プライマリケアと救急を中心とした総合誌

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入院患者の痛みの診かた

がん疼痛、術後、リウマチ、原因不明な痛みへの対処、鎮痛薬の使い分けなど、身近な疑問に答えます!

木澤義之／編

- 痛みの機序とメカニズム
- 痛みの原因の診断
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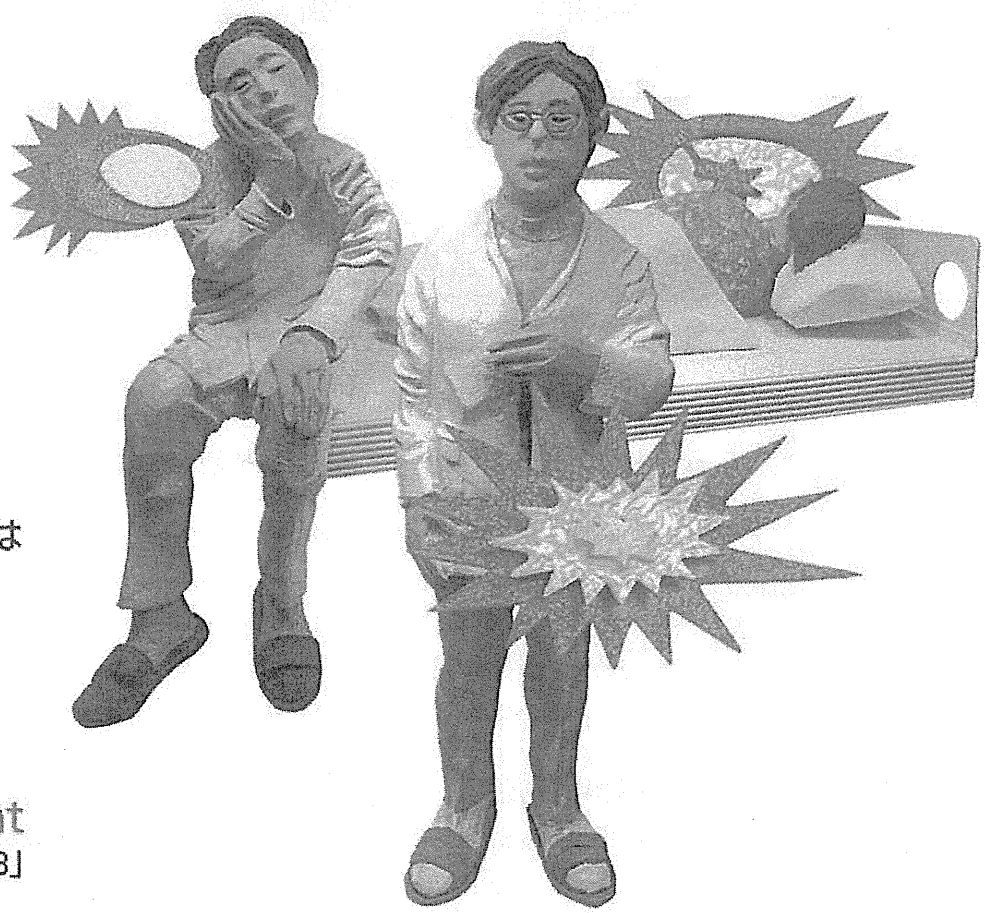

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特集

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Original Article

Improvements in Physicians' Knowledge, Difficulties, and Self-Reported Practice After a Regional Palliative Care Program

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Abstract

Context. Although several studies have explored the effects of regional palliative care programs, no studies have investigated the changes in physician-related outcomes.

Objectives. The primary aims of this study were to: 1) clarify the changes in knowledge, difficulties, and self-reported practice of physicians before and after the intervention, 2) explore the potential associations between the level of physicians' participation in the program and outcomes, and 3) identify the reasons and characteristics of physicians who did not participate in the program.

Methods. As a part of the regional palliative care intervention trial, questionnaires were sent to physicians recruited consecutively to obtain a representative sample of each region. Physician-reported knowledge, difficulty of palliative care, and self-perceived practice were measured using the Palliative Care Knowledge Test, Palliative Care Difficulty Scale, and Palliative Care Self-Reported Practice Scale (PCPS), respectively. The level of their involvement in the program and reason for non-participation were ascertained from self-reported questionnaires.

Results. The number of eligible physicians identified was 1870 in pre-intervention and 1763 in post-intervention surveys, and we obtained 911 and 706 responses. Total scores of the Palliative Care Knowledge Test, PCPS, and PCPS were significantly improved after the intervention, with effect sizes of 0.30, 0.52, and 0.17, respectively. Physicians who participated in workshops more frequently were significantly more likely to have better knowledge, less difficulties, and better self-reported practice.

Conclusion. After the regional palliative care program, there were marked improvements in physicians' knowledge and difficulties. These improvements were associated with the level of physicians' participation in the program. J Pain Symptom Manage 2015;50:232–240. © *2015 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words

Physician, knowledge, difficulty, palliative care, regional palliative care

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Introduction

Palliative care is an essential part of integrated cancer treatment.[1] It should be provided throughout an entire region, and several outcome studies have explored the effects of regional palliative care programs on place of death, the use of palliative care services, patient- and family-reported outcomes, and costs.[2–6] More recently, qualitative studies from the U.K. suggest that the most important benefit of the Gold Standards Framework is facilitating communication among health care professionals in the community.[7–9] Multiple studies from Canada, The Netherlands, and Australia revealed the perceived importance of an increase in personal and formal contact among health care professionals.[10–12]

These studies provide important insight into the potential benefits of regional palliative care programs, but, to our best knowledge, no studies have investigated the changes in physician-related outcomes despite the fact that physicians are clearly one of the most important professionals in terms of the quality of palliative care. To date, many surveys have revealed that physicians frequently have inadequate knowledge of cancer pain, opioids, symptom management, and the concept of palliative care; this could result in poor symptom control and late referrals to specialized palliative care services.[13–18] On the other hand, many physicians experience considerable difficulties when providing palliative care in a variety of areas, including symptom control, discussing death and achievable goals with patients and families, communication with multidisciplinary professionals, and obtaining support from palliative care specialists.[19–22] Although some educational intervention trials explored the effects of each program on physicians at an individual level,[23,24] understanding the changes in physician-related outcomes after a palliative care program is implemented at a regional level could be useful in interpreting how physicians should be supported to provide better palliative care for patients.

Thus, the primary aims of this study were to: 1) clarify the changes in knowledge, difficulties, and self-reported practice of physicians before and after the regional palliative care intervention program, 2) explore the potential associations between the level of physicians' participation in the program and outcomes, and 3) identify the self-reported reasons and characteristics of physicians who did not participate in the program. Our hypotheses were after the regional palliative care intervention program the knowledge, difficulties, and self-reported practice of physicians improved and the improvement was significantly associated with the level of physicians' participation in the program.

Methods

This was a part of a mixed-method regional palliative care intervention trial, the Japan Outreach Palliative care Trial of the Integrated Model (OPTIM) study.[25–27] The study methodology and results of primary endpoints of the study were reported in previous papers,[25,26] and this article reports the physician-related outcomes as secondary endpoints. This study was performed according to the ethical guidelines for epidemiological research proposed by the Ministry of Health, Labor and Welfare of Japan, and written informed consent was unnecessary. Ethical and scientific validity were confirmed by the institutional review boards for this study and of all participating hospitals.

Overview of the OPTIM Study[26]

The OPTIM study was performed in four regions of Japan. We obtained pre-intervention data for outcomes before or in the early phase of the intervention period and post-intervention data after or in the late phase of the intervention period. The intervention program was implemented from April 2008 to March 2011. The primary endpoints were home death, use of a palliative care service, and patient-reported and bereaved family-reported quality of palliative care. Secondary endpoints included patient-reported and bereaved family-reported quality of life, pain, caregiving burden, and knowledge, beliefs, and concerns about palliative care. The intervention is a comprehensive program covering four areas: 1) to improve the knowledge and skills of palliative care (i.e., dissemination of manuals and assessment tools with interactive workshops about palliative care), 2) to increase the availability of specialized palliative care services for community patients (i.e., establishment of a new community palliative care team, outreach educational visits), 3) to coordinate community palliative care resources (i.e., regional palliative care centers, whole-region multidisciplinary conferences, patient-held records, discharge-planning systems), and 4) to provide appropriate information about palliative care to the general public, patients, and families (i.e., dissemination of leaflets, posters and DVDs, workshops). During the study periods, as interventions for the main target of physicians, a total of 24,353 pocket-sized manuals and 174,891 assessment instruments were disseminated; 414 interactive workshops about a variety of palliative care topics were held and 22,189 health care workers participated; and 38 outreach visits were performed and 429 patients were referred to community palliative care teams.

