VOLUME 25 · NUMBER 33 · NOVEMBER 20 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Initiation and Discontinuation of Complementary Therapy Among Cancer Patients

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Submitted March 29, 2007; accepted August 20, 2007.

Supported by a grant from the National Cancer Center, Korea.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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0732-183X/07/2533-5267/$20.00

DOI: 10.1200/JCO.2007.11.9651

ABSTRACT

Purpose
To identify the initiation or discontinuation of complementary therapy (CT) and determine the impact of sociodemographic and clinical factors on CT use among cancer patients.

Patients and Methods
Eligible patients were age 20 or older; newly diagnosed with stomach, liver, or colorectal cancer; and started their initial treatment at the National Cancer Center, Korea, between April 1, 2001, and April 30, 2003. In total, 541 cancer patients were surveyed in face-to-face interviews at baseline, and telephone follow-up interviews were performed every 3 months for 3 years.

Results
A total of 281 patients commenced CT after diagnosis; 164 patients stopped using CT during the follow-up period. The overall cumulative probability of starting CT at 1, 2, and 3 years was 50%, 54%, and 55%, respectively. In a Cox multivariate analysis, stomach and liver cancer were associated with an increased probability of initiating CT compared with colorectal cancer. Patients who were classified as stage I, II, or III at diagnosis were associated with a decreased probability of discontinuing CT compared with stage IV.

Conclusion
Most cancer patients started to use CT during the initial treatment period. Thus, physicians should communicate with cancer patients about CT at this phase. In particular, more attention should be paid to women and individuals with higher household incomes because these groups are more likely to start CT.

J Clin Oncol 25:5267-5274. © 2007 by American Society of Clinical Oncology

INTRODUCTION

As the use of complementary and alternative medicine (CAM) has steadily gained in popularity over the past two decades, coverage of CAM in the medical literature has been increasing.[1,2] In particular, CAM, which is defined as "a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional (Western) medicine"[3] has been widely used among cancer patients throughout the world.[1,2,4-8]

The reasons for using CAM are to provide relief of cancer-related symptoms and treatment adverse effects, to treat cancer, and to promote general health or well-being.[8-14] In addition, cancer patients today have easy access to an enormous amount of information on CAM through the Internet and other media sources,[1,2] and this situation, along with patient concerns about disease recurrence, motivates cancer patients to use CAM.[2,6,15,16] As cancer incidence increases and survival time lengthens, a steady increase in CAM use by cancer patients is expected.

The main point worth mentioning is that most cancer patients combine CAM with conventional treatment.[5,8,17-21] In addition, 38% to 85% of CAM users do not consult with their conventional physicians about their CAM use.[17-20,22-24] Despite some evidence supporting the efficacy of specific CAM modalities for controlling treatment adverse effects and for survival,[25-31] insufficient clinical research data exist to indicate whether CAM is safe and efficacious, and little is known about potential adverse interactions.[32-35] Accordingly, communication between patients and physicians about various issues related to CAM (eg, patient expectations, favorable or adverse events, costs, motivations, and time of initiating CAM) is important. Many physicians can provide information to their patients to help them maintain an optimal lifestyle to cope with cancer and to promote general well-being. In this sense, it is important to investigate the pattern of CAM use in the active treatment phase.

However, most studies performed to date have been cross-sectional, in which it is not easy to elucidate the pattern of CAM use in the active treatment phase; therefore, longitudinal investigation of CAM use after cancer diagnosis is urgently needed.[2,36] In addition, most studies have been completed in Western countries. Studies of CAM use among cancer patients in Asian countries, such as Korea, have rarely been conducted,[8,13] even though Korean cancer patients often use CAM.[14]

Therefore, we performed a prospective cohort study at the National Cancer Center (NCC) of Korea to investigate the initiation or discontinuation pattern of CAM and determine the impact of sociodemographic and clinical factors of CAM use among cancer patients in the first 3 years after diagnosis. The surveyed cancer patients used complementary therapy (CT), but not alternative therapy, because they were being treated in a conventional medical institute.

PATIENTS AND METHODS

Study Sample

This study was part of a prospective cohort study performed at the NCC of Korea that sought to estimate the economic burden of cancer patients. This longitudinal study included patients age 20 or older with stomach, liver, or colorectal cancer (the most common types of cancer in Korea), who were diagnosed between April 1, 2001, and April 30, 2003. We selected patients who were referred to the NCC immediately after cancer diagnosis and started their initial treatment at the NCC without treatment at other institutes. The NCC is a research institute and hospital and is ranked third in cancer registration among hospitals in Korea.

