is also highly effective. Only a few antiemetics, such as metoclopramide, levosulpiride, and tropisetron, have been tested in randomized controlled trials, and the number of the study subjects was small [5–8]. Existing evidence about the effectiveness of each antiemetic is thus insufficient.

Scopolamine (L-hyoscine) is a naturally occurring belladonna alkaloid and it acts as a nonselective antagonist at muscarinic–cholinergic receptors in the vomiting center, vestibular nuclei, and peripheral nerve endings [9]. The scopolamine patch is effective for the prevention of motion sickness [10], postoperative nausea, and vomiting [11, 12]. Meyer reported that the addition of scopolamine patch use to a metoclopramide and dexamethasone antiemetic regimen provides an additional benefit in the control of cisplatin-induced emesis [13]. Morrow demonstrated that cancer patients with susceptibility to motion sickness have more chemotherapy side effects than cross-matched controls with no such susceptibility and suggested that such motion-sensitive cancer patients may derive further benefit from additional medication with scopolamine [14]. Scopolamine therefore may be effective to palliate nausea of cancer patients in the presence of a vestibular mechanism or movement-associated nausea.

In Japan, the scopolamine patch is not commercially available, and, thus, a solution of scopolamine has been traditionally used. A solution of scopolamine is very easy to take sublingually: the oropharyngeal absorption of scopolamine appears to lead to significant systematic absorption with a mean time to the maximum plasma concentration of 53 min (standard deviation, 8) [9]. In rabbits, the bioavailability of scopolamine after sublingual spray was 79.8 % [15]. These findings suggest that the administration of scopolamine sublingually may be useful.

In an etiology-based approach to palliate nausea of cancer patients, and in the presence of a vestibular mechanism or movement-associated nausea, scopolamine is one of the first-line agents [4, 16]. However, there have been few clinical trials on the effectiveness of scopolamine to relieve nausea unrelated to the chemotherapy or radiation of cancer patients. One before–after study of 13 cancer patients revealed that the scopolamine patch alleviates nausea in cancer patients caused by opioids [17]. To our knowledge, no studies have investigated the treatment effects of sublingually administered scopolamine for nausea in terminally ill cancer patients. Therefore, clarifying the effect of scopolamine on nausea may be useful. Thus, the primary aim of this study was to clarify the effect of sublingual scopolamine on the intensity of nausea.

Subjects and method

This was an open uncontrolled study. When the patients developed nausea, they were administered a solution of scopolamine at 0.15 mg sublingually. The intensities of nausea were assessed using the 6-point Numerical Rating Scale (NRS 0 = no nausea to 5 = worst nausea) before and 15, 30, and 60 min after administration. This study was approved by the institutional review board of Yodogawa Christian Hospital and conducted in accordance with the Helsinki Declaration. Written consent was obtained from all participants.

Patients and setting

The study participants were cancer patients consecutively admitted to the palliative care unit (PCU) in a 607-bed general hospital, Yodogawa Christian Hospital, in Japan from January to August in 2008. The PCU had 21 beds, and four full-time palliative care specialist physicians were responsible for inpatient care. Inclusion criteria were (1) adult cancer patients with metastatic or locally advanced cancer and (2) those who had not been treated with chemotherapy nor radiation therapy within a month. Exclusion criteria were as follows: (1) dementia, delirium, or other mental disorders that made oral communication difficult and (2) antiemetics had been changed within 12 h before the administration of scopolamine.

Treatments

When the patients had nausea, they were administered a solution of scopolamine at 0.15 mg sublingually. The distribution coefficient of a solution of scopolamine has a log *p* value of 0.98 [15], and its molecular mass is 438.31 M. The solvent for the solution of scopolamine was water. We decided on this dose schedule based on our clinical experience, prescribing a solution of scopolamine sublingually for nausea as the first choice, in the palliative care unit for over 10 years [18] and the Japanese clinical guidelines for gastrointestinal symptoms in cancer patients [19].

Thirty minutes after the first treatment, one additional dose of scopolamine was administered in the same way if the following criteria were met: (1) the NRS of nausea was 1 or more, (2) absence of any severe adverse effects, and (3) the patients consented to the additional administration of scopolamine. The reason why each patient did or did not agree to receive the additional dose was not recorded. Other drugs were not allowed to be changed nor added for 60 min following the first administration. On every drug administration, physicians and/or nurses explained that the medication was used with the intention to treat nausea.

Measurements

The intensity of nausea was measured using the 6-point NRS (0 = no nausea to 5 = worst nausea) before and 15, 30, and 60 min after administration. Patients reported the intensity of nausea by themselves on the NRS before and 15, 30, and 60 min after administration. To minimize the patient burden, the nurses asked the patients to report the NRS and recorded the results. If the patient was unable to report the intensity, the data were regarded as missing and no proxy evaluation was allowed.

Potential side effects investigated included drowsiness, dizziness, headache, blurred vision, dry mouth, palpitation, and delirium. All symptoms were reported by nurses as present or absent using a check list 15, 30, and 60 min after administration. We adopted a proxy evaluation of side effects despite a potential observer bias, because: (1) adopting patient-reported monitoring would decrease the feasibility of this study, and (2) patients were closely monitored in this tertiary palliative care unit by full full-time physicians and experienced nurses and thus a serious underestimation of severe side effects was unlikely. Because many patients already had some symptoms, such as dry mouth and drowsiness, we determined that the nurses should report these side effects as present only when the symptom became aggravated compared to before treatment or a new symptom developed. In addition, from the end of the study until 24 h, the attending physicians observed the patients at least twice as a part of routine practice to monitor potential adverse effects (unscheduled monitoring).

In addition, the causes of nausea were also assessed by the attending palliative care specialist physicians. They were determined based on clinical assessment (history taking, physical examination) and available investigations (blood tests, radiological investigations) [4, 20]. The causes of nausea were placed in five categories: chemically induced nausea, impaired gastric emptying, malignant bowel obstruction, movement-associated nausea, and central nervous system disturbance [3, 16].

As baseline data, the age, gender, primary tumor sites, sites of metastasis, general conditions (the Palliative Performance Scale [21]), survival days (defined as the days from the prescription of scopolamine to death), presence or absence of malignant bowel obstruction and a nasogastric tube, regular administration of opioids, corticosteroid, other antiemetic drugs, and the amount of parenteral hydration at the time of study enrollment were recorded.

Statistical analyses

Primary endpoints were (1) changes in NRS of nausea and (2) percentage of patients who achieved a decrease in NRS of 1 or more points 15 min after treatment. Secondary endpoints were the severity of nausea on NRS in 30 and 60 min and safety.

Because there is no established minimal clinically important difference in nausea of cancer patients, we provisionally set a 20 % reduction of the NRS score (1-point reduction of the 6-point NRS) as clinically significant and also assessed the median of the NRS. We chose 15 min as the primary endpoint because a potential advantage of sublingual scopolamine administration we had intended to explore in this study was its rapid effect [22, 23]. Moreover, we chose 30 and 60 min as the secondary endpoints because the mean time to the maximum plasma concentration of sublingual scopolamine is 53 min.

We statistically assessed NRS with the Wilcoxon rank sum test after 15, 30, and 60 min in comparison with before administration. Analyses were performed on the basis of intention-to-treat, and we used the last observation carried forward method to compensate for missing values. Regarding side effects, we calculated the percentages of the patients who had each side effect at any time during the study period.

We estimated the adequate sample size as 26 given meaningful difference of 1.0, standard deviation of 2.0, and correlation coefficient of 0.6 ($\alpha=0.05$; power=0.80; paired t test). Thus, we initially had determined the enrolled sample number as 30, so that 20 % might drop out.