After the interventions, the percentage of home deaths increased from 6.8% to 10.5%, and this increase was significantly greater than that in the national data.

Moreover, 88% of family members confirmed that patients who died at home had preferred a home death, and the care burden showed no significant increase. The rate of patients who received palliative care services increased significantly. The patient- and family-reported quality of care was significantly higher after intervention. The quality of life of terminally ill cancer patients, rated by proxy family members, was significantly higher after intervention. Qualitative analysis identified that the participants greatly emphasized improved communication and cooperation among regional health care professionals.

Subjects

Questionnaires were sent by mail to physicians recruited consecutively based on the inclusion criteria. Questionnaires were sent to hospital physicians via research coordinators at the study sites and clinic physicians via mail (one questionnaire for one general practice clinic). Questionnaires were accompanied with a brief letter explaining study aim, rationale for selecting subjects, and confidentiality. No reminder or rewards were used.

We intended to obtain as representative a sample of each region as possible. Data were collected in February 2008 as pre-intervention data and in January 2011 as post-intervention data. Inclusion criteria for this physician-based survey were 1) physicians of general practice clinics or those working at hospitals in cancer-related specialties (general internal medicine/family medicine, surgery, respiratory medicine, gastroenterology, gynecology, urology, otopharyncology, hematology, medical oncology, breast medicine, radiation oncology, and palliative medicine), and 2) clinical experience of three years or more (i.e., having completed residency training). Subjects were excluded if they had treated no cancer patients during the most recent year. This was a comparison of two different cross-sectional surveys, and study subjects were not the same. We identified hospitals treating cancer patients with reference to hospital lists from the Japan Hospital Association, the largest authorized organization of hospitals in Japan, and the local resource information. We finally obtained the participation of 23 of 34 hospitals in the study regions (8964 of 11,033 beds, 81%).

Measurement Instruments

Physician-reported knowledge was measured using the Palliative Care Knowledge Test.[28] This scale originally comprised five subscales, with correct, incorrect, and do not know responses. For this study, to lessen physician burden and increase response rates, we decided to use three subscales without changing items: philosophy (two items), pain (six items), and gastrointestinal symptoms (four items). The reliability and validity was conformed for each subscale.[28] The scale score was defined as the rate of correct answers, with a higher score meaning more accurate knowledge; possible range was 0–100.

Physician-reported difficulty with palliative care was measured with the Palliative Care Difficulty Scale, a validated tool to quantify the levels of difficulty when health professionals provide palliative care.[29] This scale includes five subscales: expert support, alleviating symptoms, community coordination, communication in multidisciplinary teams, and communication with patients and families. Each subscale has three items graded on a 5-point Likert-type scale from 1 = never to 5 = very much. One item example is "it is difficult to get support from experts on alleviating symptoms." A higher value means more perceived difficulties, with a possible range from 1 to 5.

Physician-reported self-perceived practice was measured using the Palliative Care Self-Reported Practice Scale, a validated tool to quantify the levels of adherence to recommended practices in palliative care fields.[29] This scale originally comprised six subscales graded on a 5-point Likert-type scale from 1 = never to 5 = very much. For this study, to lessen physician burden and increase response rates, we decided to use two subscales without changing items: pain and communication (three items each). One sample item is "I routinely inquire about the family's concerns in the dying phase." The reliability and validity was confirmed for each subscale.[29] A higher value means closer adherence to recommended practices in palliative care, with a possible range from 1 to 5.

We obtained physicians' background information (age, gender, clinical experience, clinical experience in each region, working sites, specialty, and the number of cancer patients seen per year). We also asked the physicians about the level of their involvement in the program with two questions. The first was "Did you participate in the regional palliative care program during the three years?" and physicians were asked to choose one response from "never," "participated in the program through attending workshops and reading materials," and "participated in the program through planning or operating some workshops." The second question was "How many times did you participate in workshops held by the regional palliative care program during the three years?," and physicians were asked to choose one response from "none," "one," "2–5," "6–10," and "more than 10." Furthermore, for the physicians who reported that they had never participated in the program, we asked them for the most important reason for nonparticipation: lack of information, insufficient time, lack of interest, lack of need, and others.

Statistical Analyses

To clarify the changes in knowledge, difficulties, and self-reported practice of physicians before and after the regional palliative care intervention program, we compared the total score and subscale scores of each outcome measure using the non-paired Student's *t*-test. To adjust for differences in physicians' backgrounds, a linear multivariate regression model was constructed using region, age, gender, clinical experience, working sites, and the number of cancer patients seen per year. The adjusted data were essentially the same, and we report only the crude data. To explore the potential effects of clinical experience in each region, we analyzed only the subjects who had clinical experience in each region of more than two years and obtained the same results. We calculated Hedges' g to estimate the effect size, and effect sizes of 0.2, 0.5, and 0.8 were regarded as small, moderate, and large effects, respectively.[30,31]

To explore the potential associations between the level of physicians' participation in the program and outcomes, we classified the respondents into two groups: non-participating physicians (they replied "never" participated in the program) and participating physicians (others). We then compared the total score for each outcome measure obtained in the post-intervention sample between non-participating and participating physicians using the non-paired Students' *t*-test. Furthermore, we compared the total score for each outcome measure among physicians who participated in the workshops at different times using analysis of variance (post-hoc test was not performed).

To identify the reasons for non-participation, we calculated the rates and 95% CIs of reasons given. We then compared backgrounds between participating and non-participating physicians. To identify the independent determinants, logistic regression analysis was performed using the factors investigated.

To explore the changes in the outcomes of physician subgroups, we compared the total score of knowledge and difficulties among physicians with different backgrounds: region, clinical experience (<10, 10–19, 20 years or more), working sites, specialty, and the number of cancer patients seen per year (<10, 10–49, 50 or more). For specialty, specialties with 30 or more physicians were analyzed, and physicians with a specialty of palliative medicine and others were excluded from analyses.

The *P*-value regarded as significant was 0.05 for the exploratory nature of this study, although we acknowledge that multi-comparisons could cause a Type 1 error. Analyses were performed using the Statistical Package for the Social Sciences v. 13.0 (SPSS Inc., Chicago, IL).

Results

The number of eligible physicians identified was 1870 in pre-intervention and 1763 in post-intervention surveys. Of these, 1131 (60%) and 843 (43%) returned the questionnaire, respectively; 220 and 137 responses were excluded from the analyses because of missing values or they had no opportunity to see cancer patients. In total, we obtained 911 and 706 responses, and response rates were 49 and 40%, respectively. Table 1 summarizes the backgrounds of the physicians. There were significant differences in the clinical experience, working sites, and number of cancer patients seen per year between the surveys. Mean clinical experience in each region was 13 and 14 years in pre-intervention and post-intervention surveys, respectively.

A total of 325 (46%) physicians reported that they participated in the program through attending workshops and reading materials, and an additional 67 (9.5%) physicians reported that they participated in the program through planning or operating some workshops; thus, 392 (56%) physicians were classified as participating physicians, and 296 (42%) physicians were non-participating physicians. The frequency of physicians participating in the workshops was none in 335 (47%), one in 110 (16%), two to five in 163 (23%), six to 10 in 47 (6.7%), and more than 10 in 35 (5.0%).

Changes in Knowledge, Difficulties, and Self-Reported Practice

Total scores of the Palliative Care Knowledge Test, Palliative Care Difficulties Scale, and Palliative Care Self-Reported Practice Scale significantly improved after the intervention periods, with effect sizes of 0.30, 0.52, and 0.17, respectively (Table 2). Among subscales, the effect sizes of the community coordination subscale and expert support subscale of the Palliative Care Difficulties Scale were about 0.50 or more.