All patients signed a consent form after receiving complete information about the study. In total, 541 cancer patients were surveyed in face-to-face interviews at baseline during outpatient visits to obtain information related to CT started after the cancer diagnosis, regardless of CT used before the diagnosis, as well as their sociodemographic characteristics. After the first survey, patient follow-ups were performed every 3 months for 3 years by telephone, using a questionnaire that focused on changes in the use of CT. Of the patients surveyed, 523 were analyzed after completing follow-up surveys for 3 years. The end of the study was December 31, 2005.

The survey instrument, which was developed through a literature review and discussions with experts and tested in a pilot study at the NCC, included sociodemographic questions such as age at diagnosis, sex, educational level, current residential area, household income, job status, private insurance, and use of CT. Information associated with CT, including the type of CT used, costs, initiation time, and approximate duration of use, was obtained. We also gathered information on clinical characteristics from medical records, such as the site of primary cancer, stage at diagnosis, date of diagnosis, and treatment options received during the follow-up survey period.

We defined CT as any therapy that was not currently part of the conventional medical treatment for cancer patients. CT included traditional Korean medicine, including acupuncture, Korean herbal medicine, and moxibustion; herbal agents, including ginseng, green tea, garlic, aloe, and other plant extracts; nonherbal agents, including mushrooms, chitosan, shark cartilage, honey, and other animal extracts; juices or other special diets; and vitamins or minerals. CT use was defined as the use of at least one of the above therapies after cancer diagnosis and during the 3-year follow-up period.

Statistical Analysis

Unadjusted associations between covariates and commencement or discontinuation of CT were tested using the χ^2 test. For survival analysis, the primary outcome measures were the initiation of CT and the time from the date of diagnosis to that of beginning CT. The secondary outcome measures were the discontinuation of CT and the time from the beginning to the end of CT. Because information on the dates of CT initiation and discontinuation was not clear, we used the first and last days of the 3-month follow-up intervals as the start and end times of CT use, respectively. The start and end times of CT were considered as events in our analyses, whereas subjects who died or were transferred to other institutes before beginning CT and those who had not used CT until the termination of the study were excluded.

The probability of the commencement or discontinuation of CT since cancer diagnosis was estimated using the Kaplan-Meier method, and the statistical significance of the differences between subgroups was assessed using the log-rank test. Furthermore, the relationships between prognostic factors and outcome were investigated using Cox multiple regression models.

In the first stage of the Cox analysis, univariate models were used to evaluate the effect of each specific parameter and to select covariates with $P < .20$. In the second stage, even though several covariates, such as sex, age, stage at diagnosis, and treatment type, had a $P > .20$, they were added to the final model for adjustment. In addition, unlike bivariate analysis, treatment types in the Cox models were defined as time-dependent covariates because these variables changed in value over the course of observation.[37]

To evaluate predictors of discontinuing CT, we performed further statistical analyses only for patients who used CT. Similarly, we analyzed a multivariate Cox model adjusted for sex, age, tumor site, stage at diagnosis, and treatment type after univariate model analysis. Hazard ratios indicating the effects of predictive factors on the probability of introduction or discontinuation of CT were calculated.

All data management and statistical analysis were two tailed with $P < .05$ and were performed using SAS, version 9.1 (SAS Institute, Cary, NC). This study was approved by the institutional review board of the NCC.

RESULTS

Of the 523 patients included in the analysis, 219 (41.9%) had colorectal cancer, 187 (35.7%) had stomach cancer, and 117 (22.4%) had liver cancer (Table 1); 338 (64.6%) were male, and 310 (59.3%) were age 60 or younger. Those patients diagnosed with colorectal cancer were more likely to receive surgery (99.1%), radiation therapy (29.7%), or chemotherapy (87.2%), compared with those diagnosed with stomach or liver cancer.

Approximately 54% of patients (281 of 523) commenced CT after diagnosis (Table 2). Of these, 21 patients who had multiple initiation and discontinuation points were excluded from the separate analysis of CT users. Therefore, in the analysis, 63.1% of CT users (164 of 260) actually stopped using CT during the 3-year follow-up period. In the bivariate analysis, factors associated with the initiation of CT after cancer diagnosis included age ($P < .001$), household income ($P < .001$), private insurance ($P < .001$), and tumor site ($P < .001$).

