Table 1 Subject characteristics (N = 134)

	Number of respondents (n)	% of total	Mean	SD	Median	Range
Age of children at survey (years)	134		11.1	3.7	11.0	5–18
Age at diagnosis (years)	134		7.3	4.5	7.0	0-18
Time from diagnosis (months)	134		45.8	41.6	37.0	1-202
Gender						
Male	73	54.9				
Female	60	45.1				
Tumor pathology						
Embryonal tumors	39	29.5				
Germ cell tumors	35	26.5				
Low-grade glioma	31	23.5				
High-grade glioma	15	11.4				
Other	12	9.1				
Treatment status						
On treatment	53	39.6				
Off treatment	81	60.4				
Time from treatment end (months)	79		44.7	37.1	34.0	1-160
Treatment received						
None	2	1.5				
Surgery (S)	15	11.2				
Radiation (R)	0	0.0				
Chemotherapy (C)	3	2.2				
S + R	13	9.7				
S + C	18	13.4				
R + C	4	3.0				
S + R + C	79	59.0				
Relationship of parent to child						
Mother	126	94.0				
Father	6	4.5				
Grandmother	1	0.7				
Grandfather	1	0.7				
Age of parents at survey (years)	133		41.0	5.5	41.0	26-63
Academic background of parents						
High schools						
Junior high school	1	0.8				
Senior high school	50	38.2				
Colleges and universities						
Vocational college	25	19.1				
Junior college	24	18.3				
University (undergraduate)	30	22.9				
University (graduate)	1	0.8				
Parents' time with children (hours per a day			13.1	6.5	14.0	1–24
Subjective opinion regarding parents' own e						
Affluent	84	63.6				
Not affluent	48	36.4				
Method of administration for children						
Self-administered	89	66.4				
Interviewer-administered		==::				
Interviewed by researcher	31	23.1				



Table 1 continued

	Number of respondents (n)	% of total	Mean	SD	Median	Range
Interviewed by parent	14	10.4				
State anxiety score of STAIC ^a (20-60)	104		29.9	7.8	29.0	20-52
Trait anxiety score of STAIC ^a (20-60)	97		34.9	8.8	36.0	20-52
K10 ^b score (0–40)	132		7.7	7.0	6.0	0-31
PedsQL global HRQOL score ^c (0-100)						
Self-reported	132		77.7	17.2	80.4	11-100
Parent-reported	134		73.7	17.0	75.0	20-100

Missing data were excluded

HRQOL health-related quality of life, SD standard deviation

- ^a State Trait Anxiety Inventory for Children. A higher score indicates that children have higher anxiety
- ^b Kessler-10. A higher score indicates that parents have higher psychological distress
- ^c Pediatric Quality of Life Inventory Generic Core Scales. A higher score indicates that children have higher quality of life

Table 2 Percentage-explained variance in an MTMM model of HRQOL (N = 134)

Subscales of PedsQL brain tumor module	Condition	Perception	Error
Cognitive problems			
Child	30	27	43
Parent	71	6	24
Pain and hurt			
Child	35	8	57
Parent	41	12	47
Movement and balance			
Child	45	23	32
Parent	96	3	1
Procedural anxiety			
Child	98	2	0
Parent	41	5	54
Nausea			
Child	95	5	0
Parent	43	19	37
Worry			
Child	48	14	38
Parent	7	45	48

HRQOLhealth-related quality of life, MTMM multitrait-multimethod, PedsQL Pediatric Quality of Life Inventory

down procedure excluded the method of administration as an independent variable related to the children's perception.

Trait anxiety was the strongest factor related to children's perception (r=-0.46, b=-0.43). Children with higher trait anxiety had lower perception about HRQOL (P<0.05). Older children or children from less affluent families also had a lower perception, but these results were not statistically significant. Bivariate analysis showed that children with higher state anxiety had a lower perception about HRQOL; however, this result was not confirmed on multivariate analysis and was therefore determined to be a spurious correlation. This indicates that the relationship between state anxiety and a child's perception is superficial. This relationship was clarified by conducting a staged analysis to identify which covariates attenuated the relationship (Table 5), which found that trait anxiety attenuated the relationship.

With regard to children aged 5–7 years, none of the variables tested were found to be significantly correlated with the children's perception; the strongest relationship was "interviewer" (r = -0.27, P = 0.162, n = 28). Children interviewed by a parent tended to have a lower perception about HRQOL than children interviewed by researcher.

The strongest factor influencing a parent's perception was treatment status (Table 6). The parents of children on treatment had a tendency to report that their child had a

Table 3 Correlation between calculated scores of perception and reported global HRQOL (N = 134)

	Child-report	ted global HRQOL	Parent-reported global HRQOI		
	r	P	\overline{r}	P	
Calculated scores of child's perception about HRQOL	0.55	<0.001	0.07	0.404	
Calculated scores of parent's perception about HRQOL	0.10	0.251	0.49	< 0.001	

 HRQOL health-related quality of life, r Spearman's rank correlation coefficient



Table 4 Factors related to calculated scores of children's perception about HRQOL (N = 134)

	n	r	95% CI	b	95% CI
Trait anxiety score of STAIC ^a	97	-0.46*	(-0.60, -0.29)	-0.43*	(-0.60, -0.25)
State anxiety score of STAIC ^a	104	-0.27*	(-0.44, -0.08)	_	
Age at survey	133	-0.14	(-0.30, 0.03)	-0.17	(-0.35, 0.01)
Age at diagnosis	134	0.01	(-0.16, 0.18)	_	
Time from diagnosis	134	-0.09	(-0.26, 0.08)	_	
Gender (0: Male, 1: Female)	133	0.02	(-0.15, 0.19)		
Treatment status (0: on treatment, 1: off treatment)	134	-0.06	(-0.23, 0.11)		
Subjective opinion regarding parents' own economic status and life (0: not affluent, 1: affluent)	132	0.07	(-0.10, 0.24)	0.16	(-0.01, 0.34)
Method of administration for children (0: self-administered, 1: interviewer-administered)	134	-0.06	(-0.23, 0.11)	-	
Dummy-coded variable for comparison between researcher into	rviews an	d parent inter	views		
Researcher interviews ^b	134	0.03	(-0.14, 0.20)	_	
Parent interviews ^c	134	-0.13	(-0.29, 0.04)	_	

HRQOL health-related quality of life, CI confidence interval, r Spearman's rank correlation coefficient, b Standardized partial regression coefficient by multiple linear regression analysis (n = 96, $R^2 = 0.264$)

Table 5 Factors that attenuate the relationship between children's state anxiety and lower perception about HRQOL (N = 96)

	b	b	b	<i>b</i>	b
State anxiety score of STAIC ^a	-0.29*	-0.12	-0.24*	-0.26*	-0.06
Trait anxiety score of STAIC ^a		-0.40*			-0.39*
Age at survey			-0.17		-0.17
Subjective opinion regarding parents' own economic status and life (0: not affluent, 1: affluent)				0.11	0.14

HRQOL health-related quality of life, b Standardized partial regression coefficient by multiple linear regression analysis

lower HRQOL than those of children who were off treatment. The parents with higher K10 scores who were high school graduates also had a lower perception about their child's HRQOL lower than those parents with lower K10 scores who were college or university graduates. Other variables (age, gender, time with the child per day, and subjective opinion regarding economic status and life) had no influence on a parent's perception about HRQOL.

The sensitivity analysis identified significant differences in the following parameters between child- and parent-reported scores: trait anxiety, parent's psychological distress, treatment status, or academic background of parents (Table 7). Children with elevated trait anxiety rated their HRQOL much lower on average, thereby reducing the difference between child- and parent-reported scores (Fig. 5). Parents with elevated K10 scores, those of

children on treatment, and those who were high school graduates also scored their child's HRQOL much lower than did their children themselves, thus increasing the difference between child- and parent-reported scores. Multiple regression analysis also demonstrated that the child's trait anxiety and parent's K10 score were related to the differences between child- and parent-reported HRQOL (Table 8). The relationship between these differences and the child's treatment status and parent's academic background was not statistically significant.