Associations Between the Level of Physicians' Participation in the Program and Outcomes

Compared with non-participating physicians, the participating physicians were significantly more likely to show improvements in knowledge, difficulties, and self-reported practice: knowledge, 83 (17) vs. 74 (22); difficulties, 2.1 (0.67) vs. 2.5 (0.78); self-reported practice, 3.9 (0.68) vs. 3.6 (0.81); $P < 0.001$ for all variables. There was a clear trend whereby physicians who participated in the workshop were significantly more likely to show improvements in knowledge, difficulties, and self-reported practice ($P < 0.001$ for all variables) (Fig. 1). Physicians who participated in the workshop more than 10 times had the lowest scores on all the subscales

Table 1
Physicians' Backgrounds

Background Characteristics	Before ($n = 911$)	After ($n = 706$)	P
Region, % (n)			
Tsuruoka	7.8 (71)	7.2 (51)	
Kashiwa	27 (243)	29 (202)	0.62
Hamamatsu	30 (275)	28 (195)	
Nagasaki	35 (322)	36 (258)	
Mean (SD) age (yrs)	48 (13)	47 (12)	0.025
Sex, % (n)			
Male	89 (809)	88 (621)	0.50
Female	9.3 (85)	10 (73)	
Mean (SD) clinical experience	22 (12)	21 (11)	0.012
Mean (SD) clinical experience in each region	14 (11)	13 (10)	0.12
Working sites			0.0020
Cancer hospitals	44% (405)	53% (371)	
Hospitals other than cancer hospitals	15% (139)	16% (115)	
Clinics with a home hospice function	13% (117)	10% (69)	
Clinics without a home hospice function	27% (250)	21% (151)	
Specialty			0.32
General internal medicine, family practice	33% (297)	26% (184)	
General surgery	15% (137)	16% (116)	
Gastroenterology	9.4% (86)	10% (69)	
Abdominal surgery	5.7% (52)	5.7% (40)	
Gynecology	5.6% (51)	7.1% (50)	
Urology	5.3% (48)	4.4% (31)	
Respiratory medicine	4.6% (42)	5.8% (41)	
Otorhinolaryngology	4.6% (42)	4.2% (30)	
Thoracic surgery	2.7% (25)	3.1% (22)	
Hematology	2.1% (19)	2.3% (16)	
Palliative medicine	1.4% (3)	1.4% (10)	
Breast medicine	1.0% (9)	1.1% (8)	
Radiation oncology	0.8% (7)	1.4% (10)	
Medical oncology	0.2% (2)	0.4% (3)	
Clinical oncology	0.1% (1)	0.7% (5)	
Others	8.5% (77)	10% (71)	
Number of cancer patients/y			
<10	39% (358)	32% (223)	0.005
10–49	30% (274)	33% (230)	
≥50	30% (273)	35% (249)	

The percentages do not add up 100% because of missing values.

of difficulties and the highest scores on all the subscales of knowledge and self-reported practice (data not shown). The mean scores of the subscales in the Palliative Care Difficulties Scale were communication in multidisciplinary teams (2.0, SD 1.0), alleviating symptoms (1.9, SD 0.85), communication with patients and families (1.9, SD 0.73), community coordination (1.6, SD 0.74), and expert support (1.3, SD 0.53).

Self-Reported Reasons and Characteristics of Non-Participating Physicians

Self-reported reasons were insufficient time (47%, $n = 158$; 95% CI 42, 53), lack of information (32%, $n = 106$; 95% CI 27, 37), lack of interest (16%, $n = 52$; 95% CI 12, 19), and lack of need (5.0%, $n = 16$; 95% CI 3, 8). Between the non-participating and participating physicians, there were significant differences in age, clinical experience, and working sites (Table 3). Independent determinants of non-participation were a less clinical experience and working at clinics without a home hospice function (Table 3).

Changes in Outcomes in Physician Subgroups

The total score of the physician-perceived difficulties significantly improved in all subgroups investigated (Table 4). Physicians with 20 years or more of clinical experience, working at clinics without a home hospice function, specialty of general internal medicine/family practice, and seeing less than 10 cancer patients had a lower knowledge score and higher difficulties score, but the scores were significantly improved in the post-intervention group.

Discussion

This is, to our best knowledge, the first study to systematically investigate the changes in physicians' knowledge, difficulties, and self-reported practice after a palliative care program implemented at a regional level. The most important finding of this study was that, in addition to moderate improvement in knowledge levels, physicians' difficulties markedly

Table 2
Changes in Knowledge, Difficulties, and Self-Reported Practice

Items	Before ($n = 911$)	After ($n = 706$)	Effect Size	*P*
Knowledge[a]				
Total	72 (23)	78 (20)	0.30	<0.001
Philosophy	89 (28)	92 (25)	0.11	0.025
Pain	72 (26)	79 (23)	0.28	<0.001
Gastrointestinal symptom	64 (29)	71 (27)	0.26	<0.001
Difficulties[b]				
Total	2.7 (0.80)	2.3 (0.75)	0.52	<0.001
Alleviating symptoms	2.9 (0.98)	2.8 (0.98)	0.18	<0.001
Expert support	2.4 (1.2)	1.8 (1.1)	0.49	<0.001
Communication in multidisciplinary teams	2.5 (1.0)	2.1 (0.97)	0.37	<0.001
Communication with patients and families	2.7 (0.94)	2.5 (0.92)	0.22	<0.001
Community coordination	3.0 (1.1)	2.3 (1.1)	0.63	<0.001
Self-reported practice[c]				
Total	3.6 (0.79)	3.7 (0.77)	0.17	0.001
Pain	3.4 (1.0)	3.6 (1.0)	0.20	<0.001
Communication	3.8 (0.80)	3.9 (0.80)	0.08	0.095

Values are means (SDs).
[a]Palliative Care Knowledge Test: higher value means more accurate knowledge, with a possible range from 0 to 100%.
[b]Palliative Care Difficulty Scale: higher value means more perceived difficulties, with a possible range from 1 to 5.
[c]Palliative Care Self-Reported Practice Scale: higher value means closer adherence to recommended practices in palliative care, with a possible range from 1 to 5.

improved after the regional palliative care program, especially in terms of community coordination, expert support, and communication in multidisciplinary teams. Potential reasons are 1) improved communication among health care professionals working in the same region through whole-region multidisciplinary conferences resulted in decreased difficulties in community coordination and communication in multidisciplinary teams and 2) improved expert resources available in the region resulted in decreased difficulties in expert support. These interpretations were supported by accompanying qualitative analyses.[26,27] These findings are consistent with the conclusions from multiple qualitative studies that one of the main effects of a regional palliative care program is improved communication among regional health care professionals.[7,10–12] This strongly indicates that a comprehensive regional palliative care program would decrease physicians' difficulties through facilitating interactions among community health care workers at a regional level, and this might contribute to better care coordination and symptom control for patients themselves.

The second important finding was the observation of the clear relationship between the level of physicians' participation in the programs and improvement of outcomes. Some studies suggest the potential association between the intensity of exposure and changes in outcomes in the palliative care education literature.[24] These findings indicate that ensuring multiple opportunities for physicians to participate in a regional palliative care program as a part of daily practice could lead to developing a better regional network, as well as obtaining better knowledge. The fact that the physician-reported reason for non-participation was not a lack of interest but a lack of information and time is encouraging. Non-participating physicians were younger or worked

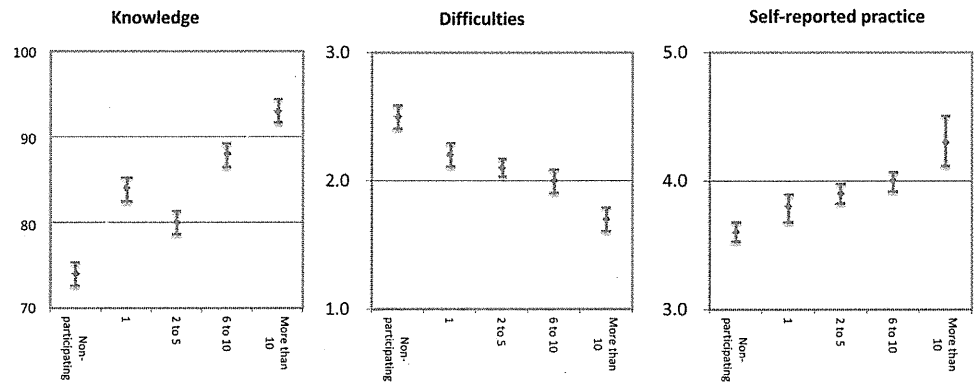

Fig. 1. Association between the number of workshops physicians participated in and outcomes. Non-participating ($n = 332$), 1 ($n = 109$), 2–5 ($n = 161$), 6–10 ($n = 47$), and more than 10 ($n = 35$). Values are expressed as the mean, with the bars showing 95% CIs.

