

Difference in the timing of cessation of palliative chemotherapy between patients with incurable cancer receiving therapy only in a local hospital and those transitioned from a tertiary medical center to a local hospital

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Background It is important to know when to decide to end palliative chemotherapy (PC) for the quality of life of patients. However, there is currently no clear agreement on when to terminate PC.

Objectives To determine whether the difference of the period between the completion of PC and death affects patients' trajectory of supportive care near end of life.

Methods This retrospective study included 52 adult patients with incurable cancer who had received PC and who were referred to our palliative care team and died in our local hospital between July 2011 and June 2014. Group A comprised patients who received anticancer therapy such as surgery and PC only in our hospital and eventually died there. Group B comprised patients who were transitioned to our hospital from tertiary medical centers after cessation of PC.

Results 17 of 22 patients (77%) in Group A conveyed the intention of continuing PC in the first interview with a physician of the palliative care team, whereas 4 of 30 patients (13%) in Group B conveyed a similar intention. The patients in Group B stopped PC a median of 43 days earlier than did the patients in Group A ($P < .0001$).

Conclusions These data showed that more patients in Group A wanted to continue PC and had a shorter interval between last PC and death. Change in the hospital where the patients are given supportive care might contribute to the cessation of futile PC at an appropriate time.

As Japan's society ages, increasing numbers of middle-aged and elderly people living in the country will be diagnosed with, and eventually die of cancer.^{1,2} With the commensurate growing call for better end-of-life (EoL) care, the role of hospitals in Japanese communities has been redefined.^{3,4} It has become necessary to shorten stays in acute-care hospitals for patients who do not need aggressive anticancer therapy. In addition, hospital restructuring has transferred many aspects of inpa-

tient care to community-based care, including EoL and palliative care of those with cancer.^{1,3}

Patients who are transitioned from a tertiary medical center (TMC) to a local hospital by their oncologists not only leave the institution, but the physicians and medical staff who had been caring for them and who were familiar with their cases. Moreover, these patients may be informed of the serious condition of their disease at the time of transition. Talking to patients and their families about

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supportive care and death is not easy, particularly when patients and/or their families want to continue aggressive therapy.⁵

Palliative chemotherapy (PC) near EoL is a commonly discussed issue nowadays. It remains the mainstay of treatment for patients with advanced malignancy in developed countries. Toxic side effects that significantly reduce patients' quality of life (QoL) and increase fatigue and anxiety are unacceptable when the aim of treatment is palliation of symptoms. Therefore, appropriately timed cessation of PC is critical.^{6,7} In most cases, use of PC in the last few weeks of a patient's life may indicate poor clinical judgment.⁸ Because it is even more complex to treat patients with a short life expectancy, treatment goals for any given patient should be clearly defined.^{5,9}

Chichibu Municipal Hospital (CMH) is a medium-sized public hospital in rural Japan; cancer patients are cared for and treated as outpatients or inpatients by a few oncologists. A full-time physician specializing in gastrointestinal surgeries and a part-time (once a week) physician specializing in PC were in charge of PC at CMH. The palliative care team of CMH comprises medical doctors and other health care professionals, such as nurses, pharmacists, and therapists. The hospital has 135 beds for acute care. It is the core community hospital in the region, but not a general hospital. Patients needing highly advanced medical care are transferred to a TMC that is about 40 km (about 25 miles) away. Patients diagnosed with gastrointestinal, pancreatic, or urological cancer at CMH can choose between CMH and a TMC for their treatment. Almost all patients who choose CMH receive anticancer therapy only throughout the course of their disease. Some patients who receive anticancer therapy at TMCs return to CMH after cessation of anticancer therapy. At TMCs, patients who do not benefit from further standard treatment or who are ineligible for participation in clinical trials may tend to cease PC earlier, even if their condition is generally good. The aim of this retrospective study was to determine whether the difference of the period between the completion of PC and death affects patients' trajectory of supportive care near EoL. The results may help physicians better understand when they should cease PC and focus instead on providing supportive care to their patients near EoL.