Differences between self- and interviewer-administered child-reports

The method of administration induced indirect effects, which resulted in a decrease of 1.1–2.5 points in child-

^{*} *P* < 0.05

⁻ variables not selected by step-down procedure

a State Trait Anxiety Inventory for Children. A higher score indicates that children have higher anxiety

^b 0: self-administered or parent-administered, 1: researcher-administered

^c 0: self-administered or researcher-administered, 1: parent-administered

^{*} *P* < 0.05

^a State Trait Anxiety Inventory for Children. A higher score indicates higher anxiety

Table 6 Factors related to calculated scores of parents' perception about child's HRQOL (N = 134)

	n	r	95% CI	b	95% CI
K10 score ^a	132	-0.24*	(-0.40, -0.07)	-0.21*	(-0.37, -0.04)
Treatment status (0: on treatment, 1: off treatment)	134	0.36*	(0.20, 0.50)	0.26*	(0.09, 0.43)
Gender of parents (0: Male, 1: Female)	134	0.05	(-0.12, 0.22)	_	
Age of parents at survey	133	-0.14	(-0.30, 0.03)	_	
Academic background of parents (0: high schools, 1: colleges and universities)	131	0.16	(-0.01, 0.32)	0.17*	(0.00, 0.34)
Parents' time with children per a day	132	-0.04	(-0.21, 0.13)	_	
Subjective opinion regarding parents' own economic status and life (0: not affluent, 1: affluent)	132	0.14	(-0.03, 0.30)	-	• .

Missing data were excluded

HRQOL health-related quality of life, CI confidence interval, r Spearman's rank correlation coefficient, b Standardized partial regression coefficient by multiple linear regression analysis

Table 7 Descriptive statistics of the differences and correlation between child- and parent-reported HRQOL (N = 134)

	n	HRQOL	a,			Difference ^b	95%	CI	Pearson's correlation coefficient
		Child-re	ported	Parent-r	eported				
		Mean	SD	Mean	SD				
Trait anxiety score of STAIG	C°								
Less than 36 (median)	48	85.8	10.2	77.1	14.9	8.7	4.3	13.2	0.30*
36 or over	49	77.3	12.9	72.2	15.7	5.2	1.9	8.5	0.69*
K10 score ^d									
Less than 6 (median)	65	83.0	12.7	79.2	12.2	3.8	0.6	6.9	0.47*
6 or over	67	75.7	15.6	65.9	15.9	9.8	6.3	13.3	0.58*
Treatment status									
On treatment	53	75.5	15.4	66.2	15.2	9.4	5.5	13.3	0.57*
Off treatment	81	81.5	13.6	76.9	14.6	4.6	1.5	7.7	0.52*
Academic background of par	rents								
High schools	51	79.1	13.9	70.1	14.9	9.0	2.0	13.0	0.53*
Colleges and universities	80	78.9	15.2	74.3	15.7	4.6	1.7	7.5	0.64*

Missing data were excluded

HRQOL health-related quality of life, CI confidence interval, SD standard deviation

reported scores for the PedsQLTM Brain Tumor Module (Table 9). For all subscales, interviewer-administration scores were lower than child-reported scores. However,

given that the 95% CIs included values of zero, the method of administration appears to have little effect on children's perception. This result was similar to that obtained on



^{*} *P* < 0.05

⁻ variables not selected by step-down procedure

^a Kessler-10. A higher score indicates that parents have higher psychological distress

^{*} P < 0.05

^a Mean of six subscale scores of PedsQL Brain Tumor Module

^b "child-reported mean HRQOL score" minus "parent-reported mean HRQOL score"

^c State Trait Anxiety Inventory for Children. A higher score indicates higher anxiety

^d Kessler-10. A higher score indicates that parents have higher psychological distress

Fig. 5 Differences between child- and parent-reported mean scores of six subscales of PedsQL Brain Tumor Module by socio-demographic and health characteristics

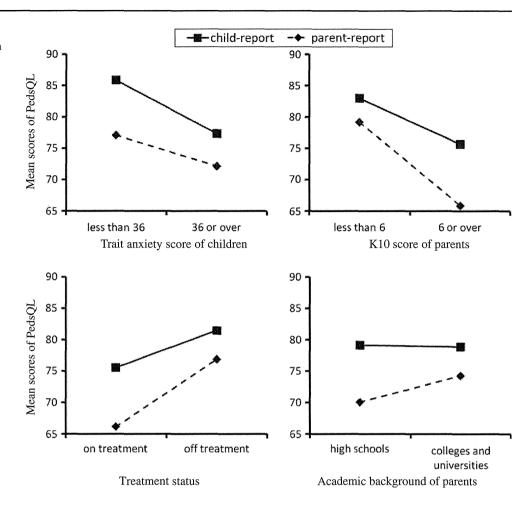


Table 8 Regression of the differences between child- and parent-reported HRQOL (N = 134)

	n	r	95% CI	b	95% CI
Trait anxiety score of STAIC ^c	97	-0.21*	(-0.39, -0.01)	-0.27*	(-0.47, -0.07)
K10 score ^d	132	0.21*	(0.04, 0.37)	0.29*	(0.09, 0.49)
Treatment status (0: on treatment, 1: off treatment)	134	-0.15	(-0.31, 0.02)	-0.13	(-0.33, 0.06)
Academic background of parents (0: high schools, 1: colleges and universities)	131	-0.14	(-0.30, 0.03)	-0.13	(-0.33, 0.06)

Missing data were excluded

CI confidence interval, HRQOL health-related quality of life, r Spearman's rank correlation coefficient, b Standardized partial regression coefficient by multiple linear regression analysis (n = 93, $R^2 = 0.168$)

analysis of factors related to children's perception (Table 4).

In contrast, children receiving interviewer-administered surveys had significantly lower scores for cognitive problems, pain and hurt, and movement and balance subscales than those who were self-administered (Table 9).

Discussion

We show that the response of children aged 5-18 to questions on HRQOL was altered by trait anxiety, while a parent's perception about their child's HRQOL was affected by the child's treatment status and the parent's



^{*} P < 0.05

^a "child-reported mean HRQOL score" minus "parent-reported mean HRQOL score"

^b Mean of six subscale scores of PedsQL Brain Tumor Module

^c State Trait Anxiety Inventory for Children. A higher score indicates higher anxiety

^d Kessler-10. A higher score indicates that parents have higher psychological distress

Table 9 Changes in child-reported HROOL score based on method of administration (N = 134)

	Direct effec	t	Indirect effect					
	\overline{D}	95% CI	I	95% CI	I1	I2		
Cognitive problems	-6.4	(-12.0, -0.8)	-2.5	(-7.5, 2.5)	-0.14	18.1		
Pain and hurt	-7.9	(-13.8, -1.9)	-1.3	(-3.8, 1.3)	-0.14	9.2		
Movement and balance	-12.6	(-19.3, -6.0)	-2.5	(-7.6, 2.6)	-0.14	18.3		
Procedural anxiety	-8.8	(-19.4, 1.8)	-1.1	(-3.5, 1.3)	-0.14	8.1		
Nausea	-2.6	(-9.8, 4.6)	-1.1	(-3.5, 1.2)	-0.14	8.2		
Worry	-0.6	(-8.0, 6.8)	-2.1	(-6.4, 2.2)	-0.14	15.3		

CI confidence interval, HRQOL health-related quality of life, D path coefficients from the method of administration to child-reported HRQOL, I indirect effect from the method of administration to child-reported HRQOL, II path coefficients from the method of administration to child-reported HRQOL path coefficients from the children's perception, I2 path coefficients from the children's perception to child-reported HRQOL

own psychological distress and academic background. Interestingly, children's HRQOL scores from self- and interviewer-administered reports were comparable, showing that the results from bivariate and multivariate analyses were not biased by the method of administration. This important result suggests interviewer measurement of HRQOL for children who are unable to self-administer the questionnaire is valid.

The correlation coefficient between the method of administration and tendency for children to score their own HRQOL highly was -0.06 (95% CI -0.23 to 0.11). Given that correlation coefficients >0.1 are regarded as small, >0.3 as medium and >0.5 as large [37], this finding suggests that the method of questionnaire administration has only a small effect on the assessment of children's perception.

All scales of PedsQLTM were scored from 0 to 100, and the actual difference in child-reported score resulting from administration method ranged from -2.5 to -1.1 points. The US Department of Health suggests methods for inferring minimum clinically significant difference (MID) [38]. Using an empirical rule (e.g., 8% of the theoretical range of scores), the MID in a PedsQLTM score is 8 points. Using a distribution-based approach (e.g., defining the MID as 0.5 times the standard deviation), the MID in the PedsQL[™] Brain Tumor Module scores reported a range from 9.2 to 17.2 points [24]. Other authors used a standard error of measurement approach to determine the MID for the PedsQLTM Generic Core Scales child-report was 4.4 [39]. Taken together, these previous findings suggest that the difference in child-reported score resulting from administration method in the present study, while not negligible, is not comparatively significant. As such, we feel confident in adopting an administration method for monitoring HROOL in clinical settings best adapted to the environment.