Table 3
Characteristics of Physicians Who Did Not Participate in the Program

	Univariate Analysis			Multivariate Analyses		
Background Characteristics	Non-Participants ($n = 296$)	Participants ($n = 396$)	*P*	Odds Ratio	95% CI	*P*
Age (yrs)	44 (12)	49 (11)	<0.001			
Sex (male)	87% (257)	88% (350)	0.38			
Clinical experience (y)	18 (12)	22 (10)	<0.001	0.95	0.93, 0.97	<0.001
Working sites			<0.001			<0.001
Cancer hospitals (reference)	57% (168)	49% (195)		1.0		
Hospitals other than cancer hospitals	16% (46)	17% (66)		0.88	0.54, 1.43	0.60
Clinics with a home hospice function	3.7% (11)	14% (54)		0.40	0.18, 0.87	0.020
Clinics without a home hospice function	24% (71)	19% (77)		2.29	1.35, 3.89	0.002
Specialty			0.23			
General internal medicine or family practice	22% (64)	29% (114)				
Surgery	24% (70)	26% (104)				
Respiratory medicine or gastroenterology	16% (48)	15% (58)				
Gynecology	8.1% (24)	6.0% (24)				
Urology	4.7% (14)	4.3% (17)				
Otorhinolaryngology	5.7% (17)	3.3% (13)				
Hematology, medical oncology, breast medicine, or radiation oncology	6.1% (18)	5.8% (23)				
Cancer patients seen per year	3.0 (0.83)	3.1 (0.83)	0.21			

Values are means (SDs) or percentages (numbers).

at clinics without a home hospice function. A strategy to provide sufficient information and time for younger busy physicians and those working at clinics without a home hospice function to allow participation in such a program could contribute to more effective results. Of note was that there might be ceiling effects in a dose-effect relationship between the improvements in physician outcomes and the degree of physician participations. As the number of physicians who participated in the program more than 10 times was small ($n = 35$), subgroup analyses were impossible. Further studies should explore

Table 4
Changes in Knowledge and Difficulties of Subgroup Physicians After Interventions

	Knowledge			Difficulties		
Background Characteristics	Before ($n = 911$)	After ($n = 706$)	*P*	Before ($n = 911$)	After ($n = 706$)	*P*
Region						
Tsuruoka	74 (17)	80 (17)	0.064	3.1 (0.81)	2.1 (0.69)	<0.001
Kashiwa	69 (25)	79 (20)	<0.001	2.6 (0.82)	2.4 (0.80)	0.005
Hamamatsu	72 (24)	81 (20)	<0.001	2.8 (0.84)	2.3 (0.78)	<0.001
Nagasaki	74 (21)	76 (21)	0.31	2.6 (0.72)	2.2 (0.67)	<0.001
Clinical experience (yrs)						
<10 ($n = 154$, 133, respectively)	78 (18)	81 (16)	0.20	2.5 (0.72)	2.3 (0.64)	0.030
10–19 ($n = 237$, 218, respectively)	80 (18)	83 (16)	0.032	2.6 (0.68)	2.2 (0.67)	<0.001
20 or more ($n = 520$, 355, respectively)	67 (25)	75 (23)	<0.001	2.8 (0.87)	2.3 (0.82)	<0.001
Working sites						
Cancer hospitals	79 (19)	84 (16)	<0.001	2.4 (0.69)	2.1 (0.59)	<0.001
Hospitals other than cancer hospitals	76 (19)	82 (17)	0.007	2.7 (0.74)	2.3 (0.77)	<0.001
Clinics with a home hospice function	74 (20)	77 (22)	0.39	2.7 (0.77)	2.0 (0.67)	<0.001
Clinics without a home hospice function	58 (26)	63 (24)	0.048	3.1 (0.89)	2.8 (0.88)	0.001
Specialty						
General internal medicine or family practice	63 (24)	69 (24)	0.007	2.9 (0.84)	2.5 (0.82)	<0.001
Surgery	75 (21)	83 (17)	<0.001	2.6 (0.72)	2.2 (0.64)	<0.001
Respiratory medicine or gastroenterology	80 (15)	84 (18)	0.15	2.5 (0.72)	2.2 (0.74)	<0.001
Gynecology	81 (20)	80 (19)	0.82	2.6 (0.82)	2.2 (0.80)	0.009
Urology	70 (21)	79 (17)	0.050	2.6 (0.72)	2.1 (0.54)	0.001
Otorhinolaryngology	72 (22)	87 (13)	0.002	2.6 (0.71)	2.2 (0.61)	0.032
Hematology, medical oncology, breast medicine, or radiation oncology	88 (12)	84 (13)	0.22	2.6 (0.70)	1.9 (0.62)	<0.001
Cancer patients seen per year						
<10	61 (25)	67 (23)	0.010	3.0 (0.87)	2.5 (0.87)	<0.001
10–49	75 (20)	81 (19)	0.001	2.6 (0.72)	2.2 (0.66)	<0.001
50 or more	82 (16)	86 (14)	0.002	2.4 (0.68)	2.1 (0.64)	<0.001

Values are means (SDs).

how many exposures were most favored in terms of cost-effectiveness.

The third important finding is the clarification of physicians who require support for palliative care. That is, physicians with 20 or more years of clinical experience, working at clinics without home hospice program, a specialty of general internal medicine/family practice, and seeing less than 10 cancer patients had lower knowledge and higher difficulty scores. This finding is reasonable because it is speculated that they had not received sufficient medical education on palliative care and had much less clinical experience with palliative care for patients. This is in contrast to the previous findings whereby senior general practitioners had more accurate knowledge of and less difficulties in palliative care in countries where a general practitioner system has been established.[32,33] Promising findings observed in this study are that, although their absolute levels of knowledge were low and difficulties were high, significant improvement was achieved after the regional intervention program, and younger physicians reported lower difficulties, probably because of improved under- and postgraduate education.[15] Because they provide palliative care only as part of their general practice, developing a multidisciplinary support system seems to be essential to decrease this burden on physicians and provide quality palliative care for patients.[34]

Of note was clarification of the areas of physician difficulties that remained relatively high, even for those who participated in workshops more than 10 times. That is, difficulties in communication in multidisciplinary teams and alleviating symptoms were relatively higher than difficulties in community coordination and expert support. This is reasonable because of the nature of the intervention, and individual interventions may be required for such areas.

This study has several limitations. First, there were no control groups, and changes observed might be national trends observed throughout Japan. There are also many factors that could influence outcomes in addition to the intervention, such as changes in the health care system and economics. Although we believe this bias may be present, it does not influence our major conclusions because the changes in outcomes observed can be well interpreted in terms of the nature of the intervention and findings from qualitative and quantitative studies.[26,27] Second, the response rate was generally low and differed between the two surveys. This may lead to overestimation of the intervention effects because responding physicians had more accurate knowledge and lower difficulties. As we had no data on non-responding physicians, we cannot exactly estimate the effects of this difference on the conclusions. We believe, however, that this bias would not influence the main conclusion because a nurse survey with a more than 80% response rate obtained in both surveys showed similar results.[26] In addition, we acknowledge that the limitation of low response rates is unavoidable in physician-based surveys because other nationwide surveys performed by the Japanese Medical Association and Ministry of Health, Labor and Welfare as a part of a national strategy achieved a similar or lower response rate, that is, 36% and 43%, respectively. Third, some physician backgrounds were significantly different between the two surveys. Although we performed statistical adjustments and subgroup analyses, there might be bias from unobserved differences. Fourth, the association between the level of physicians' participation and changes in outcomes might be influenced by unmeasured differences in physicians' characteristics, for example, physicians' willingness to see cancer patients and receive training. Finally, the comparisons of this study were at a regional and not an individual level.

Conclusion

After the regional palliative care program, physicians' knowledge and difficulties markedly improved, especially in terms of community coordination, expert support, and communication in multidisciplinary teams. This improvement was associated with the level of physicians' participation in the program. A regional palliative care program could improve physicians' knowledge and difficulties through making a network available and accessible in a region and so should be integrated into regional health care policies.