Results

Characteristics of patients and etiologies of nausea

Of the 26 patients recruited for this study, one patient could not report the NRS after 15 and 30 min because of drowsiness. All other data were fully obtained. In total, three patients were additionally administered scopolamine following the protocol. The characteristics of the patients are summarized in Table 1. The main etiologies of nausea were impaired gastric emptying and chemically induced nausea. Among all patients, 65 % (n=17) had abdominal lesions including metastases. Two patients were diagnosed with malignant bowel obstruction, and no one used a nasogastric tube. Opioids were administered in 62 % (n=16) of patients. Betamethasone was administered in 81 % (n=21) of patients, not for nausea, but for fatigue (n=6), appetite loss (n=5), and dyspnea (n=5). Some regular antiemetics except betamethasone were administered in 46 % (n=12). Also, 23 % (n=6) of patients received parenteral hydration at a mean volume of 358 ml/day.

Endpoints

The primary endpoints

The median of the 6-point NRS of nausea significantly decreased from 3.0 (range, 1–5) before treatment to 1.5 (0–5) 15 min after treatment (Table 2). Further, 84 % (n=21) showed a decrease in NRS of 1 or more points in 15 min.

Table 1 Patient characteristics (n=26)

Characteristic	Number
Gender	
Male	15
Female	11
Primary site	
Lung	7
Liver	4
Stomach, rectum, pancreas, bladder	8 (2 for each)
Esophagus, ovary, thyroid, adrenal gland, kidney, breast, skin	7 (1 for each)
Palliative Performance Scale (median, ranges)	50 (range, 20–70)
Survival days (median, ranges)	16 (range, 1–61)
Etiology of nausea	
Impaired gastric emptying	13
Chemically induced nausea	8
Movement-associated nausea	3
Malignant bowel obstruction	2
Central nervous system disturbance	0
Corticosteroid	
Betamethasone	21
Antiemetics prescribed regularly	
Haloperidol	5
Metoclopramide	4
Prochlorperazine	3
Dimenhydrinate	3
None	14

The secondary endpoints

Severity of nausea The median NRS significantly decreased from 3.0 (1–5) before treatment to 0 (0–5) 30 min after and 0 (0–4) 60 min after treatment (Table 2). The percentage of the patients who achieved a decrease in NRS of 1 or more points was 96 % (n=25) in 30 min and 100 % (n=26) in 60 min.

Adverse effects A total of 15 % (n=4) showed drowsiness, while other adverse effects, including dizziness, headache, blurred vision, dry mouth, palpitation, and delirium, were not reported. In addition, no serious adverse effect was reported in the 24-h period after administration based on unscheduled monitoring.

Discussion

This is, to our best knowledge, the first prospective study to investigate the treatment effects of sublingual scopolamine for nausea in terminally ill cancer patients. In 26 patients, the median NRS decreased significantly; 84 % (n=21) of patients showed a decrease in NRS of over 1 point on the 0–6 point scale in 15 min, and the NRS score tended to decrease further during 1 h. These findings suggest that the sublingual administration of a solution of scopolamine acts quickly and the effect lasts for at least 60 min. We also assessed the etiology of nausea and explored the effectiveness of scopolamine in subgroups with each etiology. The results suggest overall treatment success with various causes.

In this study, one patient could not undergo NRS assessment after 15 and 30 min due to drowsiness, but the patient showed improved drowsiness after 60 min and could then undergo NRS assessment. We could not conclude whether drowsiness was an adverse effect of scopolamine or a desirable consequence of symptom relief because the time of administration was midnight.

Our study had several limitations. First, we had no control groups, and symptom evaluation was performed in an unblinded manner. Second, adverse effects were evaluated through proxy assessment by nurses. Some adverse effects might have been underestimated, especially subjective symptoms such as dry mouth. Third, we could not evaluate the reasons why the patients did or did not agree to receive an additional dose, while only 12 % of the patients actually received an additional administration 30 min after. Some patients might not have wanted additional administration, not due to obtaining sufficient relief, but for other reasons (e.g., troublesome side effects or hesitating to use drugs frequently). We believe, however, this has a minimal

Table 2 Intensities of nausea assessed with the 6-point Numerical Rating Scale

Number	Before	15 min	p value	30 min	p value	60 min	p value
All patients, 26	3.0 (1–5)	1.5 (0–5)	<0.001	0 (0–5)	<0.001	0 (0–4)	<0.001
Impaired gastric emptying, 13	3.0 (1–5)	1.0 (0–5)	<0.001	0 (0–5)	<0.001	0 (0–4)	<0.001
Chemically induced nausea, 8	3.0 (1–4)	2.0 (0–3)	<0.001	0 (0–3)	<0.001	0 (0–3)	<0.001
Movement-associated nausea, 3	5.0 (5–5)	1.0 (0–3)	0.053	0 (0–3)	0.57	0 (0–0)	NC
Malignant bowel obstruction, 2	5.0 (5–5)	2.5 (0–5)	0.50	1.5 (0–3)	0.26	1.5 (0–3)	0.20

Data are expressed as median (range)

NC not calculated

influence on the conclusion because 96 % of the patients had already achieved a decrease in NRS of 1 or more points in 30 min. Other limitations included: (1) assessments of the etiologies of nausea relied on the clinical diagnoses made by the physicians; (2) scopolamine was an add-on antiemetic in most patients; (3) we did not assess the long-term effect; and (4) the sample size was too small for exploring the effectiveness of scopolamine in subgroups with each etiology.

In conclusion, sublingually administered scopolamine may be effective for managing nausea in terminally ill cancer patients. A larger randomized controlled trial is promising to assess treatment efficacy and safety.

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Effect of Nutritional Support on Terminally Ill Patients With Cancer in a Palliative Care Unit

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Abstract

The role of nutritional support on terminally ill patients with cancer in a palliative care unit has not been clarified. A total of 63 patients were retrospectively investigated; the patients receiving individualized nutritional support (intervention group [n = 22]) were compared to the others (control group [n = 41]). The intervention group received individualized nutritional support. There were no significant differences in the characteristics of patients between the groups. The prevalence of bedsores was significantly lower in the intervention group (14% vs 46%, $P = .012$). The prevalence of edema and the use of antibiotic therapies tended to be lower in the intervention group than in the control group (36% vs 54%, $P = .19$; 14% vs 27%, $P = .34$, respectively). Some terminally ill patients with cancer in a palliative care unit might benefit from nutritional support.

Keywords

nutritional support, terminally ill patients with cancer, palliative care unit

Introduction

Cancer cachexia is a complex syndrome that includes weight loss, anorexia, muscular weakness, and disturbed metabolism.[1] Weight loss is present in more than 50% of the patients with cancer at the time of diagnosis,[2] and associated with loss of independence, impaired quality of life (QOL), and shorter survival.[3,4] However, there is limited evidence from randomized trials about the treatment of cachexia in patients with advanced cancer,[5] while several studies have revealed the potential benefits of reversing or delaying progressive tissue wasting.[6,7,8] The effects of increased oral intake and long-term nutritional support have been rarely investigated, and the role of nutritional support to achieve improved QOL in terminally ill patients with cancer has not been clarified.[9, 10, 11]

The primary aim of this study was thus to explore the effect of nutritional support on the prevalence of bedsores, edema, and antibiotic therapies in terminally ill patients with cancer in a palliative care unit.

Methodology

Participants

All 117 patients with histologically proven, locally advanced, or metastatic cancer admitted to a palliative care unit in Saito-Yukoukai Hospital (Osaka, Japan) were initially screened for this study. Inclusion criteria were as follows: (1) no cognitive impairment at admission, (2) performance status of 3 or less at admission, and (3) palliative prognostic index (PPI) of less than 6 at admission.[12] Patients who died from unexpected complications, such as bleeding, unexplained cardiac arrest, and cardiovascular complications, were excluded. A total of 63 patients met the inclusion and exclusion criteria.