Similarly, results for previous comparisons of administration methods show small differences albeit in opposing

directions. Huguet and Miro, using a Catalan version of PedsQLTM, reported that interviewer-administered scores were 2 points higher than self-administered scores [40]. In their assessment of very low birth weight children aged 14 years by the TACOOL, Verrips et al. [41] found that the interviewer-administered scores were 2 points lower than the self-administered score, whereas Tsakos et al. [42] found no significant difference between self- and interviewer-administered scores for oral HROOL. Taken together, the findings from the present and previous studies suggest little difference between self- and intervieweradministered scores for child-reporting. Differences between findings for these present and previous studies may be due to differing criteria for HRQOL measured or differences in the children's diseases. To our knowledge, our present study is the first to report that the scores of self- and interviewer-administered questionnaires for HRQOL in children with brain tumors using PedsQL are comparable.

Consistent with results for other children with cancer [14], we also found that trait anxiety alters children's own perception about HRQOL. As trait anxiety has a greater effect than the other factors, it should be considered in the interpretation of child-reported scores. Given that trait anxiety is one personality characteristic that does not vary substantially over time [28], if self-reported scores from repeated measurements of a child with a brain tumor are consistently lower than parent-reported scores, the measured result may be attributed to high trait anxiety of the child.

The effect of treatment status on a parent's perception about their child's HRQOL has not been previously investigated. Parents of children on treatment tended to have a lower perception about their child's HRQOL than those of children off treatment, whereas treatment status had no influence on children's perception. As a result, clinical practice or research should use both child- and parent-reports whenever possible, particularly when



HRQOL questionnaires are needed to assess HRQOL variations during the course of treatment, changes in environment, or psychosocial intervention. For example, HRQOL reports from parents and children changed at 1, 6, and 12 months after diagnosis of brain tumor [19]. The pattern of child-reported HRQOL was different from parent-reported HRQOL over time indicating the importance of using use both child- and parent-reports.

Parents may feel a stronger impact of their child's illness than the child himself or herself [43]. In previous studies, parent-reported HRQOL scores were higher than child-reported scores for children without health problems and lower than child-reported scores for children with health problems. Our study also suggests that parents are more aware of their child's treatment through knowledge of tumor symptoms and treatment pain. In other words, the parents may feel a stronger impact of their child's treatment than the child himself or herself and accordingly tend to score the HRQOL of these children lower than the parents of children off treatment.

Vance et al. [44] suggested that parent-reported HRQOL was not influenced by parent's depression. The present study, however, which had a larger sample size than previous studies, found that the parent-reported HRQOL was affected by the parent's own psychological distress. This suggests that the parent's own prospects and cognitive tendency influence their perception about their child's HRQOL.

The present study is the first to use an MTMM model to identify factors that influence child or parent perception about HROOL. This knowledge will be useful in interpreting the discordance between child- and parent-reports of HROOL in children with brain tumors. In clinical settings, this finding will allow clinicians to take high trait anxiety in the child or high psychological distress in the parent into account. For example, when the child is off treatment, it will be less surprising that child-reported HRQOL score is low and parent-reported HRQOL score is high if the child has low trait anxiety. Routine measurements in clinical settings thus have the potential to allow the monitoring of both the child's personality and the mental state of his/her parents. This finding will also improve the selection of children for comparison of HRQOL among multiple groups. For example, in non-randomized controlled trials, children may be allocated among groups with consideration to equality of anxiety in children and mental health in parents. Our findings also suggest that single group studies should collect information on parents' academic background as well as other demographic characteristics, such as gender, age, race, etc., that influence selection bias.

Several limitations to our study warrant mention. First, as a cross-sectional study, changes in perception over time were not tested. Accordingly, we cannot conclude that the

perception of a parent or child with a brain tumor will change at the end of treatment. Clarification of intrapersonal change in perception or response shift of children with brain tumors and their parents will require a longitudinal study.

Second, we did not conduct an a priori sample size calculation because this study is a part of another study [24] that has a predetermined sample size. The effect of sample size was calculated by G*Power software [45]. If a characteristic that has a medium effect ($f^2 \ge 0.15$ [37]) on either children's or parents' perception is added to a multiple linear regression model with 3 variables, a sample of 55 would enable detection of the characteristic as the 4th independent variable with 80% power and a 5% alpha error. Similarly, a sample of 395 would be required to detect a characteristic that has a small effect ($f^2 \ge 0.02$ [37]) as the 4th independent variable. It follows that the sample size of the present study was sufficient to detect factors having a medium effect. A larger sample might discriminate additional characteristics that were not found to be statistically significant in the present study, such as children's age and economic status.

A larger sample size would also enable simultaneous modeling of responses (MTMM model, Fig. 3) and predictors (predictor model, Tables 4, 6, and Fig. 1), which might then detect any correlation between the predictors and the latent variables of rater-independent assessments of the child's condition. Further, a larger sample size should enable researchers to detect the effect of interviewer type (e.g., parent or researcher interviewer) on a child's perception. Among children aged five-to-seven and eight or more years, those interviewed by a parent tended to have a lower perception about HRQOL than those interviewed by a researcher, although this result was not statistically significant.

Third, we were unable to measure all possible factors that might influence child-parent agreement. We limited the length of our questionnaires to avoid placing further stress on the children, and therefore, measurements of the child's psychological background were limited to anxiety. Other aspects of a child's personality, such as defensiveness [14], might also influence the results, and future research should therefore investigate different personality traits. We also omitted measurements of the child's physical background, such as tumor location, tumor malignancy, relapse history, or treatment intensity [18–22]. All data in the present study were collected not from medical experts but from the children and their parents; as such, obtaining accurate, detailed answers about medical information was somewhat difficult. Additional information derived from patients with specific tumors or under specific treatment regimens will be required to identify residual confounders.

An additional constraint arises from the sample type. The present study collected data from a broad spectrum of children who had experienced brain tumors and included, for example, children diagnosed from 1 month to 17 years before the study. We could cover the broad spectrum to make up the study sample of the two subsamples. The hospitals subsample included more children with short time since diagnosis, young at survey, and on treatment than the CCAJ subsample did. To provide further insight into self- or parent-perceptions about HRQOL, further studies should focus on children at different phases of treatment or follow-up.

Families were excluded if the doctors or social workers determined that the family found the subject of the child's condition too uncomfortable to discuss. Although the number of such excluded families was not recorded, this exclusion may have limited data collection to more well-adjusted families and thereby limited the generalizability of the conclusions as well.

Finally, independent variables identified in this study accounted for 26.4% of the children's perception and 17.3% of the parents' perception. Other independent factors were not identified.

Conclusion

The method of administration—self- or interviewer-administered—had little influence on child-reporting of HRQOL. Children's perception of their own HRQOL was influenced by their trait anxiety, while parents' perception was influenced by their psychological distress, academic background, and their child's treatment status. These factors underlie the difference between child- and parent-reported HRQOL scores.

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References

- Collins, J. J., Byrnes, M. E., Dunkel, I. J., Lapin, J., Nadel, T., Thaler, H. T., et al. (2000). The measurement of symptoms in children with cancer. *Journal of Pain and Symptom Management*, 19(5), 363–377.
- Sugiyama, K., Yamasaki, F., Kurisu, K., & Kenjo, M. (2009).
 Quality of life of extremely long-time germinoma survivors mainly treated with radiotherapy. *Progress in Neurological Surgery*, 23, 130–139.
- 3. Ribi, K., Relly, C., Landolt, M. A., Alber, F. D., Boltshauser, E., & Grotzer, M. A. (2005). Outcome of medulloblastoma in children: Long-term complications and quality of life. *Neuropediatrics*, 36(6), 357–365.
- Poretti, A., Grotzer, M. A., Ribi, K., Schonle, E., & Boltshauser, E. (2004). Outcome of craniopharyngioma in children: Long-term