Disclosures and Acknowledgments

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Methadone for Patients with Malignant Psoas Syndrome: Case Series of Three Patients

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Abstract

Background: Malignant psoas syndrome (MPS) is a relatively rare syndrome that accompanies malignancy; the pain associated with MPS is often difficult to control. Methadone is known to be effective in relieving both nociceptive and neuropathic pain.
Objective: Herein we describe treatment strategies for three patients with MPS, diagnosed by imaging and clinical findings, who responded to methadone treatment.
Methods: Patient diagnoses, pain characteristics, and treatment were analyzed retrospectively.
Subjects were three patients with MPS who presented to Hyogo Cancer Center with pain. A numeric rating scale (NRS; 0–10) was used to assess patients' pain levels.
Results: All three patients were diagnosed with malignancies (prostate, cervical, and urachal) and had impaired gait and thigh extension. All had tumor invasion to the iliopsoas muscle, as determined by imaging, and were diagnosed with MPS. After starting methadone, symptoms improved in all patients and they were able to extend the thigh and walk normally. The NRS scores improved by an average of −7.3 points (95% confidence interval [CI] −4.97, −9.69) on Day 14; and the average time until symptom improvement after starting methadone was 2.3 days (95% CI 1.86, 2.80).
Conclusions: Methadone may be considered a treatment choice for MPS patients in whom pain is difficult to control.

Introduction

MALIGNANT PSOAS SYNDROME (MPS) was first described in 1990.[1] It is characterized by proximal lumbosacral plexopathy, painful fixed flexion of the ipsilateral hip with a positive psoas muscle stretch test, and radiological evidence of malignant involvement of the ipsilateral psoas major muscle. Moreover, this rare syndrome is known to be resistant to pain control with opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and adjuvant drugs.[2]

Although it has been used worldwide for more than 60 years, methadone was first approved for use in Japan in 2013. Methadone has no active metabolite and may be administered to patients with declining renal function. In addition, it has low cross-resistance with other opioids and exhibits *N*-methyl-D-aspartate (NMDA) receptor antagonist activity.[3]

However, the half-life of methadone can range from 12 to 150 hours. It takes approximately one week for stable blood concentrations to be reached, and there is a risk of drug accumulation in the body because methadone is fat soluble.[3] One of the issues considered during the approval process of methadone in Japan was the high mortality rate associated with its use compared with other opioids.[4] Following the approval of methadone in Japan, the Ministry of Health, Labour and Welfare recommends that the use of methadone be rotated with 60 mg/day morphine, or an equivalent dose of other opioids, when pain is not well controlled.

Methadone has been used primarily to treat drug addiction,[5] and although the use of methadone in cancer is increasing, there are few reports describing its use for the treatment of cancer pain.[6] We have experienced three patients who were diagnosed with MPS in whom methadone treatment was effective. Herein we describe these cases and their respective treatment strategies.

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TABLE 1. PATIENT STATUS AT TIME OF PRESENTATION

	Age/ sex	*Primary cancer site*	*Treatment*	*Imaging findings (causation MPS)*	*Walking*	*Extension of thigh*
Case I	59/M	Prostate	BSC	Invasion to IPS from right common iliac lymph node metastases	Difficult because of pain	Impossible
Case II	35/M	Urachal	Obs	Invasion to IPS from left common iliac lymph node metastases	Painful	Difficult because of pain
Case III	70/F	Cervix	BSC	Metastases to IPS	Difficult because of pain	Impossible

BSC, ; IPS, ; MPS, ; Obs,.

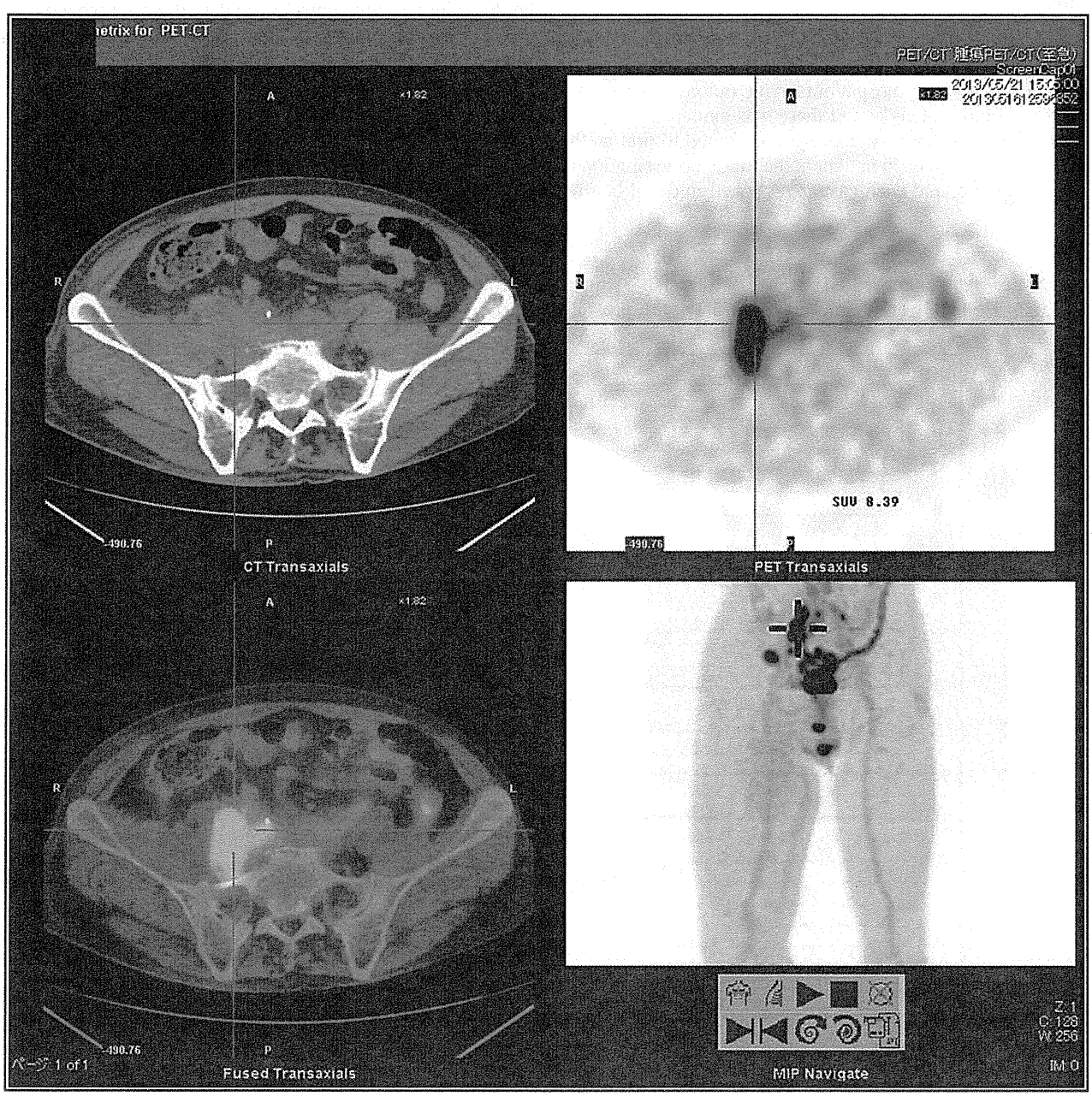

FIG. 1. Positron emission tomography/computed tomography of Case 1 on admission.

Methods

The present study was a retrospective analysis of three MPS patients who responded to methadone. The switch from morphine to methadone was made by stopping morphine with an immediate substitution of methadone using a stop-and-go (SAG) approach; in the case of transdermal fentanyl, the drug was discontinued six hours before patients were started on oral methadone.[7,8]

A numeric rating scale (NRS; 0–10) was used to assess patients' pain levels, as per the MD Anderson Symptom Inventory. The highest and lowest possible scores are referred to as the NRS_{max} and NRS_{min}, respectively. Toxicity was evaluated on the basis of Common Terminology Criteria for Adverse Events version 4.0. In this article we define the day we started oral methadone as Day 1.

Results

Three patients with MPS presented to Hyogo Cancer Center between April 2013 and July 2014. Pain was not well controlled in any of the patients with opioids (morphine, oxycodone, and fentanyl); and there was evidence of opioid toxicity; thus, all three patients were switched to oral methadone. The status of each patient at the time of presentation is given in Table 1, and each case is reviewed in detail below.