Measurement

We chose the prevalence of bedsores, edema, and use of antibiotic therapies as primary endpoints because they often occur in the final days of life and could reduce patient QOL but might be prevented by nutritional support.[13]

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Table 1. Patient Backgrounds

	Intervention group (n = 22)	Control group (n = 41)	*P* value
Age (years)			
Mean (SD)	69 (14)	69 (14)	.87
Sex (n, %)			
Female	9, 41	17, 41	.97
Male	13, 59	24, 59	
Primary tumor site (n, %)			
Lung	5, 23	11, 27	.86
Gastric	3, 14	7, 17	
Pancreatic	3, 14	5, 12	
Uterine	3, 14	2, 4.9	
Head/neck	2, 9.1	3, 7.3	
Esophageal	2, 9.1	1, 2.4	
Colorectal	2, 9.1	2, 4.9	
Biliary ductal	1, 4.6	3, 7.3	
Kidney	1, 4.6	1, 2.4	
Breast	0, 0	3, 7.3	
Ovarian	0, 0	1, 2.4	
Other	0, 0	2, 4.9	
Observation period (days)			
Median (range)	28 (8, 79)	22 (8, 130)	.54
PS (n, %)			
0	0, 0	0, 0	
1	2, 9.1	4, 9.8	.17
2	11, 50	11, 27	
3	9, 41	26, 63	
PPI			
Median (range)	3.5 (1, 4.5)	3.5 (1, 5)	.22

Abbreviations: SD, standard deviation; PS, Performance Status; PPI, Palliative Prognostic Index.

Table 2. Endpoints

	Intervention group (n = 22)	Control group (n = 41)	*P* value
Bedsore n, % (95% CI)	3, 14 (5, 34)	19, 46 (32, 61)	.012
Edema n, % (95% CI)	8, 36 (20, 57)	22, 54 (39, 68)	.19
Antibiotics n, % (95% CI)	3, 14 (5, 34)	11, 27 (16, 42)	.34
Lengths of the artificial hydration therapy (days)			
median (range)	23 (0, 53)	17 (2, 91)	.68
Lengths of the mouthfuls or less oral intake (days)			
Median (range)	3.5 (0, 50)	4 (0, 61)	.94

Abbreviation: 95% CI: 95% confidence interval.

The principal investigator (K.A.) investigated the prevalence of bedsores, edema, and use of antibiotic therapies by chart review. To confirm the reliability and validity of the evaluations, another attending physician other than the principal investigator agreed with all evaluations.

We defined that bedsores were present when identified at stage 1 or severer on the basis of the National Pressure Ulcer Advisory Panel (NPUAP) during the last 48 hours.[14] Edemas were determined as present when the patient had bilateral peripheral edema during the last 48 hours, and asymmetric or lymphatic edemas were excluded. We rated antibiotic use as positive if any antibiotics were prescribed at any time during admission. These items were routinely recorded by the physicians and/or nurses in our palliative care unit.

In addition, we investigated the lengths of artificial hydration therapy (500 mL/d or more) and the number of mouthfuls or less of oral intake.

Intervention

As a part of routine clinical practice in our palliative care unit, attending physicians ask patients whether they want to receive help from a nutrition support team on the basis of a clinical decision. If the patient agrees to receive such help, a nutritional support team, consisting of trained physicians, dietitians, pharmacists, and nurses, provides individualized nutrition support. For this study, the patients receiving nutritional support (intervention group) were compared to the others (control group).

Intervention group

Nutritional support was individualized and tailored to each patient. When the amount of oral intake of the patient was under half, the patient was monitored daily. The goal of the nutritional support was to meet or exceed the protein and energy requirements of the Nordic Recommended Allowances [15] (daily energy intake in the range of 1.5- 1.7 × basal energy expenditure [BEE], calculated from the Harris-Benedict equation,[16] and protein intake of 1.0- 1.2 g/kg body weight). The intervention included the following: (1) exploring and adjusting the causes of malnutrition; (2) encouraging patients with feeding and supporting the nurses in this role; (3) offering snacks and drinks such as dietary foods and supplements; and (4) administering total parenteral nutrition or peripheral parenteral nutrition, if indicated and agreed to.

Control group

Patients in the control group did not receive any specific nutritional support.

Statistical analyses

Comparisons were performed using Mann-Whitney *U* test or chi-square test (Fisher exact test) as appropriate. All the results were considered to be statistically significant if the *P* value was less than .05. All analyses were performed using the statistical package IBM SPSS (version 20) Statistics Base Authorized User License.

Results

A total of 63 assessable patients were divided into the intervention group (n = 22) and the control group (n = 41). At baseline, there were no significant differences in patients and clinical characteristics between the intervention and the control groups (Table 1).

The prevalence of bedsores during the last 48 hours was significantly lower in the intervention group than in the control group (14% [95% confidence interval: 5-34] vs 46% [32-61], $P = .012$; Table 2). The prevalence of edema and use of antibiotic therapies tended to be lower in the intervention group than in the control group (36% [20-57] vs 54% [39-68], $P = .19$; 14% [5-34] vs 27% [16-42], $P = .34$, respectively); the differences were not statistically significant. The lengths of the artificial hydration therapy and numbers of mouthfuls or less of oral intake were not significantly different between the groups.

Discussion

This retrospective study revealed that the patients receiving individualized nutritional support were significantly less likely to have bedsores during their final days. There have been, to the best of my knowledge, no studies investigating the effects of nutritional support on terminally ill patients with cancer with regard to the prevalence of bedsores, edema, and the use of antibiotic therapies. Nutritional intervention is generally considered as a supportive measure within the oncology strategy, and in palliative care, it focuses on controlling symptoms such as nausea, vomiting, and pain, thus improving QOL.[17,18] In patients with acute stroke, nutritional support was found to improve QOL,[19] and in acutely ill older inpatients, nutritional support reduced the need for intravenous antibiotics.[20] In a randomized controlled study, malnourished patients, with or without cancer, actually received some benefits from nutritional support intervention, especially regarding nutrition status and QOL, and they had fewer complications and needed fewer antibiotics.[21]

This study is preliminary and has major limitations: retrospective evaluation of outcomes, lack of patient-reported QOL, lack of a control group, single-institution study, and lack of detailed information on the intervention.

In conclusion, terminally ill patients with cancer receiving individualized nutrition support might be less likely to have bedsores in their final days. Some terminally ill patients with cancer might benefit from individualized nutritional support, and the role of nutritional support should be explored in the future intervention trials.

Authors' Note

This is a retrospective study in a single palliative care unit in Japan.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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REVIEW

Palliative care in Japan: a review focusing on care delivery system

Tatsuya Morita[a] *and Yoshiyuki Kizawa*[b]

Purpose of review

Providing palliative care in Japan is one of the most important health issues. Understanding palliative care delivery systems of other countries is useful when developing and modifying palliative care systems worldwide. This review summarizes the current status of palliative care in Japan, focusing on the structure and process development.

Recent findings

Palliative care units and hospital palliative care consultation teams are the two main specialized palliative care services in Japan. The number of palliative care units is 215 (involved in 8.4% of all cancer deaths), and there are approximately 500 hospital palliative care teams. Conversely, specialized home care services are one of the most undeveloped areas in Japan. However, the government has been trying to develop more efficient home care services through modifying laws, healthcare systems, and multiple educational and cooperative projects. The numbers of palliative care specialists are increasing across all disciplines: cancer pain nurses (1365), palliative care nurses (1100), palliative care physicians (646), and palliative care pharmacists (238). Postgraduate education for physicians is performed via the special nationwide efforts of the Palliative care Emphasis program on symptom management and Assessment for Continuous medical Education (PEACE) project – a 2-day program adopting a trainer–trainee strategy. Over 30 000 physicians have participated in the PEACE program. A total of 1298 and 544 physicians have completed a trainer course for palliative medicine and psycho-oncology, respectively. Multiple structure and process evaluation, bereaved family surveys in palliative care units, and patient and family evaluation in the regional palliative care program indicate many improvements.

