

Aggressiveness of Cancer-Care near the End-of-Life in Korea

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Objective: The aim of this study was to examine the appropriateness of chemotherapy and care in Korean cancer patients near the end-of-life.

Methods: We designed a retrospective cohort composed of patients diagnosed as having metastatic cancer and who received palliative chemotherapy at Seoul National University Hospital in 2002. Two hundred and ninety-eight patients who died of cancer were evaluated in terms of the appropriateness of the cancer-care they received, including chemotherapy.

Results: Median duration of chemotherapy was 6.02 months compared with 8.67 months for median overall survival. The median period between last chemotherapy and death was 2.02 months. Of the 298 patients, 50.3% received chemotherapy during the last 2 months of life. Furthermore, 17 patients (5.7%) died within 2 weeks after receiving chemotherapy. The proportion who visited an emergency room (ER) more than once during the last months of life was 33.6%, and the average number of ER visits after a diagnosis of cancer was 1.72. Only 9.1% of patients were referred to a hospice consultation service and only 11.7% of patients agreed with written DNR.

Conclusions: Among patients who died of cancer, significant proportions were found to have received chemotherapy up to the end-of-life and to have visited ERs. Hospice referrals and discussions about DNR were not conducted well during the end-of-life period in Korea.

Key words: aggressiveness – end-of-life – hospice – palliative chemotherapy

INTRODUCTION

As new anti-cancer chemotherapeutic agents with higher efficacies have been developed, the use of chemotherapy in terminal stage cancer patients has increased (1). Even after failure of various anti-cancer treatments, patients and family members usually still want another aggressive treatment, just to delay inevitable deaths. However, physicians are used to explain risks and benefits of a specific treatment, without considering whole clinical course or the quality-of-life or values. These make real confusion in preparing advance care planning of terminal cancer patients.

Much information is withheld and discussions about the end-of-life care are not conducted well, sometimes the

attitudes of patients and physicians towards chemotherapy differ markedly during the terminal stage.

When is the most appropriate time to discontinue chemotherapy? The end-of-life care and issues such as when to stop chemotherapy present huge dilemmas. To achieve death with dignity, and simultaneously prolong survival by chemotherapy, physicians should judge the discontinuation of palliative chemotherapy judiciously by comparing risks and benefits. Many physicians are concerned that patients dying of cancer are frequently over-treated (2). However, little is known on the topic, especially in Asia. Moreover, attitudes to the end-of-life care in Western and Asian countries are different for cultural reasons (3,4).

Another considerable problem concerning the end-of-life care is the level of cooperation required between hospitals and related healthcare resources. In Korea, the hospice system has not been well established, in comparison to Western countries. Hence many physicians and patients are reticent about using the hospice service (5,6).

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Thus, we conducted this study to investigate the aggressiveness of chemotherapy and the status of end-of-life care, and to assess the availabilities of related healthcare resources in Korea.

PATIENTS AND METHODS

We had designed a retrospective cohort composed of patients diagnosed as having metastatic cancer at Seoul National University Hospital (SNUH), a tertiary referral hospital. There are 1616 beds, and 37 departments, mainly for acute intervention purpose. A total of 1102 doctors (388 staffs, 163 fellows, 551 residents) are working and most patients are referred from primary care physicians and secondary hospitals. Active chemotherapy as well as cancer surgery has been conducted. For better understanding of outline of medical service, Fig. 1 shows the flow of patients in SNUH. Anti-cancer treatment is decided by the multi-disciplinary team (surgeons, radiotherapists, medical oncologists etc) and the end-of-life care is given by palliative care team (medical oncologists, pharmacists, social workers, nutritionists, nurses etc).

A total of 1050 patients newly diagnosed as having metastatic cancer in SNUH from January 1 to December 31, 2002, were included. Among them, the patients who had received palliative chemotherapy were enrolled in this study. Palliative chemotherapy is defined as the chemotherapy of which the goal is not cure but prolongation of survival or relief of the symptoms. We had followed-up this cohort till deaths of the patients due to disease progression. Exclusion criteria were as follows: (i) hematologic malignancy (leukemia, lymphoma, multiple myeloma etc), (ii) hepatocellular carcinoma only locally treated, (iii) patients who received adjuvant chemotherapy, (iv) uncertainty of last chemotherapy and (v) pediatric patients (age ≤ 16). Two hundred and ninety-eight patients who died of cancer were finally analysed for the appropriateness of cancer-care including chemotherapy.

