal fentanyl is recommended according to their expected time to achieve steady-state. In cases of severe pain that require prompt analgesia, parenteral opioids or immediate-release opioids are the desirable administration routes.

(iii) The type of opioid should be switched in patients with inadequate pain control with a certain type of opioids. [1B]

A systematic review of 21 observational studies concluded that opioid switching was an effective measure to improve the balance between analgesia and adverse events as a whole (56,57). The studies included in this analysis mainly evaluated the switch from morphine to oxycodone or fentanyl.

Therefore, available evidence suggests that opioid switching could improve analgesic effects and decrease adverse events in cancer patients with inadequate pain control with a certain type of opioid.

(iv) Another type of opioid may be added in patients with inadequate pain control with a certain type of opioid, after consultation with pain or palliative care specialists. [2C]

One observational study evaluating the effectiveness of opioid combination therapy in improving analgesic effects demonstrated that the addition of a second opioid decreased pain intensity without increasing adverse events in cancer patients with inadequate pain control after an increase in the dose of regular opioids (58).

Although the addition of another opioid may provide better analgesic effects in cancer patients with inadequately controlled pain, the present evidence is insufficient. In addition, the concurrent use of different types of opioids may affect compliance. The panel has concluded that after consultation with pain or palliative care specialists, another type of opioid may be added to patients with inadequate pain control with a certain type of opioid.

(v) The administration route may be changed to intravenous or subcutaneous infusion in patients with inadequate pain control with an oral or a transdermal preparation of opioid analgesics. [2C]

Two observational studies evaluating the efficacy of changing to a continuous parenteral route demonstrated that this change decreased pain intensity, decreased adverse events and improved the quality of life in cancer patients with inadequate pain control with oral morphine or transdermal fentanyl (59,60).

Therefore, changing to a parenteral route may facilitate an improvement in the analgesic effect in cancer patients with inadequate pain control with oral or transdermal opioids.

(vi) Ketamine may be used in combination with opioids in patients with inadequately controlled pain after a sufficient increase in opioid dose, after consultation with pain or palliative care specialists. [2B]

A systematic qualitative review including two randomized controlled trials to evaluate the efficacy of ketamine provided a modest conclusion that ketamine had a potential efficacy when used as an adjuvant to opioids for cancer pain (61).

Although the use of ketamine as an adjuvant to opioids may provide better analgesic effects in cancer patients with inadequately controlled pain after a sufficient increase in opioid dose, the present evidence is insufficient. In addition, using ketamine may increase central nervous system (CNS) side effects. The panel has concluded that, after consultation with pain or palliative care specialists, ketamine may be added in patients with inadequately controlled pain after a sufficient increase in opioid dose.

(vii) Corticosteroids may be used in combination with opioids for particular pain etiologies, paying careful attention to the risk of adverse reactions in patients who experience pain after a sufficient increase in opioid dose. [2C]

A small, randomized controlled crossover trial demonstrated that pain intensity in patients with advanced cancer decreased after the administration of methylprednisolone with weak opioids (62). On the other hand, another randomized controlled trial demonstrated that, whereas dexamethasone provided a short-term benefit for gastrointestinal adverse events and improved a patient's sense of well-being, pain intensity was not significantly different between dexamethasone–opioid combination therapy and opioid monotherapy in cancer patients with moderate-to-severe pain (63).

Therefore, there is insufficient evidence for the efficacy of corticosteroids in combination with opioids. However, corticosteroids are considered to decrease the intensity of pain caused by a specific etiology such as spinal cord compression, inflammation, increased intracranial pressure and bone metastasis. Corticosteroids can be used in combination with opioids for pain caused by such etiologies if careful attention is paid to adverse events from long-term corticosteroid use (e.g. hyperglycemia, peptic ulcer, immune suppression, Cushing's syndrome, etc.). Corticosteroids should be continued at the minimum effective dose, and should be tapered and discontinued, when ineffective.

Patients with Breakthrough Pain

(i) The rescue dose of opioids should be used in patients with breakthrough pain. [1B]
(ii) The rescue dose may be increased if adverse events are acceptable and the initial rescue dose provide inadequate analgesic effects. [2C]

Although a Cochrane review on the management of breakthrough pain concluded that a rescue dose was effective for such pain, this systematic review primarily analyzed studies of oral transmucosal fentanyl citrate, which is not available in Japan (64). Although randomized placebo-controlled trials to evaluate the efficacy of oral and parenteral opioids are lacking, there are three observational studies evaluating the efficacy of a rescue dose of subcutaneous or intravenous opioids for breakthrough pain, and two randomized controlled trials of oral transmucosal fentanyl citrate that used oral and intravenous opioids as a control treatment (65–69).