- complications and quality of life. *Developmental Medicine and Child Neurology*, 46(4), 220–229.
- Sønderkær, S., Schmiegelow, M., Carstensen, H., Nielsen, L. B., Muller, J., & Schmiegelow, K. (2003). Long-term neurological outcome of childhood brain tumors treated by surgery only. *Journal of Clinical Oncology*, 21(7), 1347–1351.
- Fuemmeler, B. F., Elkin, T. D., & Mullins, L. L. (2002). Survivors of childhood brain tumors: Behavioral, emotional, and social adjustment. *Clinical Psychology Review*, 22(4), 547–585.
- Testa, M. A., & Simonson, D. C. (1996). Assessment of qualityof-life outcomes. New England Journal of Medicine, 334(13), 835–840.
- 8. Sherifali, D., & Pinelli, J. (2007). Parent as proxy reporting: Implications and recommendations for quality of life research. *Journal of Family Nursing*, 13(1), 83–98.
- Pickard, A. S., & Knight, S. J. (2005). Proxy evaluation of healthrelated quality of life: A conceptual framework for understanding multiple proxy perspectives. *Medical Care*, 43(5), 493–499.
- Erhart, M., Ellert, U., Kurth, B. M., & Ravens-Sieberer, U. (2009). Measuring adolescents' HRQoL via self reports and parent proxy reports: An evaluation of the psychometric properties of both versions of the KINDL-R instrument. Health and Quality of Life Outcomes, 7, 77.
- Varni, J. W., Seid, M., & Kurtin, P. S. (2001). PedsQL 4.0: Reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Medical Care*, 39(8), 800–812.
- Verrips, E. G. H., Vogels, T. G. C., Koopman, H. M., & Theunissen, N. C. M. (1999). Measuring health-related quality of life in a child population. *The European Journal of Public Health*, 9, 188–193.
- 13. Landgraf, I., Abetz, L., & Ware, I. (1997). Child Health Questionnaire (CHQ): A user's manual. Boston: The Health Institute
- Jurbergs, N., Russell, K. M. W., Long, A., & Phipps, S. (2008).
 Adaptive style and differences in parent and child report of health-related quality of life in children with cancer. *Psychoon-cology*, 17(1), 83–90.
- Davis, E., Davies, B., Waters, E., & Priest, N. (2008). The relationship between proxy reported health-related quality of life and parental distress: Gender differences. *Child: Care, Health and Development*, 34(6), 830–837.
- Tamim, H., McCusker, J., & Dendukuri, N. (2002). Proxy reporting of quality of life using the EQ-5D. Medical Care, 40, 1186–1195.
- Hays, R. D., Vickrey, B. G., Hermann, B. P., Perrine, K., Cramer, J., Meador, K., et al. (1995). Agreement between self reports and proxy reports of quality of life in epilepsy patients. *Quality of Life Research*, 4, 159–168.
- Aarsen, F. K., Paquier, P. F., Reddingius, R. E., Streng, I. C., Arts, W. F. M., Evera-Preesman, M., et al. (2006). Functional outcome after low-grade astrocytoma treatment in childhood. *Cancer*, 106(2), 396–402.
- Penn, A., Lowis, S. P., Hunt, L. P., Shortman, R. I., Stevens, M. C. G., McCarter, R. L., et al. (2008). Health related quality of life in the first year after diagnosis in children with brain tumours compared with matched healthy controls; a prospective longitudinal study. *European Journal of Cancer*, 44(9), 1243–1252.
- Meeske, K. Katz., Katz, E. R., Palmer, S. N., Burwinkle, T., & Varni, J. W. (2004). Parent proxy-reported health-related quality of life and fatigue in pediatric patients diagnosed with brain tumors and acute lymphoblastic leukemia. *Cancer*, 101, 2116–2125.
- Bhat, S. R., Goodwin, T. L., Burwinkle, T. M., Landsdale, M. F., Dahl, G. V., Huhn, S. L., et al. (2005). Profile of daily life in



- children with brain tumors: An assessment of health-related quality of life. *Journal of Clinical Oncology*, 23, 5493–5500.
- Gerber, N. U., Zehnder, D., Zuzak, T. J., Poretti, A., Boltshauser, E., & Grotzer, M. A. (2008). Outcome in children with brain tumours diagnosed in the first year of life: Long-term complications and quality of life. Archives of Disease in Childhood, 93, 582–589.
- Palmer, S. N., Meeske, K. A., Katz, E. R., Burwinkle, T. M., & Varni, J. W. (2007). The PedsQL brain tumor module: Initial reliability and validity. *Pediatric Blood & Cancer*, 49(3), 287–293.
- 24. Sato, I., Higuchi, A., Yanagisawa, T., Mukasa, A., Ida, K., Sawamura, Y., et al. (2010). Development of the Japanese version of the Pediatric Quality of Life Inventory Brain Tumor Module. *Health and Quality of Life Outcomes*, 8(1), 38.
- 25. Cronbach, L. J. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika*, 16(3), 297–334.
- 26. Kobayashi, K., & Kamibeppu, K. (2010). Measuring quality of life in Japanese children: Development of the Japanese version of PedsQL™. Pediatrics International, 52(1), 80–88.
- 27. Soga, S. (1983). A study on standardization of Japanese version of the STAIC [Japanese]. *The Japanese Journal of Psychology*, 54(4), 215–221.
- 28. Spielberger, C. D., Edward, C. D., Lushene, R. E., Montouri, J., & Platzek, D. (1973). STAIC preliminary manual for the State-Trait Anxiety Inventory for Children ("How I feel questionnaire"). California: Consulting Psychological Press Inc.
- Furukawa, T. A., Kawakami, N., Saitoh, M., Ono, Y., Nakane, Y., Nakamura, Y., et al. (2008). The performance of the Japanese version of the K6 and K10 in the World Mental Health Survey Japan. *International Journal of Methods in Psychiatric Research*, 17(3), 152–158.
- 30. Furukawa, T. A., Kessler, R. C., Slade, T., & Andrews, G. (2003). The performance of the K6 and K10 screening scales for psychological distress in the Australian National Survey of Mental Health and Well-Being. *Psychological Medicine*, 33(2), 357–362.
- 31. Campbell, D. T., & Fiske, D. W. (1959). Convergent and discriminant validation by the multitrait-multimethod matrix. *Psychological Bulletin*, 56(2), 81–105.
- Theunissen, N. C., Vogels, T. G., Koopman, H. M., Verrips, G. H., Zwinderman, K. A., Verloove-Vanhorick, S. P., et al. (1998).
 The proxy problem: Child report versus parent report in health-related quality of life research. *Quality of Life Research*, 7(5), 387–397.
- 33. Hadorn, D. C. M. D., & Hays, R. D. P. (1991). Multitrait-multimethod analysis of health-related quality-of-life measures. *Medical Care*, 29(9), 829–840.

- Hu, L., & Bentler, P. M. (1999). Cutoff criteria for fit indices in covariance structure analysis: Conventional criteria versus new alternatives. Structural Equation Modeling: A Multidisciplinary Journal, 6, 1–55.
- 35. Duncan, O. D. (1966). Path analysis: Sociological examples. *American Journal of Sociology*, 72, 1–16.
- Sobel, M. E. (1982). Asymptotic confidence intervals for indirect effects in structural equation models. Sociological Methodology, 13, 290–312.
- 37. Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). New Jersey: Lawrence Erlbaum Associates.
- 38. U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research, U.S. Department of Health and Human Services FDA Center for Biologics Evaluation and Research, & U.S. Department of Health and Human Services FDA Center for Devices and Radiological Health. (2006). Guidance for industry: Patient-reported outcome measures: Use in medical product development to support labeling claims: Draft guidance. Health and Quality of Life Outcomes, 4, 79.
- Varni, J. W., Burwinkle, T. M., Seid, M., & Skarr, D. (2003). The PedsQL 4.0 as a pediatric population health measure: Feasibility, reliability, and validity. *Ambulatory Pediatrics*, 3, 329–341.
- 40. Huguet, A., & Miro, J. (2008). Development and psychometric evaluation of a Catalan self- and interviewer-administered version of the Pediatric Quality of Life Inventory version 4.0. *Journal of Pediatric Psychology*, 33(1), 63–79.
- 41. Verrips, G. H., Vogels, A. G., den Ouden, A. L., Paneth, N., & Verloove-Vanhorick, S. P. (2000). Measuring health-related quality of life in adolescents: Agreement between raters and between methods of administration. *Child: Care, Health and Development*, 26(6), 457–469.
- Tsakos, G., Bernabe, E., O'Brien, K., Sheiham, A., & de Oliveira, C. (2008). Comparison of the self-administered and intervieweradministered modes of the child-OIDP. *Health & Quality of Life Outcomes*, 6, 40.
- 43. Eiser, C., & Morse, R. (2001). Can parents rate their child's health-related quality of life? Results of a systematic review. *Quality of Life Research*, 10(4), 347–357.
- 44. Vance, Y. H., Morse, R. C., Jenney, M. E., & Eiser, C. (2001). Issues in measuring quality of life in childhood cancer: Measures, proxies, and parental mental health. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 42, 661–667.
- 45. Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39, 175–191.