In general, aggressive cancer-care presented as the intensive use of chemotherapy, low rates of hospice use and high rates of intensive care unit (ICU) admissions (7). We

identified several indicators of aggressiveness of cancer-care by empirically identifying cut offs for outliers (1,8); (i) proportion receiving chemotherapy within 14 days of death, (ii) average number of days between last chemotherapy and death, (iii) average numbers of regimens and cycles, (iv) median duration of chemotherapy, (v) proportion with >1 emergency room (ER) visits during the last months of life and (vi) proportion of ICU admission in the last month of life.

To evaluate trends in the aggressiveness of chemotherapy, we retrospectively reviewed medical records, which included chemotherapeutic regimens, no. of cycles, date of administration, do-not-resuscitate (DNR) permissions, records of ER visits. Date and place of death were obtained from the death registration database of the Korea National Statistical Office (9), and data related to hospice placement were obtained from the hospice consultation service of SNUH.

As SNUH is a tertiary referral hospital, there is no inpatient hospice unit. The major roles of hospice consultation service are (i) referring terminal cancer patients to regional hospice centers, (ii) transfer of patients to secondary hospitals for hospice care and (iii) help patients to receive home hospice service (see Fig. 1).

RESULTS

A total of 298 patients were consecutively enrolled. The clinical characteristics of patients are shown in Table 1. Two hundred and eight men and 90 women of median age 59.0 years (range: 17–86 years) were evaluated. Median duration of chemotherapy was 6.02 months (range: 0.2–19.4 months) compared to an 8.67 months median overall survival. The median period between last chemotherapy and death was 2.02 months.

INDICATORS OF AGGRESSIVE CARE

Among the 298 patients, 94.6% received chemotherapy during the last 6 months of life and 50.3% during the last 2 months of life. Furthermore, 17 patients (5.7%) died within

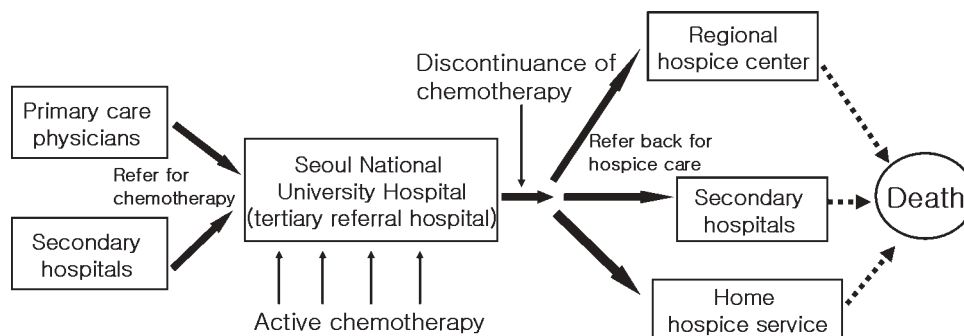


Figure 1. Outline of cancer-care in our institution.

Table 1. The clinical characteristics of patients

<i>N</i> = 298	No. of patients
Sex	
Male	208 (69.8%)
Female	90 (30.2%)
Median age	59.0 (range 17–86)
Median overall survival	8.67 months (range 0.8–22.4)
Median duration of chemotherapy	6.02 months (range 0.2–19.4)
Underlying cancer	
Lung cancer	95 (32.0%)
Advanced gastric cancer	77 (25.8%)
Colorectal cancer	18 (6.0%)
Biliary cancer	23 (7.7%)
Hepatocellular carcinoma	14 (4.7%)
Pancreas cancer	17 (5.7%)
Esophageal cancer	6 (2.0%)
Metastasis of unknown origin	15 (5.0%)
Head and neck cancer	10 (3.4%)
Others	23 (7.7%)

2 weeks after receiving chemotherapy (Table 2). Average no. of days between last chemotherapy and death were 77.1 days. Periods between last chemotherapy and death are shown in Fig. 2. The mean numbers of regimens and cycles patients received were 1.83 and 5.52, respectively.

Table 2. Indicators of cancer-care

Aggressiveness of chemotherapy	
Proportion receiving chemotherapy within 6 months of deaths	94.6% (282/298)
Proportion receiving chemotherapy within 2 months of deaths	50.3% (150/298)
Proportion receiving chemotherapy within 14 days of deaths	5.7% (17/298)
Average no. of days between last chemotherapy and death	77.1 days (range 0–286, median 60 days, SD 57.04)
Average no. of regimens	1.83 (range 1–6, median 2, SD 0.93)
Average no. of cycles	5.52 (range 1–17, median 5, SD 3.89)
Status of end-of-life care	
Average no. of ER visits after cancer diagnosed	1.72 (range 0–14, median 1, SD 1.89)
Average no. of ER visits in the last month of life	0.40 (range 0–3, median 0, SD 0.62)
Proportion with >1 ER visit in the last month of life	33.6% (100/298)
Proportion admitted to the ICU in the last month of life	2.7% (8/298)
Status of palliative care	
Proportion referred to hospice consultation service	9.1% (27/298)
Timing of referring to hospice consultation service	Median 53 days before death (range 4–471 days)
Proportion of hospital deaths*	20.8% (57/274)
Proportion of agreement with written DNR	11.7% (35/298)

*Twenty-four patients were not able to find out the place of death. Abbreviations: SD, standard deviation; ER, emergency room; ICU, intensive care unit; DNR, do-not-resuscitate.