A sub-analysis of a rescue dose of oral morphine in a randomized controlled trial demonstrated that immediate-release morphine caused a clinically significant decrease in breakthrough pain, and the mean intensity of pain decreased 60 min after administration (65). Two observational studies and a sub-analysis of a rescue dose of intravenous morphine in a randomized, controlled trial demonstrated that intravenous morphine caused a clinically significant improvement of breakthrough pain in a majority of patients (66–68). An observational trial demonstrated that subcutaneous morphine relieved breakthrough pain within 10 min in a majority of patients (69). In these studies, serious adverse events were rare.

Therefore, available evidence suggests that using a rescue dose ameliorates breakthrough pain in cancer patients receiving regular opioid doses.

The dosage used in current studies corresponded to 10–20% of the daily regular opioid dose, regardless of the administration route. These trial results suggest that this dose is safe and effective, and the panel has agreed that the starting dose of a rescue opioid should be 10–20% of the daily regular opioid dose when oral immediate-release opioids are used. On the other hand, for patients on continuous parenteral opioids, a 1 h bolus dose of regular parenteral opioid is traditionally used in Japan; therefore, the panel has recommended the 1 h bolus administration in patients on continuous parenteral opioids.

A clinical trial showed that an adequate dose of the rescue opioid would not be completely correlated with the total daily dose of regular opioids (65). Therefore, the panel has agreed that the dosage of the rescue opioid should be increased and adjusted individually if adverse events are acceptable and the initial dose provides inadequate analgesic effects.

(iii) For patients with 'end-of-dose failure,' the dose of regular opioids should be increased or the interval of regular opioid administration should be shortened [1B]

A small, randomized controlled trial comparing the effects of a dose of immediate-release morphine administered every 4 h with those of a bedtime double dose demonstrated that the pain intensity at night and the next morning as well as the requirement of a rescue opioid at night were significantly lower in the 4-h group (70). On the other hand, a small, randomized controlled trial comparing the same groups demonstrated that the pain intensity was not significantly different between the groups (71).

Although available evidence is insufficient to conclude whether an increase in the dose of regular opioids or shortening the dosing interval of regular opioids is appropriate to ameliorate 'end-of-dose failure,' the panel agreed that both the strategies can be used in cancer patients with 'end-of-dose failure' who are using regular immediate-release opioids.

There are no trials evaluating the efficacy of these 2 strategies in patients using regular sustained-release opioids. However, an increase in the dose of regular opioids presumably maintains effective blood concentration and improves 'end-of-dose failure' in patients using regular sustained-release opioids because of their prolonged duration of action. Therefore, the dose of regular opioids can be increased in cancer patients with 'end-of-dose failure' who are using regular sustained-release opioids. The dosing interval can be shortened when an increase in the dose of regular opioids is not effective or causes an adverse event.

Neuropathic Pain in Cancer Patients

(i) Adjuvant analgesics (e.g. anticonvulsants, antidepressants, antiarrhythmics, *N*-methyl-D-aspartate (NMDA) receptor antagonist or corticosteroids) may be used in cancer patients with neuropathic pain. [2B]

(a) Anticonvulsants

Two randomized, controlled trials evaluating the efficacy of gabapentin in cancer patients with neuropathic pain demonstrated that gabapentin as an adjuvant to opioids demonstrated a significantly better analgesic effect against neuropathic pain compared with placebo (72,73). Drowsiness was more frequent in the gabapentin group in both the studies. Also, in noncancer patients, a recent Cochrane systematic review concluded that gabapentin demonstrated a moderate analgesic

effect against neuropathic pain, with adverse effects such as dizziness, drowsiness and headache (74). Other than gabapentin, a randomized controlled trial comparing three arms (buprenorphine alone, phenytoin alone or buprenorphine and phenytoin) did not show any difference in analgesic effect among the three arms in cancer patients with neuropathic pain (75). A small, observational trial evaluating the efficacy of valproate as an adjuvant to opioids in cancer patients with neuropathic pain demonstrated that 56% patients exhibited a decrease in pain intensity (76). Another small, observational trial evaluating the efficacy of clonazepam as an adjuvant to opioids in cancer patients with neuropathic pain demonstrated that although the mean pain intensity decreased from three to one in five patients who completed the study protocol, another five patients dropped out because of worsening pain or drowsiness (77).