Based on the Kaplan-Meier method, the overall cumulative probability of starting CT at 1, 2, and 3 years after diagnosis was 50%, 54%, and 55%, respectively (Fig 1). In addition, 45% of patients started CT within the first 6 months. Significant differences were observed in the probability of initiating CT in relation to tumor site ($P < .0001$). The time at which 50% of the patients had begun CT after diagnosis was 9 months for liver cancer patients and 4 months for those with stomach cancer.

For CT users (n = 260), the overall cumulative probabilities of stopping CT at 1, 2, and 3 years after the initiation of CT were 43%, 60%, and 68%, respectively (Fig 2). In addition, significant differences were found in the probability of stopping CT in relation to tumor site ($P = .003$). The time at which 50% of users had stopped CT after beginning CT was 6 months for colorectal cancer patients, 21 months for liver cancer patients, and 24 months for those with stomach cancer.

Female sex and higher household income were significantly associated with an increased probability of commencing CT after cancer

Table 1. Distribution of Patients by Cancer Site

Variable	Colorectal (n = 219)		Stomach (n = 187)		Liver (n = 117)		All (n = 523)	
	No.	%	No.	%	No.	%	No.	%
Sex								
Male	133	60.7	116	62.0	89	76.1	338	64.6
Female	86	39.3	71	38.0	28	23.9	185	35.4
Age, years								
≤ 60	125	57.1	112	59.9	73	62.4	310	59.3
> 60	94	42.9	75	40.1	44	37.6	213	40.7
Education								
High school or less	162	74.0	157	84.0	98	83.8	417	79.7
Post-high school	57	26.0	30	16.0	19	16.2	106	20.3
Occupation								
No	69	31.5	36	19.3	17	14.5	122	23.3
Yes	150	68.5	151	80.8	100	85.5	401	76.7
Place of residence								
Metropolitan	85	38.8	60	32.1	45	38.5	190	36.3
Other	134	61.2	127	67.9	72	61.5	333	63.7
Household income, US $/month								
≤ 1,000	72	32.9	61	32.6	35	29.9	168	32.1
1,001-3,000	99	45.2	90	48.1	53	45.3	242	46.3
> 3,000	48	21.9	36	19.3	29	24.8	113	21.6
Private insurance								
No	136	62.1	101	54.0	73	62.4	310	59.3
Yes	83	37.9	86	46.0	44	37.6	213	40.7
Stage at diagnosis								
I	28	12.8	60	32.1	5	4.3	93	17.8
II	66	30.1	30	16.0	49	41.9	145	27.7
III	82	37.4	44	23.5	46	39.3	172	32.9
IV	43	19.6	53	28.3	17	14.5	113	21.6
Surgery*								
No	2	0.9	27	14.4	86	73.5	115	22.0
Yes†	217	99.1	160	85.6	31	26.5	408	78.0
Radiation therapy*								
No	154	70.3	185	98.9	101	86.3	440	84.1
Yes	65	29.7	2	1.1	16	13.7	83	15.9
Chemotherapy*								
No	28	12.8	49	26.2	109	93.2	186	35.6
Yes	191	87.2	138	73.8	8	6.8	337	64.4

*Time-constant covariate because this treatment was completed within 6 months after cancer diagnosis.
†Includes both palliative surgery and surgery for metastases.

diagnosis (Table 3). Compared with colorectal cancer, stomach and liver cancer were associated with an increased probability of commencing CT (for stomach cancer: hazard ratio [HR], 1.91; 95% CI, 1.41 to 2.60; for liver cancer: HR, 1.58; 95% CI, 1.01 to 2.46).

Stomach cancer patients were less likely to stop using CT compared with those with colorectal cancer (stomach cancer: HR, 0.49; 95% CI, 0.33 to 0.75; Table 4). Compared with stage IV cancer, stages I, II, and III at diagnosis were associated with a significantly reduced probability of discontinuing CT (stage I: HR, 0.49; 95% CI, 0.27 to 0.92; stage II: HR, 0.40; 95% CI, 0.24 to 0.66; stage III: HR, 0.58; 95% CI, 0.37 to 0.91).