Prevalence of Analgesic Prescriptions among Patients with Cancer in Japan: An Analysis of Health Insurance Claims Data

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Abstract

Objectives: To promote effective management of cancer pain as a nationwide health policy, it is necessary to monitor the performance of health care providers in managing pain in their patients. To plan a system that monitors the performance of pain management, the exact methods of measurement, including the range of target patients, and estimate the resources must be defined. Performance in pain management can be evaluated either in all patients with cancer or restricted to patients with cancer who are already taking analgesics. Restricting the target patient group to patients on analgesics may be more efficient but the extent of that efficiency remains uncertain.

Methods: Using insurance claims from eight employer-sponsored insurance companies, we analyzed data from patients (N = 2858) who had received anti-cancer treatment (ie, surgery, chemotherapy, and radiation therapy) for the five major cancers in Japan (ie, breast, colorectal, liver, lung, and stomach cancers).

Results: Overall, 22.9% of patients received some kind of analgesic prescription in the course of a month. Lung cancer patients were more likely to be prescribed analgesic prescriptions (any analgesics 34.8%; opioids 18.2%) than patients with the other four cancers. The observed percentage of patients who received analgesic prescriptions over the study period (ie, January 2005 to November 2009) decreased.

Conclusion: If we limit the target patient group to patients with cancer already on analgesics, we can reduce the number of persons to be contacted by about three-fourths, compared to assessing pain in all patients with cancer. Although we do not wish to ignore the problem of undetected pain among patients with cancer, beginning our systematic evaluation with patients with cancer already on analgesics may be a realistic option.

Keywords: analgesic prescription, pain management, performance measurement, cancer, opioid

1. Introduction

While pain is the most focused-on part of palliative care in cancer patients (Portenoy, 2011), management of pain is reportedly inadequate in many settings (Cleeland et al., 1994; Deandrea, Montanari, Moja, & Apolone, 2008; Okuyama et al., 2004; Uki, Mendoza, Cleeland, Nakamura, & Takeda, 1998). Few studies have examined the adequacy of pain management in cancer care in Japan (Okuyama et al., 2004; Uki, Mendoza, Cleeland, Nakamura, & Takeda, 1998). Even though cancer is the leading cause of death (Ministry of Health, 2010) in Japan, opioid consumption is relatively small compared to opioid consumption in other industrialized counties. According to a report by the International Narcotics Control Board, opioid consumption in Japan is the lowest among the G7 countries (The International Narcotics Control Board, 2010).

Concern over low opioid consumption in Japan has led policy makers to pay extra attention to pain control. The Cancer Control Act of 2007, which delegated comprehensive responsibility for cancer control to the Japanese government, specifically states that both national and local governments should "take measures to enable palliative care, such as pain control, from the early stages of cancer care processes" (Japan Law Data Archives, 2006). And The Basic Plan to Promote Cancer Control Programs established adequate pain control as a central agenda (Ministry of Health, 2007).

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One way to foster adequate pain management in hospitals throughout Japan would be to establish a system to monitor their pain management programs. Measurement and feedback of hospital performance of pain management, preferably in comparison to other medical facilities, would motivate hospitals to improve their pain management (Hibbard, Stockard, & Tusler, 2003). Establishment of a pain management monitoring system would require that consistent methods be clearly defined to measure pain management in target patients and in the success/failure of treatment.

There are several ways to define the target patients who need pain management. The ideal way, which would be to include all patients with cancer who suffer from any kind of pain, would require a process of asking all patients with cancer (perhaps before definitive diagnoses are made) about their pain, since some patients may not have discussed their pain with their health providers. An alternative way may be to target only patients under some type of pain management or patients taking analgesic drugs. This way overlooks patients with pain not recognized by health providers, and thus fails to consider providers' ability or efforts to thoroughly detect patients' suffering. On the other hand, because this way does not rely on obtaining patients' reports, it provides a more defined range of target patients and saves the time and effort of interviewing individual patients about pain.

While the theoretical limitation associated with focusing on patients already being treated for pain is clear, an important unanswered question is: How much labor can we expect to save by limiting the number of target patients? We have found no studies in the literature that report the percentage of patients with cancer being treated for pain in Japan. Although surveys from other countries have reported their prevalence of pain (Breivik et al., 2009; van den Beuken-van Everdingen et al., 2007) and proportion of treatment for moderate to severe pain (Breivik et al., 2009), they have not focused on the frequency of prescribing pain medications associated with resource allocation for monitoring of pain management in hospitals. The purpose of this study was to gain insight into the current status and recent time trend of the use of pain medications in Japan. We analyzed a large database of insurance claims from multiple employer-sponsored insurance companies.

2. Methods

2.1 Dataset

2.1.1 The Health Insurance System in Japan

We analyzed insurance claims data sets from 8 employer-sponsored insurance companies. In Japan, all residents have health insurance from either their employment or their place of residence. Many large companies work with associated insurance companies (1435 insurance companies as of April 2012 (National Federation of Health Insurance Societies (Kenporen), 2012)). Relatively small companies who do not work with associated insurance company provide coverage through the Japan Health Insurance Association. Unemployed or retired persons and persons aged 75 years or older have coverage based on their place of residence from city or region-based insurance entities, respectively.

Health services are reimbursed on a fee-for-service basis according to a nationally defined fee schedule. The healthcare facilities submit claims every month for each patient. The claims list all the services and medications provided to patients in the facility as well as the diagnoses corresponding to those services and medications. For patients who receive drug prescriptions, claims for the medications are submitted by the pharmacy that has dispensed the prescription. These pharmacy claims also contain the names of the prescribing facilities, thus providing links to the prescribing claims.

2.1.2 Study Sample

For our study, eight insurance companies provided data from a total of 750 000 members consisting of the employees of affiliated companies and their dependents. Among them, three insurance companies provided claims from January 2005 to December 2009 and five provided claims from January 2008 to December 2009. The claims from these eight insurance companies included a total of 84652 patients with any type of cancer diagnosis, including tentative diagnoses. To avoid ambiguity of diagnosis on the insurance claims, we analyzed data on patients who had received anti-cancer treatment for the five major cancers in Japan, namely, breast, colorectal, stomach, lung, and liver cancers. Anti-cancer treatment included surgery, chemotherapy, hormone therapy, and radiation therapy. We excluded patients who had undergone only endoscopic treatment, because we suspected that cancer painmay not have been an issue for them.

2.2 Statistical Analyses

Analgesic drugs were classified according to the World Health Organization Pain Control Ladder (World Health Organization., 1996); non-steroidal anti-inflammatory drugs (NSAIDs) including acetaminophen, weak opioids (ie, codeine, dihydrocodeine, tramadol, and pentazocine), and strong opioids (ie, morphine, oxycodone, fentanyl,

pethidine, and buprenorphine). Low-dose aspirin (100mg/tablet) and the codeine contained in cold medicines were not regarded as painkillers. For each month during the study period, the proportion of patients with cancer who received each type of drugs was recorded.

The proportion of analgesic prescriptions were compared between patients' treatment phases (ie, after surgery, after chemotherapy, and after radiation) and primary cancer site. Definition of the treatment phase was based on the last anti-cancer therapy. For example, patients who received surgery followed by chemotherapy (at a later time) were considered to be "after surgery" for the period between surgery and chemotherapy, and "after chemotherapy" after the chemotherapy had been received. Primary cancer sites were determined on the basis of both the cancer treatment and diagnosis recorded on insurance claims. For those patients who had undergone surgery, including site-specific intervention (eg, radio frequency ablation therapy to the liver), the primary site of cancer was considered to be the target organ. For those patients who had received only systemic chemotherapy, where the target cancer had not been clearly established, or radiation therapy where the insurance reimbursement code was the same across different target sites, the diagnoses in the insurance claims were accepted as they had been recorded. The differences in the proportions were statistically tested using the chi-square tests.

The trend of prescribing analgesic drugs for cancer patients was described as the proportion of patient-prescribed analgesic drugs among the cancer patients who had used any health services during a given month. The person-month was the unit of analysis. The change in the trends was analyzed graphically. Also the beta coefficients to represent the trend was calculated using linear regression analyses where the percentage of analgesic prescriptions and the time variable were the dependent and independent variables, respectively, assuming the linearity of the relationship. Because the assumption of homoscedastic errors did not hold for some regression models, the robust standard errors were calculated with the White correction. No correlation between error terms and the independent variable was confirmed. All analyses were performed using Stata 11.2 (StataCorp LP, College Station, Texas).