Therefore, available evidence suggests that gabapentin improves neuropathic pain in cancer patients. Although some other anticonvulsants may improve neuropathic pain in cancer patients, current evidence for the efficacy of these agents is insufficient.

(b) Antidepressants

A randomized controlled, crossover trial comparing the efficacy of amitriptyline, a tricyclic antidepressant (TCA), as an adjuvant to opioids with that of placebo in cancer patients with neuropathic pain showed that amitriptyline caused a small but significant improvement in maximum pain intensity (78). However, the incidence of adverse effects, such as drowsiness, confusion and dry mouth, was also significantly higher with amitriptyline. In noncancer patients, a recent Cochrane systematic review concluded that TCAs and venlafaxine, a serotonin norepinephrine reuptake inhibitor (SNRI), are effective for achieving at least moderate pain relief in patients with neuropathic pain (79).

Although available evidence is insufficient to establish the efficacy of antidepressants in cancer patients with neuropathic pain, on the basis of data from patients without cancer, TCAs and SNRIs can be used as an adjuvant to opioids in cancer patients with neuropathic pain.

(c) Antiarrhythmics

A randomized, controlled trial evaluating the efficacy of lidocaine (2 mg/kg by bolus infusion followed by a 2 mg/kg drip infusion for 1 h) for the treatment of opioid-refractory neuropathic and other types of pain in cancer patients demonstrated that lidocaine provided a significantly better analgesic effect compared with placebo, with minor adverse effects such as tinnitus and perioral numbness (80). In contrast, two small, randomized controlled, crossover trials evaluating the efficacy of lidocaine in cancer patients with neuropathic pain demonstrated no significant analgesic effect (81,82).

In noncancer patients, a recent Cochrane systematic review concluded that lidocaine and other oral analogs demonstrated better analgesic effects in cancer patients with neuropathic pain compared with placebo, and were as effective as other analgesics (83).

Although the results of available evidence are conflicting and insufficient, the panel concluded that, on the basis of data from patients without cancer, antiarrhythmics may be used as adjuvants to opioids in cancer patients with neuropathic pain.

(d) NMDA receptor antagonists

A small, randomized, controlled, crossover trial evaluating the efficacy of ketamine against opioid-refractory neuropathic or mixed pain in cancer patients demonstrated that ketamine demonstrated a significantly better analgesic effect compared with placebo, with moderate adverse effects such as hallucination and sensation of insobriety (84). In two other small observational studies, ketamine demonstrated a clinically significant decrease in opioid-refractory neuropathic pain in 61–77% patients with cancer (85,86).

Although available evidence is insufficient and there is a well-documented risk of a CNS adverse effect, ketamine may be used as an adjuvant to opioids in cancer patients with opioid-refractory neuropathic pain.

(e) Corticosteroids

Although to date, no clinical trials have evaluated the efficacy of corticosteroids in the treatment of neuropathic pain in cancer patients, corticosteroids are considered to improve the intensity of pain caused by a specific etiology such as spinal cord compression, nerve compression or inflammation.

The panel agreed that corticosteroids can be used as an adjuvant to opioids for neuropathic pain caused by spinal cord compression, other nerve compression by tumor invasion or inflammation in the nervous system.

DISCUSSION

We reported the summary of recommendations of a new Japanese clinical guideline for the management of cancer pain. Although we used a formal evidence-based methodology for constructing this clinical guideline, a majority of the recommendations are based on poor-quality controlled trials, observational studies or expert opinions. This finding confirms that a worldwide effort for conducting well-designed, controlled trials is essential for improving the clinical guideline and management of cancer pain. During our efforts, the European Association of Palliative Care guideline was recently published (16). In this guideline, the key messages and recommendations are essentially the same as in the Japanese guideline; but their recommendation levels are generally weak because of the lack of confirmatory evidence in the majority of fields. The results highlight the importance of conducting well-designed, controlled trials to identify the best practice in cancer pain management.