Summary

Palliative care in Japan has progressed rapidly, and the Cancer Control Act has played a very important role in developing palliative medicine. Challenges include developing a structure for palliative care in the community or regional palliative care programs, establishing a method to measure and improve the quality of palliative care at a national level, developing evidence-based medicine and policy making, and palliative care for the noncancerous population.

Keywords

delivery, Japan, palliative care

INTRODUCTION

This brief review summarizes the current status of palliative care in Japan, focusing on the structure and process development.

GENERAL HEALTH SYSTEM

The medical system in Japan is characterized by free access, fully covered by national insurance, and lack of general practitioner (GP) system [1–3]. Patients can freely access all medical institutions, including university hospitals and cancer centers. Japan achieved universal health coverage in 1961, and all Japanese are insured. Every patient pays 30% of all medical cost, except for elderly people and children, and when the monthly co-payment exceeds a threshold amount (ranging 80 000–110 000 yen per month according to their income),

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KEY POINTS

- Palliative care in Japan has rapidly progressed in this decade, and the Cancer Control Act has played a very important role.
- Palliative care units and palliative care teams are two main specialized palliative care services.
- To improve home care service, the government is trying to develop more efficient home care services through modifying laws, healthcare systems, and multiple educational and cooperative projects.
- The numbers of palliative care specialists are increasing across all disciplines.
- Postgraduate education for physicians is performed via the special nationwide efforts of the PEACE project, and the total number of physician participants is over 30 000.

the co-payment is decreased to 1%. Physicians working at clinics are basically specialists (not trained GP); typically, specialists such as surgeons and cardiologists work in hospitals for 10 or more years, and then they establish a clinic and see patients with common diseases in addition to patients with diseases they specialize in.

HISTORY OF PALLIATIVE MEDICINE

The beginning of systematic palliative care in modern medicine in Japan was developed at the Yodogawa Christian Hospital, Osaka, in 1973. This was organized care for terminally ill cancer patients, led by Dr Kashiwagi, one of the pioneer hospice physicians in Japan. In the late 1970s to 1980s, the hospice movement was introduced and, initially, Christian hospitals developed the hospice care program. The first palliative care unit or inpatient hospice, the Seirei Hospice, was established in 1981 in Shizuoka. Almost palliative care units in Japan belong to a general hospital and are called as palliative care units or inpatient hospice. For approximately 10 years, the number of palliative care units gradually increased and, in 1990, palliative care units became covered by national insurance. To exchange information with healthcare professionals working in palliative care units, the Japanese Hospice Palliative Care Association was established in the following year, and representatives from almost all palliative care units participated in the association. In the 1990s, palliative care was gradually disseminated to general hospital wards, outpatient services, and the community. Home care nursing services (1992), hospital palliative care teams (2002), clinics with a home hospice function (2006), and day care hospices (2006) became covered by national insurance. In 2007, the Cancer Control Act was legalized with a special focus on improving palliative care, chemotherapy, and radiation therapy. Under the national policy led by the Cancer Control Act, many projects started, including the Palliative care Emphasis program on symptom management and Assessment for Continuous medical Education (PEACE) program to ensure all physicians had an opportunity to receive a 2-day palliative care education. The Orange Balloon Project was developed to provide information to the general public about palliative care, and the Outreach Palliative care Trial of Integrated Regional Model (OPTIM) study was conducted in order to measure the effects of a regional palliative care program on a variety of outcomes. Palliative care is rapidly progressing in Japan, especially in the oncology field since the Cancer Control Act, and the evaluation and modification of these programs are ongoing.

CANCER CONTROL POLICY AND PALLIATIVE CARE

The Cancer Control Act has played a very important role in developing palliative medicine in oncology. The Cancer Control Act promotes a national network of hospitals treating cancer patients, consisting of a national cancer center, 47 prefectural cancer hospitals, and 397 designated cancer hospitals. All designated cancer hospitals should fulfill the requirement of structural and process evaluation for palliative care. A series of nationwide surveys has clarified the structural and process aspects of palliative care in a designated cancer hospital network, which has led to a marked improvement in care (Fig. 1).

PALLIATIVE CARE UNITS (INPATIENT HOSPICES)

Palliative care units (inpatient hospices) have been the mainstream of specialized palliative care services in Japan. The number of palliative care units is now 215 and they are involved in 8.4% of all cancer deaths (Fig. 2). Typical palliative care units belong to general hospitals and have an average of 20 inpatient beds to provide end-of-life care for cancer patients (Table 1). They should fulfill the criteria for certification: space, private rooms, availability of attending physicians, and rooms and equipment for families. They are designed to accommodate terminally ill patients so they can stay for several weeks or months in a home-like environment in their last period of life. Recently, however, the

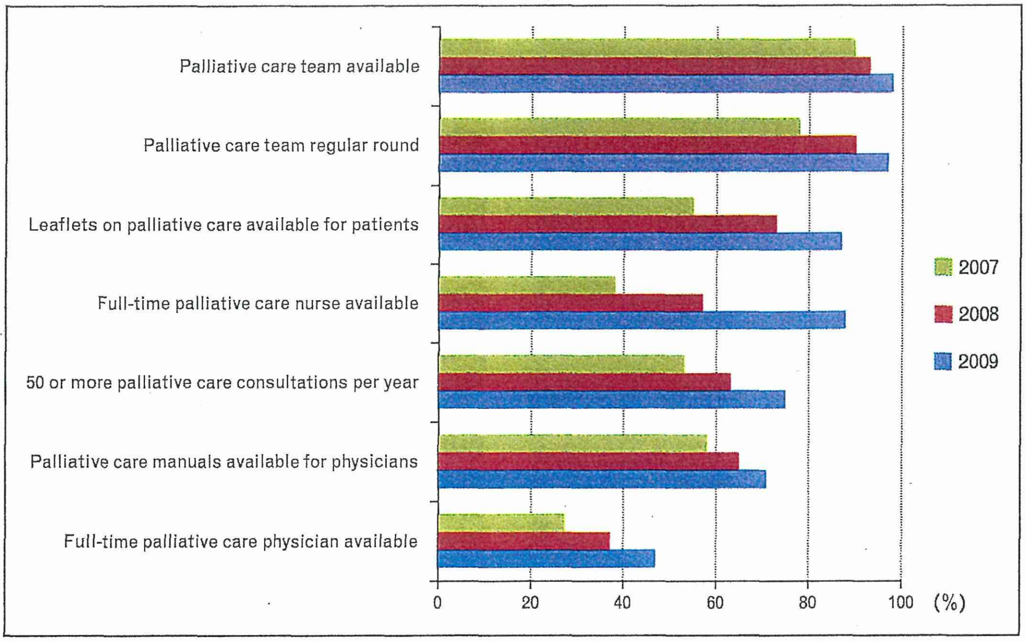

FIGURE 1. Improvement in palliative care in 500 cancer hospitals.

increased availability of home care services and increased use of anticancer treatment have resulted in a shorter duration of use of palliative care units. Most palliative care units provide outpatient services and half provide home care services as a decision of the belonging hospitals. One important achievement of the palliative care unit network is the Japan HOspice and Palliative Care Evaluation (J-HOPE) survey [4–6]. Through the nationwide palliative care unit network, a family bereavement survey involving more than 8000 participants was performed, and the results were fed back to all institutions every 3 years [4–6]. Clinical studies to obtain insights in the challenging areas were successfully completed.