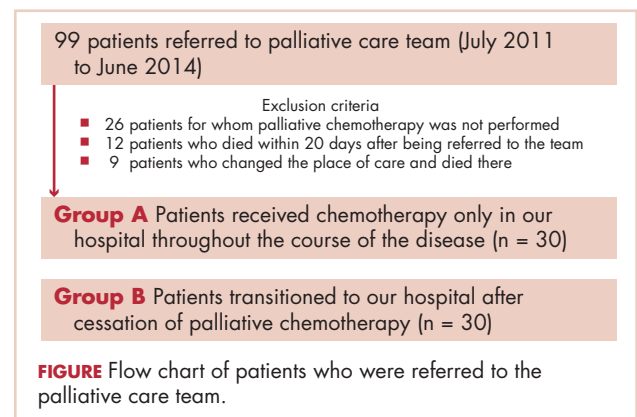
Methods

This study used a retrospective cohort design. All adult patients with incurable cancer, such as metastatic and recurrent cancer, who had received PC and supportive care from the palliative care team at CMH and subsequently died there during July 2011-June 2014 were identified from the medical records. PC was defined as chemotherapy treatment with noncurative intent.

Patients who were diagnosed with incurable cancer and

died at CMH but did not receive PC throughout the course of the disease were not included in this study. Patients who had already been referred before the start of the study period and those who were referred during the period and were alive at the end of the study period were not included. In addition, patients who eventually died at home or in a nearby hospital and those referred to our palliative care team who died within 20 days were not included (Figure). For the latter group of patients, confirmation regarding their preference for cessation of PC and location of EoL during the interview with a physician of our palliative care team was considered difficult because of the patients' poor general condition

When the patients were referred to the palliative care team, a physician member of the team would conduct a face-to-face interview of about 20 minutes with each patient during a regularly scheduled treatment appointment at our hospital. After the interview, the physician was in charge of the patient's medical care with other members of the palliative care team, in place of the oncologist. We recorded the following variables: age, gender, site of cancer, date of death, date of first visit to our hospital, date of the first interview with a physician of our palliative care team, number of days spent in our hospital, number of admissions for palliative care, date of cessation of anticancer therapy, and date of patients' perception of supportive care. Patients' perception of palliative care was defined as their decision to switch to best supportive care only. We focused on the following factors: patients' willingness to continue anticancer therapy, the preferred location for EoL therapy, patients' expression of fear of abandonment, the period between cessation of PC and death, the interval between talking to patients about supportive care and death, and the length of hospital stay immediately before death. Expression of fear of abandonment was defined as use of descriptions such as "I was abandoned by my physician (or oncologist)" in the medical records at the time of the first interview with the physician at our palliative care team or in subsequent daily medical records until the death of the patient.



Patients were divided into 2 groups: Group A, which comprised patients who received chemotherapy only in our hospital throughout the course of their disease; and Group B, which comprised patients who were transitioned to our hospital after cessation of PC. In Group A, the date of progression of the cancer with the current line of treatment was determined retrospectively. Progressive disease was defined as levels of one or more tumor marker being significantly above normal, according to the RECIST [Response Evaluation Criteria in Solid Tumors] guidelines for imaging.¹⁰ QoL could not be assessed with specific scales because this was a retrospective study. CMH's institutional review board approved the project protocol. Statistical tests included the Fisher exact test, chi-square test, and the Mann-Whitney test, as appropriate. A *P* value of <.05 was considered statistically significant. All statistical analyses were performed with StatView (SAS Institute, Cary, NC).

Results

During July 2011-June 2014, 99 consecutive patients with incurable cancer who were referred to the palliative care team were screened. Of those patients, 26 were excluded because they had not received PC, 12 were excluded because they died within 20 days of being referred to our team because of deterioration in the disease, and 9 were excluded because they changed the hospital of care and died there after an intervention of our team. In all, 52 patients (25 men, 27 women) who met our inclusion criteria were included in this study (Group A, n = 22; Group B, n = 30). The patient characteristics are shown in Table 1. Of the patients in whose charts were reviewed, 64% and 37% (Group A and Group B, respectively) were men, and the respective median ages were 71 years and 72.5 years. The primary cancer sites were pancreatic and biliary (45% and 27%), colorectal (23% and 13%), gynecological (0% and 20%), and lung (0% and 17%), as shown in Table 2.

TABLE 1 Characteristics and attributes of patients (N = 52)