3. Results

A total of 6656 patients had one of the five major cancers on the health insurance claims, among whom 2585 patients received treatment with surgery, chemotherapy, and/or radiotherapy during the study period, and thus were entered into the analyses. Patient characteristics are presented in Table 1. Average patient age was 53.4 years (Standard deviation: 10.6); 57.7% of patients were female. The most common cancer was breast cancer (n =923 [35.7%]), followed by colorectal cancer (n =615 [23.8%]) and stomach cancer (n =465 [18.0%]). The average duration of the observation period (ie, from first cancer treatment to last visit) was 33.8 months.

Table 1. Patient characteristics

Age				
<20	21	(0.8%)
20-39	243	(9.4%)
40-59	1619	(62.6%)
60-69	548	(21.2%)
>70	154	(6.0%)
Gender				
Female	1491	(57.7%)
Cancer site				
Breast	923	(35.7%)
Colorectal	615	(23.8%)
Liver	179	(6.6%)
Lung	412	(15.9%)
Stomach	465	(18.0%)
Treatment received				
Surgical Intervention	1586	(61.4%)
Chemotherapy	1629	(63.0%)
Radiation	594	(23.0%)_

Tables 2 and 3 show the percentages of patients receiving analgesic prescriptions every month by treatment phase and by site of cancer, respectively. Overall, 22.9% of patients who used healthcare each month received analgesic prescriptions (Table 2). Analyses for each drug class revealed that NSAIDs or acetaminophen and opioids were prescribed in 19.8% and 9.1% of the patients, respectively. Strong and weak opioids were prescribed 6.2% and 4.0% of visits, respectively. When we separated patients by treatment received, patients after chemotherapy were most frequently prescribed analgesics (23.7%), while opioids were most frequently prescribed for patients after radiation therapy (9.8%). The analysis by site of cancer revealed that patients with lung cancer were more likely to receive analgesics (overall, 33.3%) than patients with other types of cancer (Table 3).

Table 2. Average proportion of analgesic prescriptions every month by treatment phase

	Overall	After surgery	After chemotherapy	After radiation	P value
Any analgesics	22.9%	21.4%	23.7%	22.8%	< 0.001
ACA	1.9%	1.9%	2.2%	2.6%	< 0.001
ACA/NSAIDs	19.8%	18.8%	20.7%	20.8%	< 0.001
Opioid	9.1%	6.7%	9.4%	9.8%	< 0.001
Weak opioid	4.0%	4.2%	3.8%	4.3%	0.16
Strong opioid	6.2%	3.6%	6.7%	6.5%	< 0.001

Abbreviations: ACA acetaminophen; NSAID non-steroidal anti-inflammatory drug.

Table 3. Average proportion of analgesic prescriptions every month by site of cancer

	Breast	Colorectal	Liver	Lung	Stomach	P value
Any analgesics	20.0%	20.8%	23.8%	33.3%	17.1%	< 0.001
ACA	1.9%	1.9%	2.5%	2.5%	1.9%	0.01
ACA/NSAIDs	18.4%	17.7%	19.9%	28.7%	14.4%	< 0.001
Opioid	4.2%	8.9%	9.6%	17.6%	7.0%	< 0.001
Weak opioid	2.1%	3.5%	7.0%	6.1%	2.8%	< 0.001
Strong opioid	2.4%	6.6%	3.1%	13.2%	5.3%	< 0.001

Abbreviations: ACA acetaminophen; NSAID non-steroidal anti-inflammatory drug.

Figure 1 shows a decrease in the percentage of patients who received analgesic prescriptions over the observation period (ie, January 2005 to November 2009). Table 4 shows that analgesic prescriptions decreased by 0.13% per month as calculated via regression analysis.

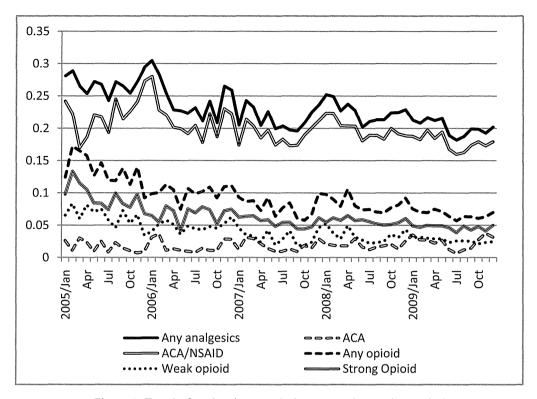


Figure 1. Trend of analgesic prescriptions over observation period

Table 4. Monthly decrease of proportion of analysis prescriptions (linear regression analyses)

	Beta		(95% CI)	P value
Any analgesics	-0.13%	-0.15%	-0.11%	< 0.001
ACA	0.01%	0.00%	0.02%	0.13
ACA/NSAIDs	-0.08%	-0.11%	-0.05%	< 0.001
Opioid	-0.13%	-0.15%	-0.10%	< 0.001
Weak opioid	-0.07%	-0.09%	-0.06%	< 0.001
Strong opioid	-0.09%	-0.11%	-0.07%	< 0.001

Abbreviations: ACA acetaminophen; NSAID non-steroidal anti-inflammatory drug.

4. Discussion

Our study, using health insurance claims data from employee-sponsored insurance companies, showed that about one fourth of the patients treated for the five major cancers in Japan received analgesic prescriptions. Since the patients counted in our study were in treatment, the true prevalence of pain that include patients with pain but not in treatment among these patients will be higher. Restricting our target group of patients to patients taking analgesic medications will facilitate selection of patients for evaluating the performance measurement of pain management. By selecting patients in treatment for this evaluation, we will be getting by with only one-fourth to one-fifth of the all the patients. In addition, restricting our target group to patients taking analgesic medication is likely to be more efficient for systematic evaluation purposes than identifying and assessing patients with pain from all patients with cancer.

It must be noted that our study neither implies that identifying patients with untreated pain is of little value nor does it advocate limiting target patients for the monitoring of pain management. Although the prevalence of pain among Japanese patients with cancer is unknown, the prevalence of analgesic prescriptions is much lower than prevalence of pain itself reported in other countries. One systematic review showed that about half of all diseases stages and a third of patients after curative treatment reported pain (van den Beuken-van Everdingen et al., 2007). A population-based survey from Europe and Israel showed that 74% of patients with cancer reported pain

(Breivik et al., 2009). Although the patients with cancer in our study were younger and in better condition than the average patient with cancer (Center for Cancer Control and Information Services, National Cancer Center, 2011), the gap between the prevalence of pain among patients with cancer and our finding that 22.9% of patients received analgesics may be an indication of the undertreatment of pain in Japan. This gap underscores the importance of detecting pain among cancer patients.

We need to implement better pain management for cancer pain nationwide. While we are not satisfied with a limited target patient group for assessment in planning a nationwide system, we understand that starting with a limited group is a realistic option. Uniform application of the assessment with clear definition is essential to encourage improvement. Even if we start small, we will eventually assess all patients with cancer who are experiencing pain and ensure that they have access to pain management and appropriate treatment.

In order to work toward a nationwide pain management system for cancer pain, we need to be cautiously aware of the nature of the data to be used and the findings on opioid consumption in Japan. The decreasing trend of patients receiving analgesic drugs in the observed data may be associated with the composition of patients in treatment phases shifted from acute-phase dominant to chronic follow-up phase dominant over time. Because we enrolled patients from the month in which they began cancer therapy and followed up later, patients under observation in the early years of the study period were usually enrolled right after the treatment, making them more likely to receive analgesic medications for pain that arose from the anti-cancer treatment (eg, wound pain after surgery, dermatitis after radiation therapy). In the later years of the study we observed patients both in regular follow-up and patients receiving acute treatment. Thus, a larger proportion of more stable patients in regular follow-up may have caused the overall proportion of analgesic prescriptions to decrease. Nonetheless, the decrease was not steep and therefore did not greatly influence our findings.