HOSPITAL PALLIATIVE CARE TEAMS AND OUTPATIENT PALLIATIVE CARE SERVICES

In contrast to palliative care units where active cancer treatment is not usually performed, hospital palliative care teams and outpatient palliative care services provide specialized palliative care for any patient irrespective of their treatment status. Two nationwide surveys are available, and both indicated there are about 500 hospital palliative care teams in Japan [7]. The Cancer Control Act obliges all designated cancer hospitals to establish hospital palliative care teams and to obtain payment from national insurance. The hospital palliative care team should meet the following criteria: at least one full-time physician, at least one full-time nurse, and a

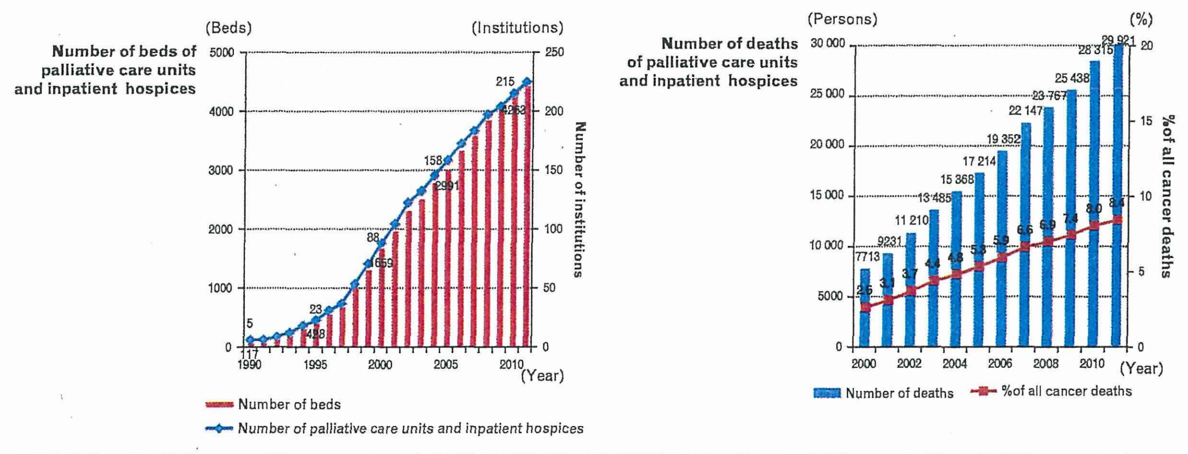

FIGURE 2. Development of palliative care units and inpatient hospices.

Table 1. Activity of palliative care units and inpatient hospices (*n* = 195)

		%	*n*
Types	Palliative care units	98	191
	Inpatient hospices	2	4
Number of admitted patients per year			
	Mean (25–75‰)		134 (100, 178)
	≤100	26	51
	101–200	57	113
	>201	18	36
Duration of admission			
	Median (25–75‰)		39 (31, 52)
	<30	23	47
	30–59	67	134
	≥60	10	19
Percentages of patients who died during the admission			
	Median (25–75‰)		89 (83, 95)
	<75	11	22
	75–89	41	81
	≥90	48	97
Availability of outpatient service		92	180
Availability of home care service		40	78

Data are from the report of Hospice Palliative Care Japan, 2009.

psychiatrist should be available. Many hospital palliative care teams have a full-time nurse, and half have a full-time physician (Table 2). The activity of palliative care teams shows a large variation among institutions with a median number of patients from 0 to over 1000 per year. On average, a hospital palliative care team sees about 100 patients per year, and reasons for referrals are pain in 70% of patients and other physical symptoms and psychological problems in 30–40% of patients.

HOME CARE SERVICES

Specialized home care services are one of the most undeveloped areas in Japan. Because of the lack of a GP system, there are three types of provider of home care services for terminally ill patients: physicians working at clinics, specialized home care clinics (focusing on home care rather than outpatient care), and home care divisions of hospitals. The number of community palliative care teams is small, with only 74 nationwide and they are usually working as part of hospital palliative care teams. Specialized palliative care nurses who can prescribe essential medications and perform death certification are still unavailable in Japan, such as McMillan nurses in the UK and the hospice care program in the USA. Very recently, the government has been trying to develop more efficient home care services through modifying laws, healthcare systems, and multiple educational and cooperative projects. One of them is establishing 'clinics with a home hospice function', in which high payment is assured if a physician provides a 24-h 7-day home care. Unfortunately, although the number of clinics with a home hospice function has rapidly increased over the last 5 years, the effect is limited and thus the home death rate of cancer patients has not markedly increased (Fig. 3).

ORGANIZATION OF REGIONAL PALLIATIVE CARE RESOURCES

Similar to home care services, there is also a wide variation in the organization of palliative care resources in the region. This is mainly because of free access and no GP system. In typical cases, patients receive anticancer treatment in cancer centers, university hospitals, or acute general hospitals. As the disease progresses, cancer and university hospitals typically refer patients to community hospitals (usually small and palliative care specialists unavailable), and some patients additionally receive general medical management from clinic physicians. In their terminal stage, a patient average of approximately 10% die at home, another 10% die in palliative care units or inpatient hospices, and the remaining a majority of patients die in hospitals. To measure the effect of a regional palliative care program and understand how to improve palliative

Table 2. Activity of palliative care teams and outpatient palliative care services

	Hospital palliative care teams		Outpatient service
	National survey (2010)	JSPM registry (2010)[a]	National survey (2010)
Number of services	541	371	401
Number of patients (/year)			
Mean (SD)	99 (104)	119	27
Median (ranges)	70	89 (0, 1532)	9
≤49	186 (34%)		
50–99	151 (28%)		
100–199	115 (21%)		
≥>=200	63 (12%)		
Full-time physicians	214 (40%)		
Full-time nurses	374 (69%)		
Reasons for referral[a]			
Pain		67%	
Other physical symptoms		37%	
Psychological problems		33%	
Care coordination		14%	
Family care		9.3%	
Ethics		2.5%	
Performance status on referral			
0, 1		24%	
2		24%	
3		29%	
4		22%	
Outcomes			
Discharge and follow-up as outpatient		38%	
Discharge to home care services		10%	
Discharge to palliative care units		10%	
Discharge to other institutions		8.1%	
Death		35%	
Ending follow-up		16%	

JSPM, Japanese Society of Palliative Medicine.
[a] For all 22 101 consultations. Data are available from 192 palliative care teams. Some data do not add up 100% because of missing data.

care at a regional level, the OPTIM study was completed [8▪▪,9]. The main results are promising that comprehensive regional palliative care program has improved length of stay at home, patient-perceived and family-perceived quality of care and quality of life, and physician-reported and nurse-reported difficulties [8▪▪,9]. A process analyses identified improving networking among multiple healthcare professionals as a core element of successful palliative care program in the region.

SPECIALTY AND NATIONAL ASSOCIATIONS

There are certification systems for palliative care physicians, nurses, and pharmacists (Fig. 4). The numbers of each specialist have all increased during this 5-year period. For certification, physicians should have at least 2-year clinical activity in the palliative care specialized services, and accomplishment of academic and education activity.

Regarding the nationwide organization, Hospice Palliative Care Japan was originally an association of palliative care units and inpatient hospices, and almost all certified palliative care units participated. In addition, the Japanese Society of Palliative Medicine is the most noteworthy academic association for palliative care, to which more than 4000 physicians are members. Regarding home care services, there are again various associations with different backgrounds and policies.