STATUS OF END-OF-LIFE CARE

The proportion of patients that visited an ER more than once during the last months of life was 33.6% and average number of ER visits after a diagnosis of cancer was 1.72 (range 0–14). One month before death, patients had visited an ER an average of 0.40 times. Among the 298 patients, only 9.1% of patients were referred to a hospice consultation service, at a median 53 days before death (range 4–471 days). The proportions of hospital death were 20.8 and 2.7% of patients admitted to the ICU in the last month of life.

Place of death was not associated with referral to hospice service (12.3% in hospital death versus 10.1% in home death, *P* = 0.470 by the Student *t*-test) and average no. of days between last chemotherapy and death (84.27 days for in hospital deaths versus 76.71 days for at home deaths, *P* = 0.564 by the Student *t*-test). The agreement rate of written DNR was only 11.7%.

Timing of discontinuance chemotherapy affected to cancer-care. The patients received chemotherapy within 2 months of deaths showed higher proportion of ER visiting and admission to ICU in the last month of life comparing with those received chemotherapy 3 months or later before death (Table 3). Even though direct comparison has some limitation, median overall survival was rather shorter in the patients received chemotherapy within 2 months of deaths (7.4 versus 10.5 months, *P* < 0.001 by log-rank test). Mean number of regimens and cycles were not different according to each group. Agreement rate of written DNR issue and hospice referral and proportion of hospital death were not associated with the timing of discontinuation chemotherapy.

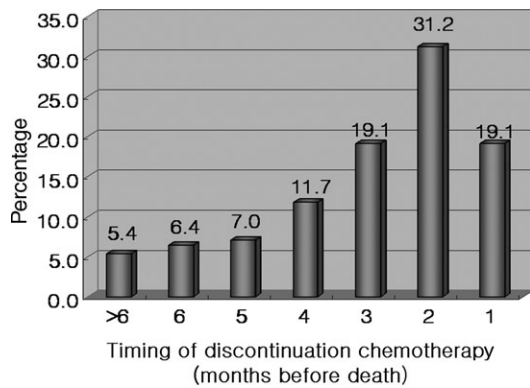


Figure 2. Periods between last chemotherapy and deaths.

DISCUSSION

Significant proportions of patients have received aggressive chemotherapy up to the end-of-life in Korea. When should we discontinue chemotherapy near the end-of-life? This is not a simple problem, because the end-of-life care decisions are complex with personal, medical, social and psychological dimensions (10). In general, physicians use chemotherapy prudently only when it is likely to extend life or relieve symptoms, and should discontinue chemotherapy when its benefits are outweighed by its disadvantages (i.e. its associated toxicities). Hence physicians should try to balance the risks and benefits involved and organize related health care resources appropriately.

In the present study, we evaluated the status of the end-of-life care and found that a significant proportion of patients received inappropriate chemotherapy. According to our results, the patients received chemotherapy during a median 6.02 months in the median overall survival was

8.67 months with average 1.83 regimens and 5.52 cycles of chemotherapy. We also found that 94.6% of patients received chemotherapy in the last 6 months of life, which is higher than that reported in USA (33% by Emanuel et al., and 37.5% by Gagnon et al.) (11,12) and in Italy of 79.7% (13). In addition, the average number of days between last chemotherapy and death was 77.1 days, which is similar to data reported in the USA (65.3 days in 1996) (1). However, direct comparisons with previous reports are difficult due to different settings and patient characteristics. Furthermore, SNUH is a tertiary referral hospital, in which patients tend to receive more aggressive care and chemotherapy (14). In contrast, patients who are reluctant to chemotherapy would not be referred to the university hospital. However, the present study indicates that chemotherapy is administered more aggressively than was expected.