The impact of the insurance claims on our findings also warrants mention. First, the insurance companies that provided the data were employer-sponsored. As such, they exclusively enroll employees and employees' dependents. We suspect therefore that our target patient group tended to be younger than the average cancer patient. In fact, while the national statistics on the hospital-based cancer registries showed that most cancer patients to be in their 60s and 70s (Center for Cancer Control and Information Services & National Cancer Center, 2011), most of the patients with cancer in our studies were their 50s and 40s. Second, the accuracy of the diagnosis may be questionable. Since insurance claims place more emphasis on consistency between diagnoses and services provided than clinical accuracy, determining whether a diagnosis is tentative or final is difficult. Third, claims data do not describe the symptoms for which the drugs were prescribed. Therefore, we cannot determine whether NSAIDs were prescribed for pain, fever, or some other anti-inflammatory malady. Fourth, claims submitted to insurance companies lack information on services out of the fee-for-service reimbursement. In 2003 the Japanese health insurance system started paying per-diem based on predefined information from diagnosis-procedure groups in 82 participating hospitals. The number of participating hospitals gradually increased, and in 2011, a total of 1447 hospitals (19% of total) in Japan were participating (Bureau of Health Insurance, Ministry of Health, Labor, & Welfare, 2012). Most services and medications provided during hospitalization to these hospitals were not captured in regular insurance claims, increasing the likelihood of underestimating analyses use during hospitalization. Fifth, we limited our analyses to the patients who received therapy for the five major cancers in Japan. By limiting the cancer type to the five major cancers, we could match the match the claim diagnoses with the treatment. This enabled us to exclude patients with a tentative diagnosis who turned out not to have cancer later or inactive diagnosis that was treated could remain on the claims even after treatments were over. However, in real clinical practice, the target for pain management should include all cancer types. We need to bear in mind that the results may have been different if we included all cancer types. Finally, since our data are derived from health insurance companies, the number of patients per hospital was small for many hospitals. Given that taking analgesic prescriptions in small denominators is not likely to produce stable results, we did not perform analyses at the level of individual providers.

5. Conclusion

Our study showed the prevalence of analgesic prescriptions among five major cancers in Japan. When planning for a system that monitors the performance of pain management, it is important to balance the resources used with the range of the target for the measurement. The frequency of analgesic prescription provided information for an evidence-based discussion on how to restrict or broaden the target population for monitoring using available resources. Even if we decide to begin systematic evaluation with a smaller target patient group (ie, patients already taking analgesics), we will do so keeping in mind that our ultimate goal is to provide pain relief to all patients with cancer in our country.

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References

- Breivik, H., Cherny, N., Collett, B., de Conno, F., Filbet, M., Foubert, A. J., ... Dow, L. (2009). Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. *Ann Oncol*, 20, 1420-33. http://dx.doi.org/10.1093/annonc/mdp001
- Bureau of Health Insurance, Ministry of Health, Labor, and Welfare, Japan. (2012). Overview of revision of fee-schedule 2012. Retrieved August 27, 2012, from http://www.mhlw.go.jp/bunya/iryouhoken/iryouhoken15/dl/h24 01-05.pdf
- Center for Cancer Control and Information Services, National Cancer Center. (2011). Statistics of 2008 Cancer Cases from Hospital-based Cancer Registries in Japan. Retrieved August 18, 2012, from http://ganjoho.jp/professional/statistics/hosp_c_registry.html
- Cleeland, C. S., Gonin, R., Hatfield, A. K., Edmonson, J. H., Blum, R. H., Stewart, J. A., & Pandya, K. J. (1994). Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med*, 330, 592-6. http://dx.doi.org/10.1056/NEJM199403033300902
- Deandrea, S., Montanari, M., Moja, L., & Apolone, G. (2008). Prevalence of undertreatment in cancer pain. A review of published literature. *Ann Oncol*, 19, 1985-91. http://dx.doi.org/10.1093/annonc/mdn419
- Hibbard, J. H., Stockard, J., & Tusler, M. (2003). Does publicizing hospital performance stimulate quality improvement efforts? *Health Aff (Millwood)*, 22, 84-94. http://dx.doi.org/10.1377/hlthaff.22.2.84
- Japan Law Data Archives. (2006). Cancer Control Act. Retrieved August 8, 2012, from http://law.e-gov.go.jp/announce/H18HO098.html
- Ministry of Health, Labor, and Welfare, Japan. (2007). Basic Plans to Promote Cancer Control Programs.
- Ministry of Health, Labor, and Welfare, Japan. (2010). Vital statistics of Japan. Retrieved August 8, 2012, from http://www.mhlw.go.jp/toukei/list/dl/81-1a2.pdf
- National Federation of Health Insurance Societies (Kenporen). (2012). About Kenporen. Retrieved August 9, 2012, from http://www.kenporen.com/outline/
- Okuyama, T., Wang, X. S., Akechi, T., Mendoza, T. R., Hosaka, T., Cleeland, C. S., & Uchitomi, Y. (2004). Adequacy of cancer pain management in a Japanese Cancer Hospital. *Japan J Clin Oncol*, *34*, 37-42. http://dx.doi.org/10.1093/jjco/hyh004
- Portenoy, R. K. (2011). Treatment of cancer pain. *Lancet*, 377, 2236-47. http://dx.doi.org/10.1016/S0140-6736(11)60236-5
- The International Narcotics Control Board. (2010). Report of the International Narcotics Control Board on the Availability of Internationally Controlled Drugs: Ensuring Adequate Access for Medical and Scientific Purposes. Retrieved August 8, 2012, from http://www.incb.org/pdf/annual-report/2010/en/supp/AR10_Supp_E.pdf
- Uki, J., Mendoza, T., Cleeland, C. S., Nakamura, Y., & Takeda, F. (1998). A brief cancer pain assessment tool in Japanese: the utility of the Japanese Brief Pain Inventory--BPI-J. *J Pain Symptom Manage*, *16*, 364-73. http://dx.doi.org/10.1016/S0885-3924(98)00098-0
- van den Beuken-van Everdingen, M. H., de Rijke, J. M., Kessels, A. G., Schouten, H. C., van Kleef, M., & Patijn, J. (2007). Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol*, 18, 1437-49. http://dx.doi.org/10.1093/annonc/mdm056
- World Health Organization. (1996). Cancer Pain Relief. Geneva, Switzerland: World Health Organization.

ORIGINAL ARTICLE

Survey on recognition of post-mastectomy pain syndrome by breast specialist physician and present status of treatment in Japan

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Abstract

Background Post-mastectomy pain syndrome (PMPS) is chronic pain after breast cancer surgery and is reported to influence quality of life (QOL). Although the results of a survey in Japan showed high incidence, at 21–65 %, many of the patients had never been treated for PMPS. One reason for this low treatment rate may be poor understanding of PMPS by medical personnel. In this study, we conducted the survey by using questionnaire to assess current treatment and the recognitions of the medical personnel.

Methods We mailed a questionnaire to 647 specialist members of the Breast Cancer Society.

Results Of those, 34.7 % responsed. While PMPS was recognized by as much as 70.5 % of responding physicians, it was treated by as little as 47.7 % of the responders. In addition, while non-steroidal anti-inflammatory drugs (NSAIDs), which were ineffective in relieving PMPS, were used by 78.4 % of the responders, effective drugs were rarely used; therefore, treatment was considered ineffective by 69.5 %. This indicates that appropriate therapies are not

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widely used, and none of the current therapies are very effective.

Conclusions The results showed high recognition of PMPS pathology among physicians, but the treatment rate was as low as 47.7 %. NSAIDs were the main treatment, and the treatment effects were not satisfactory. It was revealed that currently appropriate treatment modalities have not been widely used. Education of physicians, distribution of treatment information and further studies are considered necessary for the spread of appropriate treatment modality.

Keywords Breast Cancer ·
Post-mastectomy pain syndrome ·
Recognition by physicians · Quality of life · Treatment

Introduction

Post-mastectomy pain syndrome (PMPS) is chronic pain after breast cancer surgery that remains for a long time. PMPS is reported to have influence on postoperative quality of life (QOL) [1-11]. Although recent studies indicate that the PMPS incidence is as high as 30-70 % [8, 12-15], the number of patients treated has been limited and treatment effects have been poor, which is considered to be a problem in Europe and the US [4, 5, 8, 9, 14, 16, 17]. The pain appears to be caused by peripheral neuropathy primarily in the intercostobrachial nerve [6, 7]. Recent reports have shown that this pain occurs not only after mastectomy, but also after other procedures for treating breast cancer, breast conserving surgery, tumor enucleation, and breast reconstructing surgery [8, 13, 18]. It has also been reported that the pain occurs after sentinel lymph node biopsy and in patients in whom the intercostobrachial nerve

was preserved [5, 15, 18]. Breast cancer is the most common cancer among women in Japan, affecting 1 in 20 women, and the incidence is increasing every year. Younger women in their 40s and 50s, who are busy with child care and work, are most affected by the disease. Survival rates of breast cancer in Japan are high, with 10-year survival rates of approximately 90 % at stage I and 80 % at stage II [19]. Postoperative QOL has large influence on the family and society, as well as on the patient herself. Recently, the problem of chronic pain has risen with the improvement of cancer survival rates [11, 15, 20]. Although the results of a survey in Japan showed high incidence, at 21-65 % (2-9 years post-surgery), many PMPS patients who have sought outpatient consultation have never been treated for the pain. Not knowing that there are treatment methods available, many gave up the idea that their pain could be alleviated [5, 8, 17]. One reason for this could be a poor understanding of PMPS by medical personnel. In addition, surveys of present status of PMPS treatment in Japan have rarely been conducted. We planned this study to better understand awareness of and current treatment of PMPS in patients undergoing breast cancer surgery by physicians in Japan to identify the problems faced and thus facilitate development of more appropriate treatments to improve the quality of life of patients.