Case I

A 59-year-old man presented because of intractable pain in May 2013. He had been diagnosed previously with prostate cancer and had been undergoing hormone therapy and chemotherapy since September 2010. No other clinical history was noted.

The patient had pain in his back and left lower abdomen and had difficulty walking and extending his thigh because of the pain. The psoas muscle stretch test was positive. On positron emission tomography (PET)/ computed tomography (CT), high uptake (maximum standardized uptake value 8.39) was observed at the right common iliac lymph nodes, indicating metastases. These metastases directly infiltrated the iliopsoas muscle. In addition, external iliac lymph node metastases and spinal metastasis to L2 were observed (see Figure 1).

Upon presentation, the patient was administered transdermal fentanyl (nearly equivalent to 1.75 mg fentanyl by continuous intravenous infusion [c.i.v.]), morphine hydrochloride hydrate as a rescue dose, and 1 mg dexamethasone, but his pain was not controlled and he did not respond to the rescue dose of morphine other than becoming extremely sleepy. Despite the addition of 400 mg etodolac, the patient's pain did not improve.

Six hours after discontinuing transdermal fentanyl, the patient was started on oral methadone (30 mg/day). On Day 3 his pain had resolved such that he was able to extend his thigh and walk. On Day 5, Grade 2 nausea developed. On Day 7 the methadone dose was reduced to 20 mg/day. On Day 13 the patient was admitted to hospital because of cellulitis of the right lower limb, but he soon recovered with intravenous antibiotics. On Day 14 the patient's NRS_{max} was reduced from 10 (on Day 1) to 2, and the NRS_{min} was reduced from 2

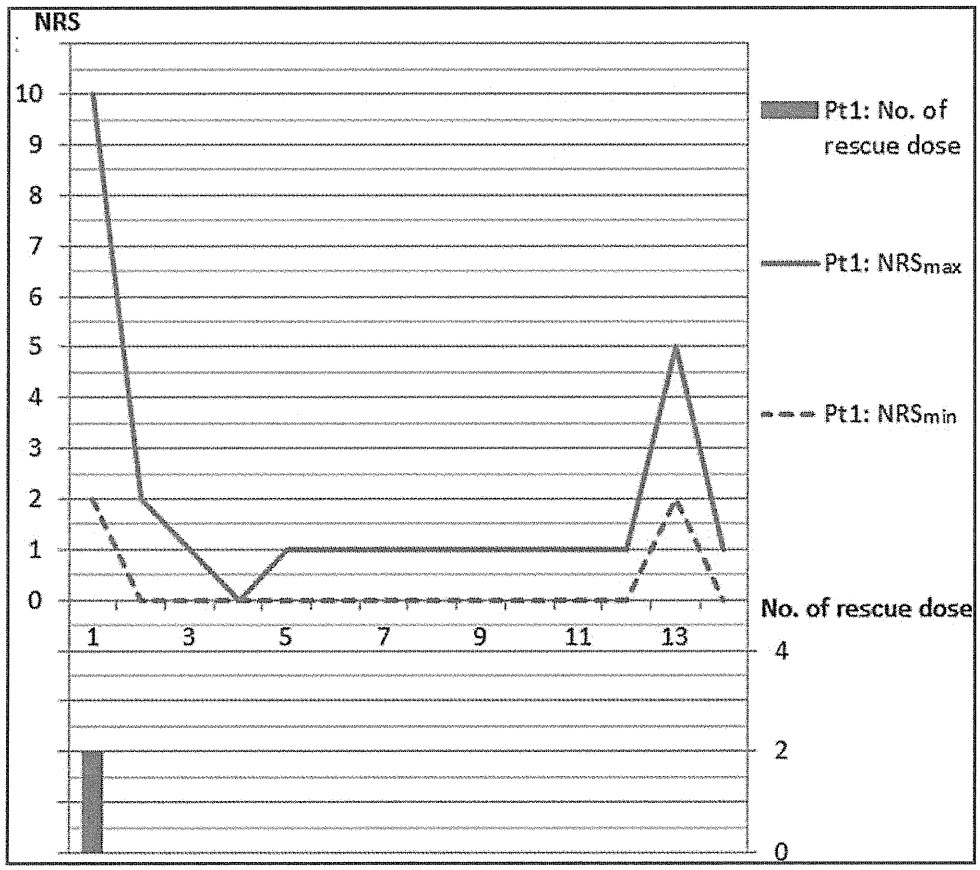

FIG. 2. The change of NRS and the number of rescue doses in Case 1.

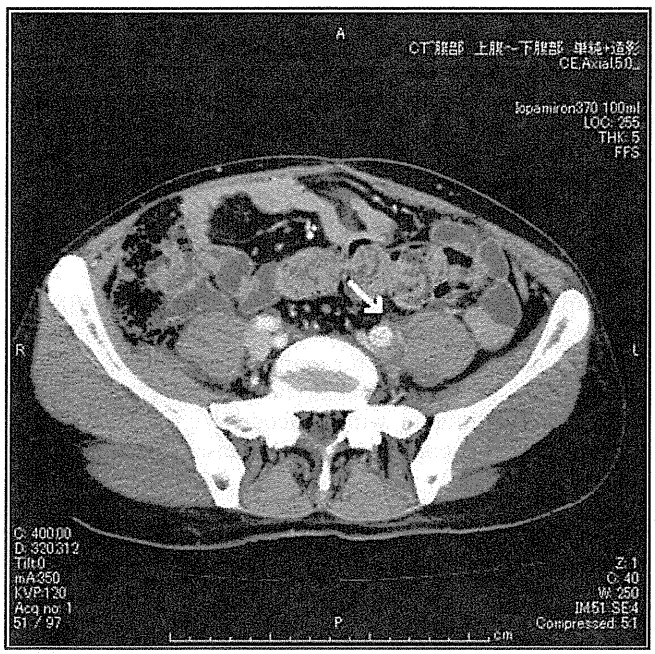

FIG. 3. Computed tomography of Case 2 on admission.

(on Day 1) to 0. Although the patient died approximately six months after starting methadone treatment, his pain was well controlled up until one week before he died, at which time he was no longer able to take oral medication. The changes in NRS scores and doses are shown in Figure 2.

Case II

A 35-year-old man was referred to Hyogo Cancer Center in February 2014 because of pain in his left leg. He had been diagnosed previously with urachal cancer and treated surgically (in 2008, 2009, and 2012) and with adjuvant chemotherapy with cisplatin and S-1 in 2010. No other clinical history was noted.

The patient had left inguinal and thigh pain with leg edema. He also had strong pain when we straightened his left knee, such that he was unable to lie on a bed. The psoas muscle stretch test was positive. CT revealed swelling of the left common iliac lymph node to 11 mm and infiltration into the left iliopsoas muscle; the left inguinal lymph nodes were also swollen, but there was no apparent obstruction of the circulation (see Figure 3).

The patient had been given 200 mg tramadol hydrochloride for pain control, but this did not work, so he was switched to oxycodone SR (60 mg/day). In addition, the patient was on 75 mg/day pregabalin and 180 mg/day loxoprofen sodium hydrate. Despite this, the patient's pain remained uncontrolled and the rescue medication (10 mg oxycodone) was ineffective, inducing only strong sleepiness.