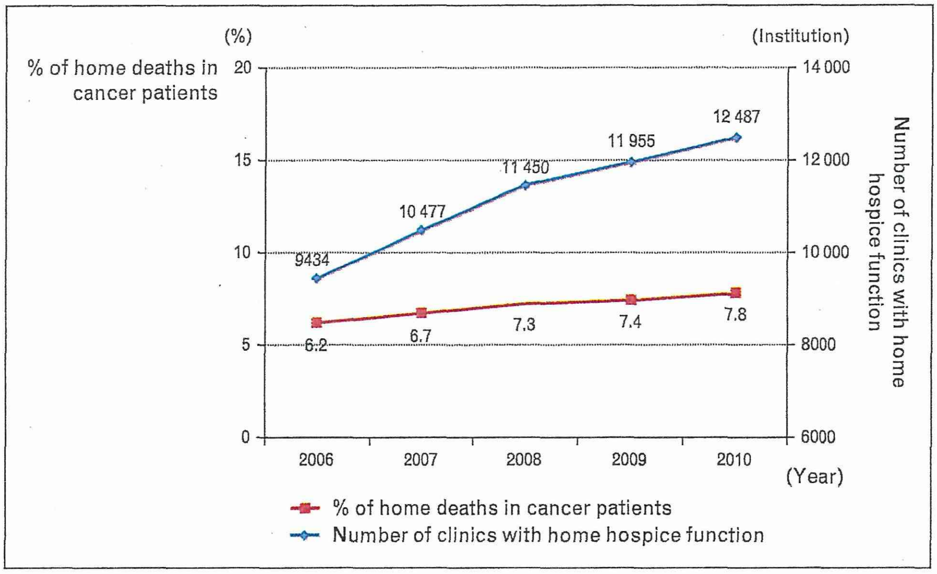

FIGURE 3. Trends in home deaths.

UNDERGRADUATE, POSTGRADUATE, AND CONTINUING MEDICAL EDUCATION

A 2009 nationwide survey demonstrated that many medical universities provide undergraduate education (Table 3), although bedside teaching and palliative care specialists are not frequently involved. This is because many medical universities still have no faculties specialized in palliative medicine.

Postgraduate and continuing medical education is performed via the special nationwide efforts of the PEACE project (Fig. 5). This 2-day interactive education program adopts a trainer–trainee strategy using original manuals, and the

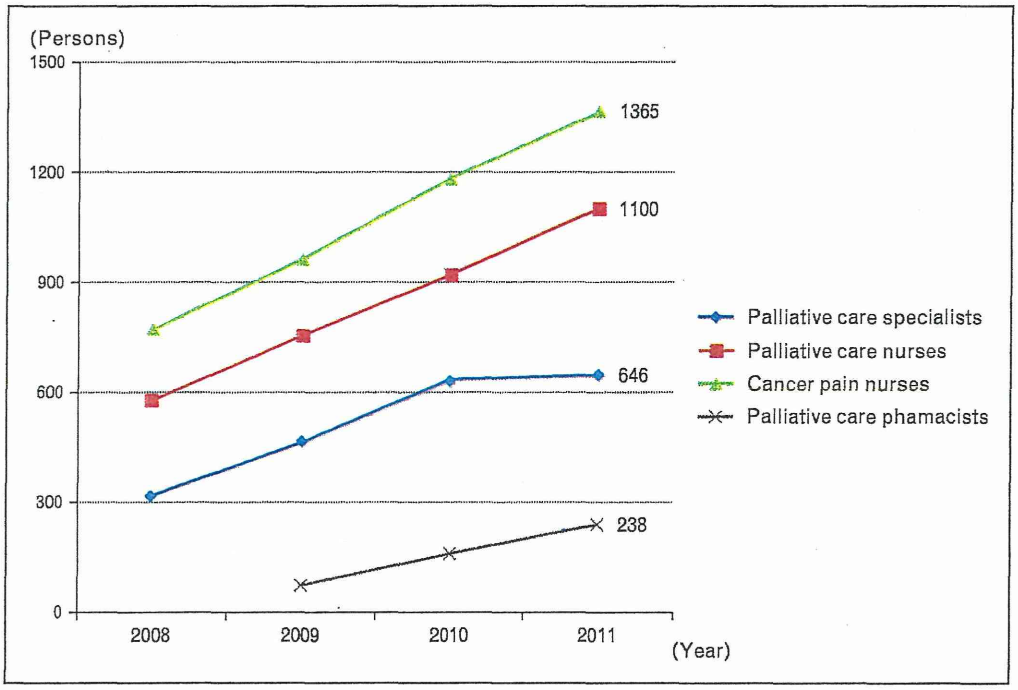

FIGURE 4. Certified specialties in palliative care.

Table 3. Undergraduate education (*n*=60, 2009)

	n	%
Educational opportunity in palliative medicine	65	99
Mean school hours per 6 years (SD)	5.5 (3.9)	
Faculty responsible for education[a]		
Anesthesiology	45	68
Internal medicine	20	56
Surgery	17	30
Psychiatry	14	26
Pediatrics	3	21
Gynecology	1	4.5
Contents[a]		
Pain control	62	94
Symptom control	52	79
Informed consent	35	53
Team collaboration	34	52
Hospice	32	49
Giving bad news	29	44
Family support	29	44
Methods[a]		
Lecture	65	99
Case discussion	17	26
Group work	12	18
Role play	11	17
Bedside teaching	5	7.6

[a] Duplicated answers.

total number of physicians who have participated in the PEACE program is over 30 000. A total of 1298 and 544 physicians have completed a trainer course for palliative medicine and psycho-oncology, respectively.

FUNDING AND POLICY SUPPORT

In principle, all activities are funded by the national insurance and national project. Some private funding has provided small grants for research or trial activities. Each palliative care service usually has volunteers to provide broader services for patients and families.

ACCESS TO PALLIATIVE CARE ACROSS THE COUNTRY

Figure 6 details the number of palliative care units/inpatient hospices and clinics with home hospice functions in regions throughout Japan. Recently, the disparities among regions, that is, among prefectures and among towns/cities within a prefecture, are becoming wider in Japan, not only in palliative care, but also in general areas. Resolving the discrepancies among the regions in one country is regarded as one of the high-priority issues.

CONCLUSION

Palliative care in Japan is being rapidly disseminated, especially since the Cancer Control Act. Multiple structure and process evaluation, bereaved family surveys in palliative care units, and patient and family evaluation in the regional palliative care program indicate many improvements observed in this period.

The next challenges include developing a structure for palliative care in the community or regional palliative care programs, establishing a method to measure and improve the quality of palliative care at a national level, developing evidence-based

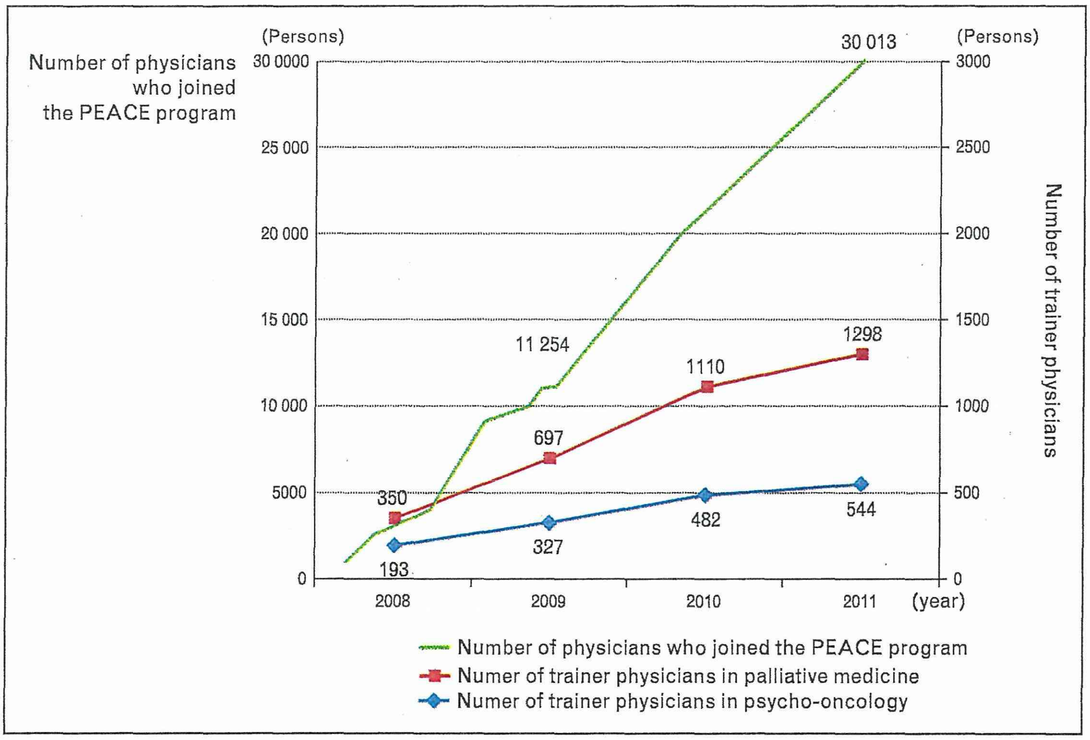

FIGURE 5. Continuing education in palliative medicine.