What makes this aggressive chemotherapy? The older generations view cancer as a sentence for death—the quintessential incurable disease. However, with developments of novel therapeutics in the modern oncology field, cancer is generally considered as a chronic disease that can be controlled by anti-cancer drugs. As more anti-cancer treatment options are available, we are frequently confronted by disagreements between old cancer patients and young family members, and even physicians have different attitudes to elderly and young cancer patients (15). Sometimes family members do not want patients to have insight of the disease, and prefer that information on diagnosis, stage, and prognosis be withheld, whereas usually patients want to be informed if they reach the terminal stage (16). Sometimes family members request aggressive chemotherapy and that every effort be made to prolong survival because of the obligations they feel for their parents, which are accentuated in the orient by confucianism (17). In Asian countries, family caregivers had a

Table 3. Indicators of cancer-care according to timing of discontinuation chemotherapy

	Timing of discontinuation chemotherapy		
	Within 2 months before death (N = 150)	3 or more later before death (N = 148)	P value
Aggressiveness of chemotherapy			
Average no. of regimens	1.83 (range 1–5)	1.82 (range 1–6)	0.980*
Average no. of cycles	5.10 (range 1–17)	5.95 (range 1–18)	0.600*
Status of cancer-care			
Proportion with >1 ER visit in the last month of life	42.0% (87/150)	25% (37/148)	0.002 [†]
Proportion admitted to the ICU in the last month of life	4.7% (7/150)	0.7% (1/147)	0.067 [†]
Proportion of hospital deaths	19.0% (26/137)	22.6% (31/137)	0.512 [†]
Proportion referred to hospice consultation service	8.7% (13/150)	10.8% (16/148)	0.532 [†]
Proportion with agreement of written DNR	15.3% (23/150)	8.1% (12/148)	0.053 [†]
Median overall survival	7.4 months (range 0.8–20.2)	10.5 months (range 2.5–22.4)	<0.001 [‡]

*P value based on the Student t-test.

[†]P value based on the Pearson, χ^2 -test.

[‡]P value based on the log-rank test.

significantly more aggressive attitude toward the end-of-life care than the patients' own stated preferences (18). However, these discrepancies and the generation gap often make family members a huge communication barrier between patient and doctor (3).

Many social and cultural factors might contribute to aggressive cancer treatment in Korea. One possible explanation is low cost of treating cancer in Korea. Mean medical expense of cancer patients for 1 year in Korea is lower than in USA; \$11 600 per patient in Korea (19) versus \$29 000–48 000 per patient in USA (20,21).

Even though not all emergency patients visit ER, the current study shows that 33.6% visited an ER (in tertiary referral hospital) more than once during the last months of life, which is markedly higher than reported in the USA (9.2% in 1996) (1). This might be explained by the lack of role of regional medical facilities in Korea, because less than 5% of terminal cancer patients are covered by regional hospice centers or secondary hospitals. And in our results, the patients received chemotherapy till the end-of-life visited ER and admitted to ICU more frequently in the last month of life. The decision to discontinue chemotherapy is also related to the decision to enter a hospice (11), and in the present study we found that only 9.1% of patients were referred to a hospice consultation service comparing to 26.9% in the USA (22). The lack of decent hospice centers and poor coordination between major hospitals and the hospice programs in Korea may explain the low referral figure, because rates of hospice use have been reported to be closely related to the ready availability of hospice services (23,24). Furthermore, a well established family physician-based continuity of care system for cancer patient might be able to lower the ER visit rate near the end-of-life (6).

We also found that the patients with agreement of written DNR were only 11.7%, which reflects the small proportion of patients and family members prepared to agree with the issuance of a DNR. Although the frequency of DNR issuance during the terminal stage is dependent on many influencing factors (25,26), our results are disappointing. The possible explanations for this low rate were as follows. First, DNR has not yet been authorized legally in Korea. Second, issuance of DNR decision is raised at a late stage in Korea (27), because breaking bad news (like discussions about death) has been done by physicians or family members in only limited numbers of cases. It is a concern that as a result patients have insufficient time to prepare for death with dignity after discussions about the end-of-life decisions.

The present study has some limitations. First, our study represents only a single center, and thus, we cannot exclude the possibility of a selection bias. Hence the representativeness of our findings should be validated by further nationwide larger studies. Second, we did not include quality-of-life data. Nevertheless, to the best of our knowledge, the present study is the first conducted in Asia to evaluate the status of chemotherapy and cancer-care.

A significant proportion of our study cohort received chemotherapy till the end-of-life, and ER visits. Moreover, the study finds that hospice referrals and discussions about DNR were not conducted well. Thus, physicians should be concerned as to whether patients dying of cancer are being over-treated and whether this constitutes inappropriate care that interferes with the dignity of life. Whole clinical course of the individual patient, quality-of-life and values should be considered in medical decision for the end-of-life care in terminal cancer patients.

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Conflict of interest statement

None declared.

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