After admission, the patient was started on oral methadone (15 mg/day) with a rescue dose of 10 mg oxycodone. On Day 2 his symptoms had improved and he could lie on a bed and walk with less pain. On Day 5 the patient could assume the position for palliative irradiation, so he was treated with palliative irradiation to the pelvis with a total dose of 37.5 Gy (15 fractions [Fr]). On Day 14, despite the fact that the palliative irradiation had not been completed, the patient's

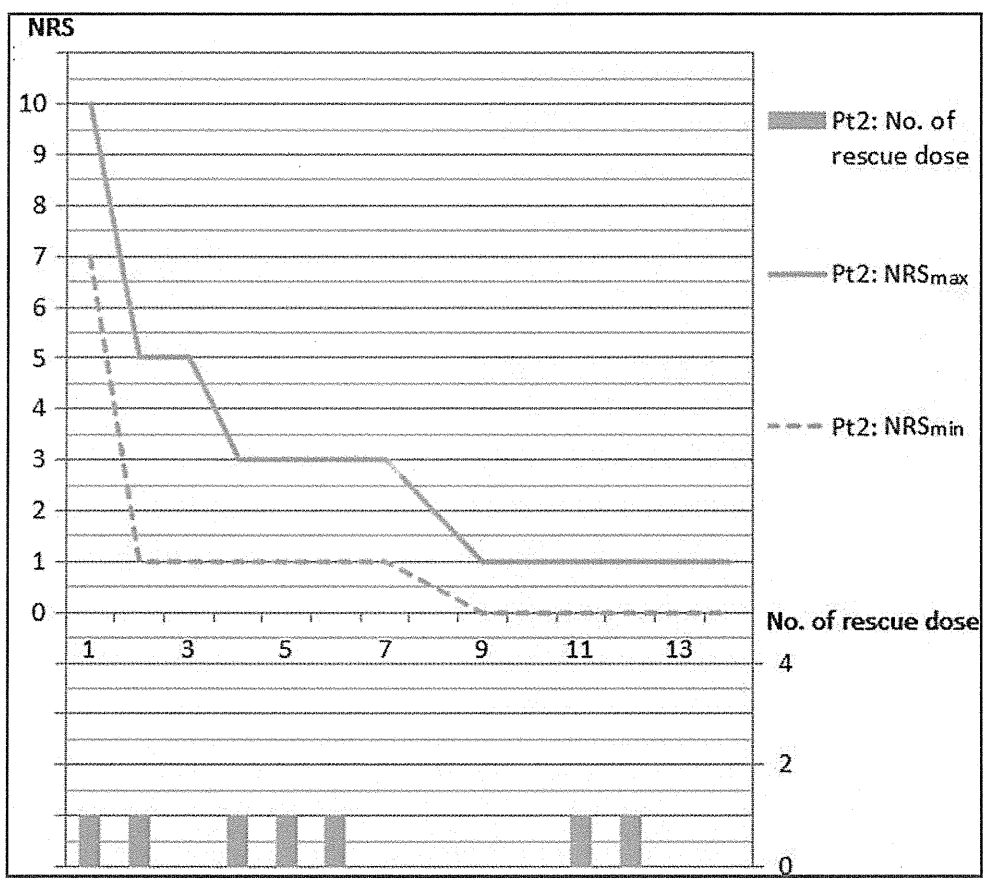

FIG. 4. The change of NRS and the number of rescue doses in Case 2.

NRS_{max} was reduced from 10 (on Day 1) to 1, and the NRS_{min} was reduced from 7 (on Day 1) to 1. At the time of writing, the patient is still alive and undergoing chemotherapy; his pain continues to be well controlled with methadone. The change in NRS scores and doses are shown in Figure 4.

Case III

A 70-year-old woman was referred to Hyogo Cancer Center in April 2014 because of pain when moving. She had been diagnosed with cervical cancer in 2013 and had been treated with chemoradiation, including radiation to the pelvis (65 Gy/35 Fr) and uterovaginal brachytherapy (14.83 Gy/3 Fr), and chemotherapy with cisplatin. The patient had also been diagnosed previously with oropharyngeal carcinoma and treated with induction chemotherapy followed by chemoradiation, but it is unlikely that this tumor was associated with her current pain. A clinical history of an appendectomy at 18 years of age was noted.

The patient had pain in the left lower abdomen, along with left inguinal and thigh pain; she also had difficulty moving, especially walking. The psoas muscle stretch test was positive. Direct invasion to the left iliopsoas muscle was observed on PET/CT, as were lung metastases, invasion into the right muscle under the shoulder blade, and a residual lesion at the cervix and urethra (see Figure 5).

Despite being treated with 10 mg/day oxycodone SR and 180 mg/day loxoprofen, the patient was admitted to Hyogo Cancer Center because of her pain. Loxoprofen was stopped at the time of hospitalization because of reduced renal function, and titration with oxycodone c.i.v. was started. However, the patient felt strong, unpleasant sleepiness with

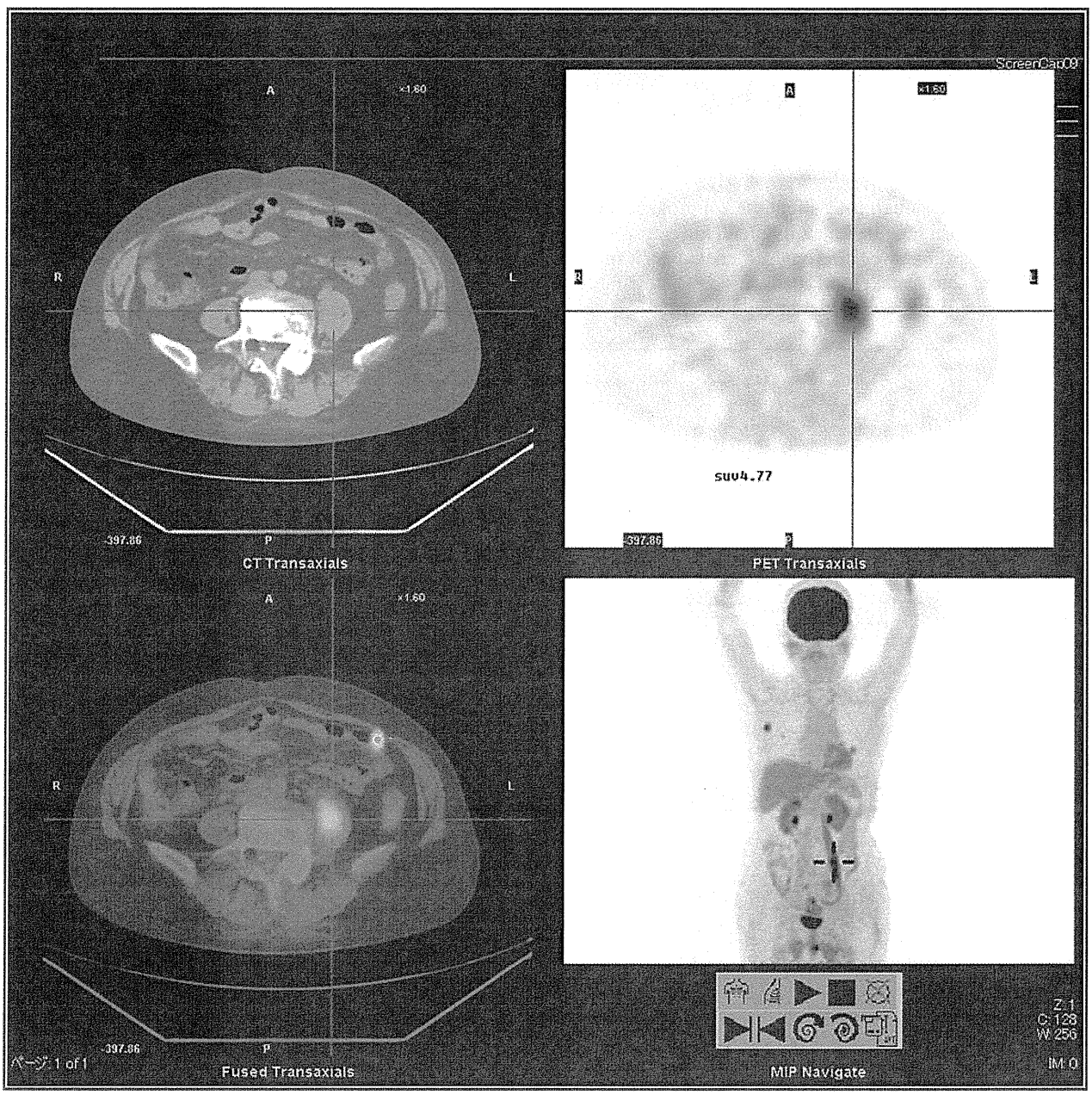

FIG. 5. Positron emission tomography/computed tomography of Case 3 on admission.