Patients and methods

As no similar survey on the recognition of chronic postoperative pain in patients with cancer has been conducted, a questionnaire was initially prepared based on other studies of chronic pain and surveys of physicians [5, 9, 10, 15, 20-25], as shown in Table 1. Before conducting the survey, we explained the purpose of the survey to the Board of Directors of the Japanese Breast Cancer Society and received approval for the survey. We then requested the Head Office of the Society to disclose information on members of the Society, but were not given permission in light of protection of personal information. Only labels with the postal address and name of specialists required for the postal survey were provided. A request for cooperation, explaining the purpose of the research, and a questionnaire were posted to all 647 specialists of the Japanese Breast Cancer Society in March 2007. The responses were collected by fax. The responding period was 3 weeks. Each specialist signed the questionnaire. The questionnaire consisted of questions regarding recognition of postoperative chronic pain, recognition and experience of PMPS, and current treatment of PMPS and its efficacy. After tallying the results, their opinions on the remaining pain, and relationship between their recognition of PMPS and their

experience and policy of treatment of PMPS were evaluated. Statistical analysis was performed using the Mann-Whitney U-test, and p < 0.05 was considered statistically significant.

Results

The recovery rate of the questionnaire was 34.7 % (647 distributed; 224 responded; 2 returned as undeliverable).

Background of respondents

The backgrounds of respondents are shown in Table 2.

Questions regarding recognition of postoperative chronic pain

A total of 223 respondents answered the question about prolonged pain associated with surgery, and 1 respondent did not answer the question. The results are shown in Table 3.

Questions regarding recognition and experience of PMPS

Table 4 shows the recognition and duration of PMPS. The incidence of PMPS was 0 % for 4.5 % of the responders, 20 % for 49.5 %, 40 % for 16.2 %, 60 % for 3.2 %, 80 % for 5.0 %, 100 % for 0.9 %, and unknown for 20.7 %. The current number of patients who were diagnosed with PMPS was 0 for 16.4 % of the responders, 5 or fewer for 40 %, 10 or fewer for 10.9 %, less than 20 for 8.2 %, 20 or more for 7.3 %, and unknown for 17.3 %. Regarding the treatment of PMPS, 51.8 % experienced difficulty, while 48.2 % did not experience difficulty.

Questions regarding the current treatment modality and its effects

A total of 222 respondents answered the question about current management of patients with pain, and 2 respondents did not answer the question. The results are shown in Table 5. In addition to 106 physicians who answered the previous question with a reply that "treatment is administered by myself," 10 answered the question regarding current treatment modality. The results are shown in Table 6. Treatment effects are shown in Table 7. The anticonvulsants gabapentin and pregabalin were not included among the test drugs, because the former had only recently entered the market and the latter was not yet on the market in Japan at the time of the survey.



Table 1 Questionnaire

Affiliation	Name
Specialty	Experience yrs Gender male • female
A. Basic information	
(excluding biopsy only)	incer operation did you have in your hospital last year?/year prolonged postoperative pain? (Multiple choice)
	. ② Pain rarely occurred. ③ There is no need for
treatment.	-
④ Pain will resolve with	time course. ⑤ I should focus on the cancer treatment
because pain is a secondar	y symptom. 6 It is difficult to explain to the patients.
I want to do somethin	g for my patients. 8 Pain needs to be treated. 9 I
want to know how pain c	an be treated. [®] I should consult a pain specialist.
① Other ()
B. Regarding Postmastectomy	Pain Syndrome (PMPS)
1) Do you know what PMPS is?)
① Yes ② No	
2) How often do you think the I	PMPS occurred after surgery?
① 0% ② 20% ③	40% 4 $60%$ 5 $80%$ 6 $100%$ 7 I don't
know.	
3) How long do you think PMP	_
· · · · · · · · · · · · · · · · · · ·	5 years 4 7 years 5 More than 10 years 6 I
don't know. 4) How many patients with PM	PS do you have now?
	4 $11 \sim 20 5$ $21 \sim 6$ I don't know.
5) Have you ever experienced a	
① Yes ② No	in the state of th
	th PMPS now? (Multiple choice)
① No treatment, with	observation 2 Treat by myself 3 Alternative
medicine	
-	nselves in their own way 5 Consult pain specialist
6 Other ()
7) Questions for those who chos	
	tment now? (Multiple choice)
-	ls ③ Tranquilizers ④ Antidepressants
(5) Herbal medicines (6) injections	Topical preparations T Nerve blocks 8 Local
3	Acupuncture ① Other ()
b) How effective do you this	*
	Slightly effective ③ Moderately effective ④ Very
effective ⑤ I don't know	
_	lose treatment information regarding PMPS to patients?
① Yes② No③ I don	n't know.

Question regarding the recognition of patient education by physicians

Disclosure of the rapeutic information to patients was considered to be necessary by 77.4 % of the responders, unnecessary by 3.0 %, and unknown by 19.6 %. Other

Furthermore, we investigated the recognition of PMPS and presence/absence of treatment. Current treatment was investigated in the recognizing group (n=158) and the unrecognizing group (n=66). The number of physicians

Table 2 Responder's characteristics

	No. (%)	
Responders	224	
Sex		
Male	197 (87.9)	
Female	27 (12.1)	
Experience (years)		
Median	20	
Range	6-52	
Specialty		
Surgery	189 (84.4)	
Medical oncology	30 (13.4)	
Obstetrics and gynecology	1 (0.4)	
No answer	4 (1.8)	
Surgeries performed at the attending institution (2006)		
Median	80	
Range	0–960	

Table 3 Opinions on prolongation of postoperative pain (responses based on multiple choices)

Opinion	No.	%
Nothing can be done	33	14.8
Pain rarely occurred	19	8.5
There is no need for treatment	65	29.1
Pain will resolve with time course	109	48.9
I should focus on the cancer treatment because pain is a secondary symptom	14	6.3
It is difficult to explain to the patients	23	10.3
I want to do something for my patients	92	41.3
Pain needs to be treated	63	28.3
I want to know how it can be treated	112	50.2
I should consult a pain specialist	30	13.5
Other	12	5.4

Table 4 Recognition and duration of PMPS

	No.	%
Recognition of PMPS		
Known	158	70.5
Unknown	66	29.5
Duration of PMPS (years)		
1	11	5.0
3	52	23.4
5	27	12.2
7	5	2.3
More than 10	61	27.5
Unknown	66	29.7

Table 5 Current measures taken for PMPS patients (responses based on multiple choices)

Measures to be taken	No.	%
No treatment, with observation	145	65.3
Treat by myself	106	47.7
Alternative medicine	3	1.4
Let patients treat themselves in their own way	27	12.2
Consult pain specialist	69	31.1
Other	13	5.9

Table 6 Therapies currently used for PMPS patients (responses based on multiple choices)

Treatment	No.	%
NSAIDs	91	78.4
Opioids	10	8.6
Tranquilizers	38	32.8
Antidepressants	40	34.5
Herbal medicines	14	12.1
Topical preparations	31	26.7
Nerve blocks	10	8.6
Local injections	7	6.0
Rehabilitation	29	25.0
Acupuncture	0	0
Other	9	7.8

Table 7 Current treatment effects

No.	%	
25	21.6	
56	48.3	
25	21.6	
2	1.7	
8	6.9	
	25 56 25 2	

who responded "treatment is administered by myself" in the recognition group and unrecognizing group was 83 and 22, respectively, a significantly greater response by members of the recognition group than by the unrecognizing group (p < 0.01).

Patients were classified into an effective group (very effective or moderately effective) and an ineffective group (not effective or slightly effective) according to the therapeutic effect to compare the current treatment modality and its effects. For the NSAIDs, antidepressants, tranquilizers, and opioids that were frequently used in the treatment, the therapeutic efficacy is shown in Table 8. For all drug classes indicated for the treatment of PMPS, more