Characteristic/attribute	Group		P value
	A (n = 22)	B (n = 30)	
Median age, y (range)	71 (43-82)	72.5 (43-86)	.95*
Sex – male, n (%)	14 (63.6)	11 (36.6)	.09*
Median distance between home and a TMC, km/miles ^a (range)	Not available	41.5/28.0 (30.6-114/19.0-70.8)	Not applicable
Median distance between home and CMH, km/miles ^a (range)	2.75/1.7 (0.1-18.8/0.06-11.7)	4.75/3.0 (1-17.6/0.62-11.0)	.13†
Median time interval between first visit to CMH and death, d (range)	258.5 (55-1,395)	58.5 (21-279)	.0001†
Median time interval between referral to PCT to death, d (range)	53 (22-91)	58.5 (21-279)	.18†
Median time interval between progressive disease and death, d (range)	58 (15-199)	Not available	Not applicable
Median time interval between last chemotherapy and death, d (range)	54 (6-199)	97 (53-353)	<.0001†
Median time interval between perception of supportive care and death, d (range)	32 (0-199)	75.5 (32-340)	<.0001†
Median no. of admissions for palliative care (range)	2 (1-4)	2 (1-10)	.43†
Total median length of hospital stay for symptom control, d (range)	31 (13-82)	29 (11-74)	.35†
Final length of hospital stay before death, d (range)	24 (2-59)	18.5 (2-54)	0.55†

TMC, tertiary medical center; CMH, Chichibu Municipal Hospital; PCT, palliative care team

^aValues for miles are rounded to 1 decimal point.

**P* value by Fisher exact test. †*P* value by Mann-Whitney test.

TABLE 2 Primary cancer diagnosis (N = 52)*

Type of malignancy	Group	
	A (n = 22)	B (n = 30)
Pancreatic and biliary	10	8
Colorectal	5	4
Gastric	5	1
Esophageal	1	2
Urological	1	0
Gynecologic	0	6
Lung	0	5
Head and neck	0	4

*P value by chi-square test = .005.

Pancreatic, biliary, and colorectal cancers were more common primary cancer sites in Group A than in Group B (Table 2). In Group A, 17 patients (77%) conveyed the intention of continuing PC in the first interview with a physician of the palliative care team, compared with 4 patients (13%) in Group B (Table 3). The patients in Group B stopped PC a median of 43 days earlier than did the patients in Group A (Table 1). The patients in Group B decided to switch to best supportive care a median of 43 days earlier than did the patients in Group A (Table 1).

Retrospectively, the objective timing of progressive disease according to the radiological findings or changes in tumor markers and the timing of cessation of PC was not significant for the patients in Group A (Table 1). However, 10 patients (45%) in Group A continued PC after the evaluation that their cancer was progressive.

Patients in Group B, who were referred to CMH from TMCs, were interviewed by a physician of the palliative care team at the first visit. Therefore, the time interval between the first visit to CMH and death and that between referral to the palliative care team of CMH and death was equal for patients in Group B. The time interval between referral to the palliative care team of CMH and death was

not significantly different between Group A and Group B patients (Table 1).

We performed subgroup analyses to exclude the difference in primary cancer sites between the groups. We extracted patients with pancreatic, biliary, colorectal, gastric, or esophageal cancers from both groups and defined them as Subgroup A (extracted from Group A) and Subgroup B (from Group B). We compared patient characteristics between Subgroup A and Subgroup B. Subgroup A also had the following significant findings in relation to Subgroup B: a larger proportion of patients willing to continue PC ($P < .0001$), a longer length of time between first visit to CMH and death ($P < .0001$), a shorter length of time between cessation of PC and death ($P < .0001$), and a shorter length of time between perception of supportive care and death ($P < .0001$), shown in Table 4.

Discussion

The primary cancer sites were different between Group A and Group B. One possible reason for that could be the lack of oncologists who specialize in gynecology, respiratory organs, and head and neck regions at CMH. However, without such oncologists, patients with gynecologic, lung, or head and neck cancers who needed supportive care near EoL required transfer to a local hospital. The patients in Group B visited several TMCs for treatment about 40 km (about 25 miles) away from their homes. The distance from the patients' homes to CMH was not significantly different between Group A and Group B. In addition, there was no significant difference between Group A and Group B with respect to the total length of hospital stay for symptom control, number of admissions for palliative care, and length of final hospital stay before death.

Patients' attitudes and wishes vary widely when faced with a life-threatening or terminal illness; some patients are unwilling to undergo any treatment, whereas others are willing to undergo almost any treatment even if it has a small chance of being beneficial.^{5,11} When the oncologist deems the continuation of PC to be futile, the patients cannot continue the treatment at TMC. They are forced

TABLE 3 Comparison of patients' attitudes at the interview by a physician of palliative care team

Attitude	Group		P value
	A (n = 22)	B (n = 30)	
Willing to continue PC when recommended supportive care, Yes:No	17:5	4:26	<.0001*
Preferred location of EoL when recommended supportive care, Home:Hospital:Unknown	15:7:0	19:9:2	.46†
Expression of fear of abandonment, Yes; n (%)	0 (0%)	4 (13.3%)	.12*

PC, palliative chemotherapy; EoL, end of life

*P value by Fisher's exact test. †P value by chi-square test.