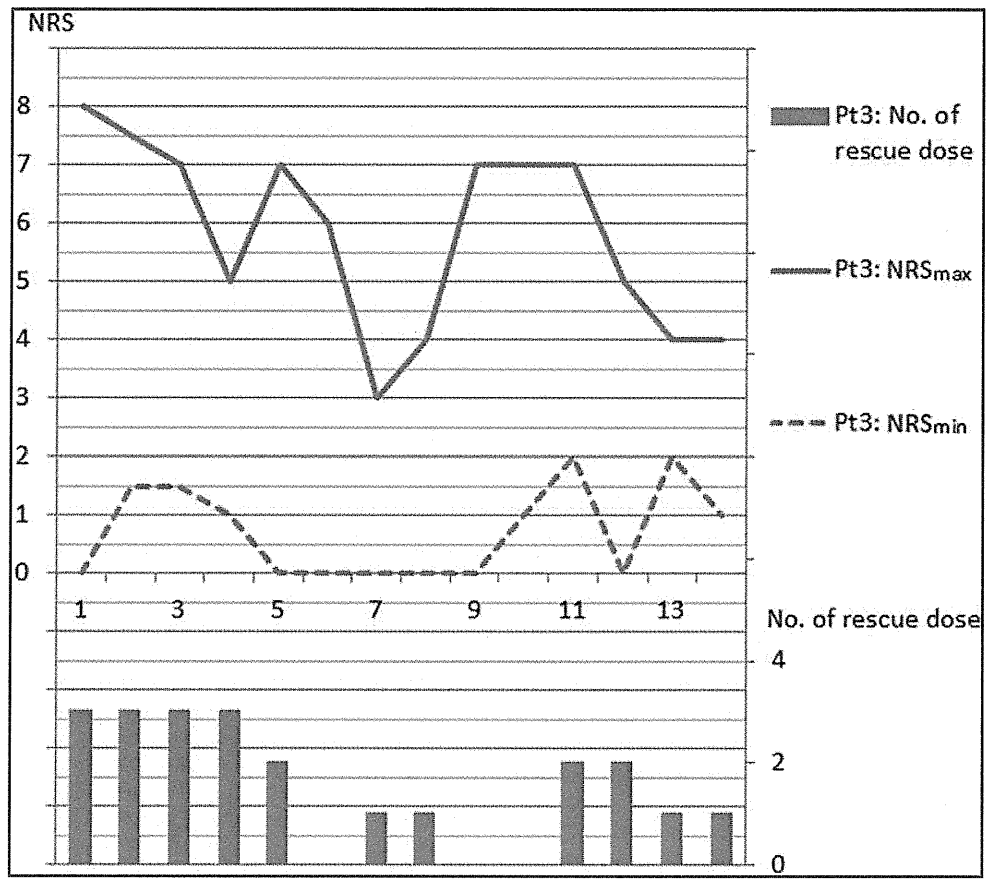

FIG. 6. The change of NRS and the number of rescue doses in Case 3.

14.4 mg/day oxycodone c.i.v. The dose of oxycodone was reduced to 12 mg/day c.i.v., but the patient's pain was not controlled with this dose. The patient was switched to 1.2 mg fentanyl c.i.v. in an attempt to decrease her sleepiness, but she remained sleepy and her pain remained uncontrolled.

The patient was then started on oral methadone (15 mg/day), and at the end of Day 1 of treatment she was able to extend her left thigh; on Day 2 her movement-related pain had improved. On Day 7, despite good pain control, the dose of oral methadone was reduced from 15 mg/day to 10 mg/day because delirium was observed. On Day 8 the patient was able to start rehabilitation, but her NRS score worsened. The pain symptoms differed from the MPS pain and were thought to be due to vesical tenesmus caused by bladder invasion. The patient was started on loxoprofen again because her renal function had recovered by that time. On Day 11 the patient's pain levels were again reduced. On Day 14 the patient's NRS_{max} was reduced from 8 (Day 1) to 4, but her NRS_{min} was relatively stable at 1 (0 on Day 1). The patient died approximately two months after starting methadone, but her pain was well controlled up until three days before her death, at which time she was no longer able to take oral medication. The changes in NRS scores and doses are shown in Figure 6.

Efficacy

After methadone initiation, the patients' pain symptoms had improved within three days (average 2.3 days; 95% confidence interval [CI] 1.86, 2.80), and they could all extend their thigh and walk. The NRS_{max} was reduced by an average of −7.3 points (95% CI −4.97, −9.69) by Day 14. Pain was well controlled in two of the three patients up until they were no longer able to take oral medication.

Discussion

With methadone treatment, all three MPS patients experienced an improvement in their symptoms and could extend their thigh and walk. The NRS scores also clearly improved in a relatively short period of time, and the number of rescue doses used decreased in two of the three patients. In the third patient, the NRS score and the number of rescue doses decreased once, but when she started rehabilitation, her pain worsened transiently due to vesical tenesmus. This pain was resistant to the rescue medication and the patient did not want to use rescue doses. Furthermore, the development of delirium between Days 7 and 10 was another reason for the temporary reduction in rescue doses. This patient's symptoms improved soon after she was restarted on loxoprofen, but some residual pain remained while moving. From the aspect of morphine equivalent daily dose (MEDD), the MEDD of all three patients was decreased by switching to oral methadone (Case I, 175.0 mg to 47.0 mg MEDD/day; Case II, 90.0 mg to 70.5 mg MEDD/day; Case III, 120.0 mg to 47.0 mg MEDD/day).[9]

Although there are no standard criteria for the switch from other opioids to methadone, all three patients in the present series had tried up to two different opioids before switching to methadone—Case I: morphine rescue and fentanyl; Case II:

tramadol and oxycodone; Case III: oxycodone and fentanyl—which had resulted in a poor response and unacceptable toxicity. For these reasons we decided to use methadone. The switch to methadone was made using the SAG approach.[7,8] While switching from the other opioids to methadone, rescue doses were used for breakthrough pain. The rescue doses were effective for Case II, and we continued. For Case I, the rescue medication was changed to a diclofenac suppository, which was used only a few times. Case III continued with fentanyl i.v. at first, but her pain control was not good. After the addition of sublingual fentanyl, this patient's pain improved.

If rescue doses prove to be useful even slightly, we continue them at first. If there is no response at all to rescue doses, changing to another rescue medication is preferable. Furthermore, the addition of rapid-onset opioids may be beneficial. A recent study has reported that switching over three days is preferable to the SAG strategy when changing from high-dose morphine to methadone.[10] However, more information from a greater number of case studies is necessary before definitive recommendations can be made about how best to switch from opioids to methadone.

According to several previous reports, pain associated with MPS is often difficult to control. Of course, the best treatment to control pain is to control the tumor itself.[2,11] However, in most cases the tumor is metastatic and inoperable. Chemotherapy or palliative radiation may then be administered. This requires more time to control the tumor, and sometimes the continuation of treatment is difficult because of tumor pain. Other palliative treatment is essential for continuing tumor control.

One reason why MPS pain is difficult to control is that the pain is not purely nociceptive, because neuropathic pain may also be involved.[1,11] Neuropathic pain is often difficult to control, and there are currently few drugs effective against this type of pain. In addition, MPS is often resistant to nerve blocks, extradural blocks, and subarachnoid blocks.[2,11]

Methadone is a newly introduced opioid in Japan. The most important characteristic of this drug is that it acts not only on μ-opioid receptors, but also on NMDA receptors.[12–14] In Japan, methadone is to be used only if other opioids are not effective; therefore, prior opioid use is noted in most patients. In a previous study, approximately 80% of patients whose pain was not well controlled with other opioids responded to oral methadone.[8] Intractable pain is one of the most common problems that results in deterioration of cancer patients' quality of life.[15] In previous studies, less than 50% of MPS patients were able to control their pain with multimodal treatments, including NSAIDs, opioids, adjuvant drugs, and epidural or intrathecal anesthesia.[1,2,11] It is currently unclear why the pain in these MPS patients responds to methadone, but it seems that methadone may be one of the treatment choices for MPS refractory to other opioid therapy and with difficult-to-control pain.

Furthermore, the recognition of MPS is low, and so MPS may be underdiagnosed.[11] Both clinical symptoms and imaging scans are important in the diagnosis of MPS. If patients have difficulty extending their thigh and walking, imaging or reevaluation of imaging may be considered to assess involvement of the iliopsoas muscle. Although not unique to MPS, it is necessary to accurately assess the origin of pain to appropriately control cancer-related pain.

There are certain limitations to the present study. In particular, the study was a retrospective study with very few cases. All patients had severe pain, and two patients did not have enough time to try other adjuvant drugs except for NSAIDs. However, no previous study has described highly effective treatment choices for MPS. The findings of the present study indicate that there is the possibility that MPS will respond to methadone, but further studies are required to prove the benefits of methadone in these patients.

In conclusion, further studies are needed to validate the efficacy of methadone treatment for MPS. In addition, it will be beneficial to identify predictive markers or symptoms of responsiveness to methadone.

Author Disclosure Statement

No competing financial interests exist.

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