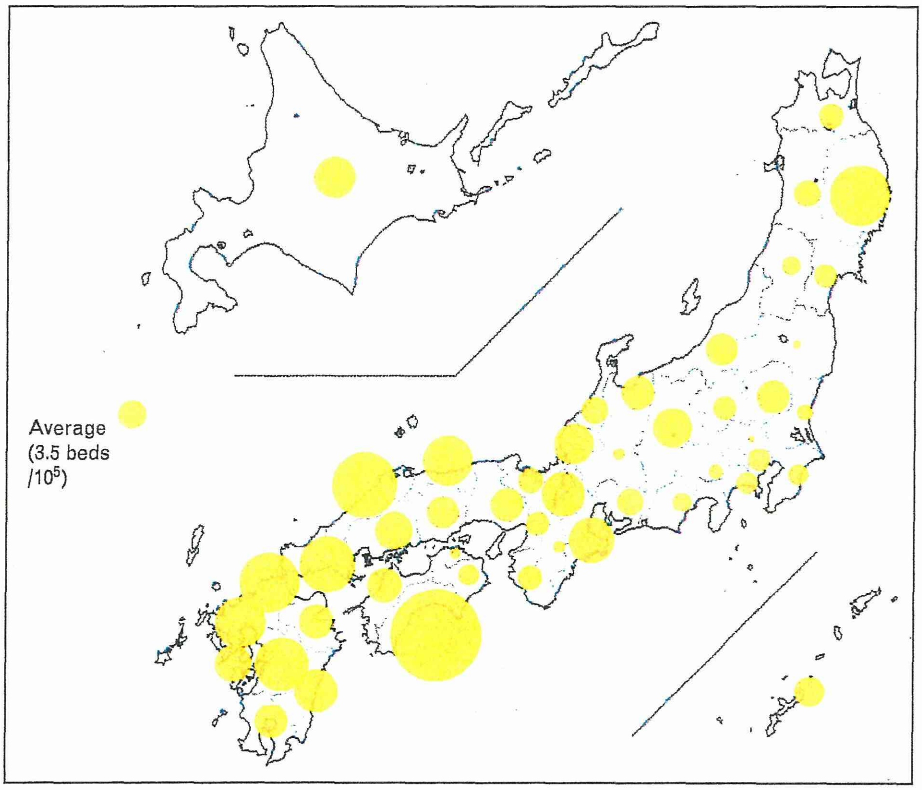

FIGURE 6. Availability of palliative care units and inpatient hospices among prefectures.

medicine and policy making, and palliative care for the noncancerous population.

Acknowledgements

None.

Conflicts of interest

The authors have no conflicts of interests for completing this study.

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- ■■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 242).

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Original Article

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Specialized Palliative Care Services in Japan: A Nationwide Survey of Resources and Utilization by Patients With Cancer

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Abstract

Objective: The aim of this study was to investigate the availability and utilization of specialized palliative care services among patients with cancer in Japan. **Methods:** We conducted a nationwide cross-sectional survey of 828 institutions predicted to provide specialized palliative care services. **Results:** Responses were received from 751 institutions (response rate, 91%); of these, 541 had specialized palliative care services. Adding the census data of palliative care units, the total estimated number of institutions with specialized palliative care services was 659. Of all the patients with cancer who died in the period from April 2009 to May 2010 in Japan, the estimated proportion who utilized specialized palliative care services was 24%. **Conclusions:** Usage of specialized palliative care services in Japan have increased explosively in the past decade.

Keywords

nationwide survey, Japan, specialized palliative care, neoplasms

Introduction

Palliative care has become an essential part of medical services, mainly among patients with cancer, in the past 30 years in Japan. In 2006, the Cancer Control Act was approved to improve the quality of life of all the patients with cancer, and one of the most important policies was the dissemination of palliative care throughout the country.[1] The number of palliative care units increased dramatically from 5 in 1990 to 235 in 2010.[2] In 2000, 7366 patients with cancer died in palliative care units,[3] and this increased to 25 529 in 2009,[2] comprising 7.4% of all cancer deaths in Japan. To further disseminate palliative care, the activities of palliative care teams were approved by the National Healthcare Insurance system in 2002. In 2007, the Ministry of Health, Welfare, and Labor obliged each regional cancer center to establish a palliative care team. In 2010, Japan had 377 regional cancer centers and 133 centers (35%) had a palliative care team that was certified by the National Healthcare Insurance system.[2] Because of this rapid expansion of specialized palliative care services in Japan, we conducted a nationwide survey to investigate the resources and utilization of specialized palliative care services in Japan.

Methods

Design

In this survey, a service was defined as specialized palliative care if it fulfilled all of the following 4 criteria: (1) use of palliative care specialists to provide management of pain, physical symptoms, psychosocial issues, and spiritual issues based on comprehensive assessment of patients and their families; (2) use of a palliative care team including at least a specialized palliative care physician and a specialized palliative care nurse; (3) at least 1 physician within the palliative care team to be a full-time employee; and (4) public notice of a specialized palliative care service to be given by the institution. Types of specialized palliative care services were classified as follows: (1) palliative care unit, (2) hospital-based palliative care team, (3) community palliative care consultation, (4) palliative care

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Table 1. Characteristics of Participating Institutions (n = 751).

Characteristics	n (%[a])
Types of institution[b]	
Regional cancer center	272 (36%)
University hospital	84 (11%)
Other hospital	370 (49%)
Clinic	47 (6%)
Others	3 (0.4%)
Total number of beds[c]	
<250	173 (23%)
250-499	244 (32%)
500-749	190 (25%)
≤750	72 (10%)
Providing specialized palliative care service	
Yes	541 (72%)
No	210 (28%)

[a] Percentage of all participating institutions.
[b] The total of the percentages is not 100% due to duplicated counts.
[c] The total of the percentages is not 100% due to missing values.

outpatient clinic, (5) home palliative care, and (6) day care service. We surveyed all service types, with the exception of home palliative services and day care services, for which no definitions or nationwide organizations were available. We assume that day care service is currently rare in Japan.