TABLE 4 Comparison of factors between Subgroup A and Subgroup B

Factor	Subgroup		P value
	A (n = 21)	B (n = 15)	
Median time interval between first visit to CMH and death, d (range)	247 (55-991)	60 (23-187)	.0001*
Median time interval between last chemotherapy and death, d (range)	50 (6-88)	89 (53-250)	.0004*
Median time interval between perception of supportive care and death, d (range)	32 (0-78)	90 (36-199)	<.0001*
Willing to continue anticancer therapy when recommended supportive care, Yes:No	17:4	4:11	.0019†

CMH, Chichibu Municipal Hospital

*P value by Mann-Whitney test. †P value by Fisher exact test.

to change the location of care, which may lead to them to express fears of abandonment, as seen in the Group B patients. To minimize this fear, oncologists must consider how to change the location of palliative care near the residence of patients or their family when PC becomes futile.

Oncologists at the previous medical institutions discussed the cessation of PC with the patients in Group B. Thus, few patients were willing to continue PC at the time of interview at CMH. However, many patients in Group A hoped to continue PC when referred to our palliative care team. Patient-related factors that may contribute to patients receiving futile PC at EoL include the personality traits of the patient and/or the family in not wanting to give up the hope of cure.¹² The physicians at our relatively small local hospital could meet these patients' expectations and would not want to disappoint them. Retrospectively, according to the data regarding the radiological findings or changes in tumor markers, 10 patients (45%) in Group A continued PC after the evaluation that their cancer was progressive. Although oncologists recognized disease progression in the patients in Group A, they continued PC for these patients to give them hope. An independent factor correlated with a shorter interval between the completion of PC and death was the presence of symptoms. Patients may believe that the outcomes of PC may be overly optimistic and PC is the only way to palliate their symptom because the tumor evokes the symptom.¹³⁻¹⁵ Oncologists should tell their patients that PC is not the only way to eliminate symptoms and that its efficacy is limited if their general condition is poor.¹⁶

Although talking to patients and their families about cessation of PC and supportive care is not easy, oncologists must inform patients and their families in advance about the timing of cessation and help them make important EoL decisions.^{5,17,18} Patients have few opportunities to discuss their preferences about EoL care with physicians throughout the course of their disease.¹⁹ Ideally, oncologists

should start PC with informed patient consent to the fact that PC is not for cure and that patients need to be referred to palliative care units at the same time as they receive PC. However, because data have shown that 19.6% of patients start PC without having been given information about palliative care units, this has not yet been achieved in clinical practice.²⁰ This is because physicians do not yet have sufficient data to enable them to decide whether they should stop PC or recommend hospice admission.¹⁶

Some limitations to this study need to be considered. First, our study was confined to a single institution within the specific subset of patients with incurable cancer and a limited number of oncologists at CMH. In particular, because of the small number of patients who received anticancer therapy only at CMH throughout the course of the disease, we cannot generalize our findings to other settings. However, Subgroup A showed a significantly shorter length of time between cessation of anticancer therapy and death, and a significantly shorter length of time between perception of supportive care and death after performing analyses to correct for the small sample size. Second, this study was retrospective in design; therefore, the findings may not be fully validated. To obtain more accurate data regarding EoL care, prospective cohort studies are needed to identify terminally ill patients and subsequently follow them until death.

It is assumed that the patients in Group B had been able to have an appropriate discussion with their oncologists about stopping PC before they transferred to CMH. We did not examine how many of the patients who had received anticancer therapy at TMCs did not transfer to CMH for supportive care and eventually died at the TMCs. Those patients may well be the patients who were more likely to continue PC until close to death. Therefore, we assumed that it would be easier for oncologists at a local hospital to discuss PC with patients who transferred there from a TMC after cessation of PC because the patients

would already have discussed the matter with the TMC oncologists before they transferred.

In conclusion, patients transferred to a local hospital from TMCs after cessation of anticancer therapy (Group B) stopped PC a median of 43 days earlier than those receiving therapy only in a local hospital (Group A). Four patients in Group B expressed fear of abandonment over the course of their disease, whereas no patient in Group A expressed similar fears. Change in the hospital where the patients are given supportive care may provide patients an opportunity to cease futile PC at an appropriate time after discussion with their oncologists. When changing a hospital, few patients expect the continuation of PC; however, the physician needs to consider the fear of abandonment of such patients.

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