The number of patients with cancer who utilized specialized palliative care services was defined as the total number of patients with cancer listed in specialized palliative care services, according to our previous study.[4] If 1 patient received 2 types of specialized palliative care services, the number of the patients who received specialized palliative care service would be classed as 2. Although avoiding duplicates would be ideal, we were unable to do so because it could cause privacy issues in participating institutions. The estimated proportion of patients with cancer who utilized specialized palliative care services was calculated relative to the number of all cancer deaths listed in the statistics database of the Ministry of Health, Welfare, and Labor in Japan.[5]

To estimate the number of patients with cancer who utilized a hospital-based palliative care team, community palliative care consultation, or palliative care outpatient clinic in the 1-year period from April 2009 to March 2010, we conducted a nationwide cross-sectional survey. We mailed a survey questionnaire to a responsible member of the specialized palliative care services in 828 medical institutions that we predicted might provide these services because they met 1 or more of the following criteria: (1) having a certified palliative care unit; (2) being a certified regional cancer center; (3) having a certified palliative care team; (4) being a training institution certified by the Japanese Society for Palliative Medicine (JSPM); (5) employing a specialized palliative care physician (diplomate or tentative faculty member of the specialty board of palliative medicine) certified by the JSPM; or (6) employing a trainer who has completed a 2-day faculty development program of fundamental palliative care education called Palliative Care Emphasis Program on Symptom management and Assessment for Continuous Medical Education (PEACE) conducted by the JSPM or National Cancer Center from September 2008 to September 2010. We mailed a reminder letter to nonrespondents 4 weeks after mailing the survey questionnaires, followed by a telephone or e-mail reminder at 8 weeks.

To estimate the number of patients with cancer who utilized a palliative care unit, we accessed data in the census database from April 2009 to March 2010 through the annual survey of this database conducted by the Association for Hospice Palliative Care Japan in July 2010.[2] The census database covered 201 (93%) of the 217 certified palliative care units.

Measurements

Survey questionnaire. An envelope containing a cover letter stating that the survey was anonymous, instructions for the survey, a copy of the survey questionnaire about specialized palliative care service, and a self-addressed stamped envelope for returning the questionnaire was mailed to each institute. The questionnaire was organized into 3 parts: (1) characteristics of the institution such as total number of hospital beds and types of specialized palliative care services (if any); (2) numbers of patients with cancer who received specialized palliative care by a hospital-based palliative care team, palliative care outpatient clinic, or community palliative care consultation in the period from April 2009 to March 2010; and (3) structure, process, and staffing of specialized palliative care services (results not reported here). Survey questions were generated based on a literature review and discussions among researchers. The face validity of the draft survey was confirmed by 10 palliative care physicians, 2 oncologists, and 3 specialized palliative care nurses in September 2009, and the survey was revised by researchers. The survey was conducted from September 2010 to January 2011. The protocol was approved by the institutional review board of the Graduate School of Comprehensive Human Sciences, University of Tsukuba.

Data extraction from the census database of palliative care units. We accessed the census database of the Association of Hospice Palliative Care Japan regarding the statistics for palliative care units from April 2009 to March 2010. We obtained data such as the annual number of admitted patients, the annual number of deaths, the total number of beds, and the average length of stay in the units.

Descriptive statistics were used to summarize the data. Analyses were performed using IBM SPSS19.0–J software (IBM, Tokyo, Japan).

Results

Of the 828 institutions targeted, 751 responded to the questionnaire (response rate, 91%): these comprised 686 institutions that returned the questionnaire and 65 institutions that provided data via telephone or e-mail. The characteristics of the 751 participating institutions are listed in Table 1: 417 (55%) had less than 500 beds and 541 (72%) provided specialized palliative care.

Table 2. Number of Institutions Providing Each Type of Specialized Palliative Care Service in Participating Institutions.

Types	n	%[a]	95% Confidence Interval
Hospital-based palliative care team	538	99	(99, 100)
Palliative care outpatient clinic	410	76	(72, 79)
Palliative care units	109	20	(17, 24)
Certified[b]	99	18	(15, 22)
Noncertified[b]	10	2	(1, 3)
Community palliative care consultation	74	14	(11, 17)

[a] Number of institutes expressed as a percentage of the number of participating institutions providing specialized palliative care services (n = 541).

[b] Certification status according to National Health Insurance system in Japan.

Table 3. Numbers of Patients With Cancer Who Utilized Specialist Palliative Care Services in Japan in the 1-Year Period (April 2009-March 2010).

Types	n	Institution, Mean ± SD, Median
Annual number of patients with cancer who utilized		
Hospital-based palliative care team	43 716	86 ± 87, 62
Palliative care outpatient clinic	10 216	21 ± 50, 5
Community palliative care consultation	519	8 ± 17, 2
Total	54 451	101 ± 116, 67
Annual number of patients with cancer		
Who were admitted to palliative care units[a]	29 844	148 ± 73, 133
Who died in palliative care units[a]	25 529	127 ± 57, 118

Abbreviation: SD, standard deviation.

[a] Data extracted from the census database of Hospice Palliative Care Japan.

Number of Institutions Providing Specialized Palliative Care Services

Table 2 lists the numbers of participating institutions providing each type of specialized palliative care service. A hospital-based palliative care team, palliative care outpatient clinic, palliative care unit, and community palliative care consultation were available in 538, 410, 109, and 74 institutions, respectively, of those participating institutions that provided specialized palliative care services.

From the census database of the Association of Hospice Palliative Care Japan, 217 certified palliative care units were available in 2009.[2] Thus, we assumed that 118 nonparticipating institutions (217 − 99 = 118) provided specialized palliative care services in a certified palliative care unit. The total estimated number of institutions providing specialized palliative care service was 659 (541 + 118 = 659) in 2009 in Japan.

Estimated Total Number of Patients With Cancer Who Utilized Specialized Palliative Care Services

In the participating institutions, the annual numbers of patients who used hospital-based palliative care team, palliative care outpatient clinic, or community palliative care consultation service were 43 716, 10 216, and 519, respectively, in the period from April 2009 to March 2010 (Table 3, upper section). The annual numbers of new patients who were admitted to or died in a palliative care unit were 29 794 and 25 438, respectively, according to the data from the census database of Hospice Palliative Care Japan for the same period (Table 3, lower section). According to the census database, 3934 beds were available for a total of all palliative care units (average 18 beds/palliative care unit) and the average length of stay in a palliative care unit was 41.8 ± 15.2 (standard deviation) days. The estimated total number of patients with cancer who utilized specialized palliative care services in 2009 in Japan was 84 295 (43 716 + 10 216 + 519 + 29 844 = 84 295). According to the national death statistics database of the Ministry of Health, Welfare, and Labor in Japan, the number of patients with cancer that died during the period April 2009 to March 2010 was 344 105.[5] Therefore, an estimated 24% (confidence interval, 24%-25%) of patients with cancer who died in Japan in 2009 used specialized palliative care services.

Discussion

We conducted a nationwide survey for the 1-year period from April 2009 to March 2010 in Japan to clarify the number of institutions that provided a specialized palliative care service and to estimate the number of patients with cancer who utilized such services. Three of the most important findings of this survey were that (1) the number of palliative care teams was approximately 540; (2) approximately 660 institutions provided specialized palliative care services; and (3) an estimated 24% of patients with cancer who died during the period utilized a specialized palliative care service.

In the early 2000s in Japan, there were few specialized palliative care services exists except for palliative care units. The results of our survey indicate that the types and quantity of specialized palliative care services have increased explosively in the past decade. Multiple studies have revealed the beneficial effects of specialized palliative care services on patient outcomes.[6,7] Thus, if the trend of increased usage of specialized palliative care continues, we expect that there will be great improvements in patient outcomes as well as the quality of life of patients and their families in the future.[8]

Although the utilization of specialized palliative care services by patients with cancer has greatly increased, as described above, the usage is still lower than the 50% rate observed in some other developed countries. For example, the annual cancer deaths were 140 497 in 2009 in the United Kingdom,[9] and 19% (27 257) of these patients with cancer utilized palliative care units, 37% (51 644) utilized palliative care teams, 17% (24 138) utilized palliative care outpatient clinics, 8% (10 958) utilized day care services, and 37% (51 744) utilized home palliative care.[10] Sixty-eight percent of patients with cancer who died between July 1, 2000, and December 31, 2002, utilized specialized palliative care in Western