DISCUSSION

In this longitudinal study of 523 cancer patients at the NCC of Korea, 50% commenced CT within the first year after cancer diagnosis. The cumulative probability of starting CT was 54% at 2 years and 55% at 3 years. Therefore, the start of CT was established mainly within the first year of diagnosis. Most previous studies, which had cross-sectional and retrospective designs, have estimated the prevalence of CT use,[5,6,8-10,17,20-22,38-40] but the results did not reveal the changing pattern of CT use over time.

Approximately 45% of patients started CT use within the first 6 months after diagnosis. Generally, during this time, most cancer patients receive intensive initial treatment. In fact, a total of 519 patients (99%) received initial treatment, such as surgery, chemotherapy, radiation therapy, or other therapy, in the first 6 months. A longitudinal study has reported that most patients start their use of CT during the 4 months after being informed of their cancer.[36] Moreover, a hospital-based study found that the majority of patients (70%) use CT within the first 3 months of diagnosis.[20] These results indicate that a combination of CT with conventional treatment during the initial treatment

Table 2. Baseline Characteristics by Initiation and Discontinuation of CT

Characteristic	Initiation of CT (n = 523)			Discontinuation of CT (n = 260)*		
	No.	%	*P*	No.	%	*P*
No. of patients	281			164		
Sex						
Male	173	51.2	.11	99	62.3	.73
Female	108	58.4		65	64.4	
Age, years						
≤ 60	183	59.0	< .001	104	61.5	.48
> 60	98	46.0		60	65.9	
Education						
High school or less	215	51.6	.05	129	64.2	.50
Post-high school	66	62.3		35	59.3	
Occupation						
No	58	47.5	.12	37	66.1	.60
Yes	223	55.6		127	62.3	
Place of residence						
Metropolitan	110	57.9	.15	65	62.5	.87
Other	171	51.4		99	63.5	
Household income, US $/month						
≤ 1,000	66	39.3	< .001	40	62.5	.44
1,001-3,000	136	56.2		73	59.8	
> 3,000	79	69.9		51	68.9	
Private insurance						
No	148	47.7	< .001	84	60.9	.43
Yes	133	62.4		80	65.6	
Diagnosis site						
Colorectal	95	43.4	< .001	65	72.2	.07
Stomach	115	61.5		59	56.2	
Liver	71	60.7		40	61.5	
Stage at diagnosis						
I	51	54.8	.43	24	53.3	.10
II	85	58.6		44	56.4	
III	90	52.3		58	69.1	
IV	55	48.7		38	71.7	
Surgery†						
No	67	58.3	.27	41	67.2	.44
Yes‡	214	52.5		123	61.8	
Radiation therapy†						
No	243	55.2	.11	143	63.6	.68
Yes	38	45.8		21	60.0	
Chemotherapy†						
No	108	58.1	.14	61	62.9	.96
Yes	173	51.3		103	63.2	

Abbreviation: CT, complementary therapy.
*Twenty-one patients were excluded because the period of using CT was not continuous.
†Time-constant covariate because this treatment was completed within 6 months after cancer diagnosis.
‡Includes both palliative surgery and surgery for metastases.

period is widespread among cancer patients. In fact, most previous studies have reported that more than 50% of CT users combined CT with conventional treatment.[5,8,17,18,20,21] Although several studies have shown that the concurrent use of CT may reduce adverse effects or enhance standard chemotherapy,[29,41] this is restricted to a few particular types of CT. Thus, the potential for harmful interaction and the underlying mistrust of CT still exist at the heart of orthodox medicine.[7,35,42-44] In addition, appropriately evaluating the outcome of conventional treatment is difficult in this case because a combination of CT and conventional therapy may affect health in general and influence responses to cancer treatment.

For a more useful approach to these problems, a need for greater patient-provider communication has been addressed.[13,17] Although we did not assess patient-provider communication, most studies have shown that a significant number of cancer patients use CT without discussing their plans with their oncologist,[8,11,45] which is similar to results published in Korea,[13,14] and that the main information sources on CT are the numerous health columns in the mass media and on the Internet, and family and close friends.[8,20] Furthermore, other studies have shown that doctor-patient relationships are worse among CT users than nonusers,[6,46] and CT users are less satisfied with conventional treatment.[47,48]

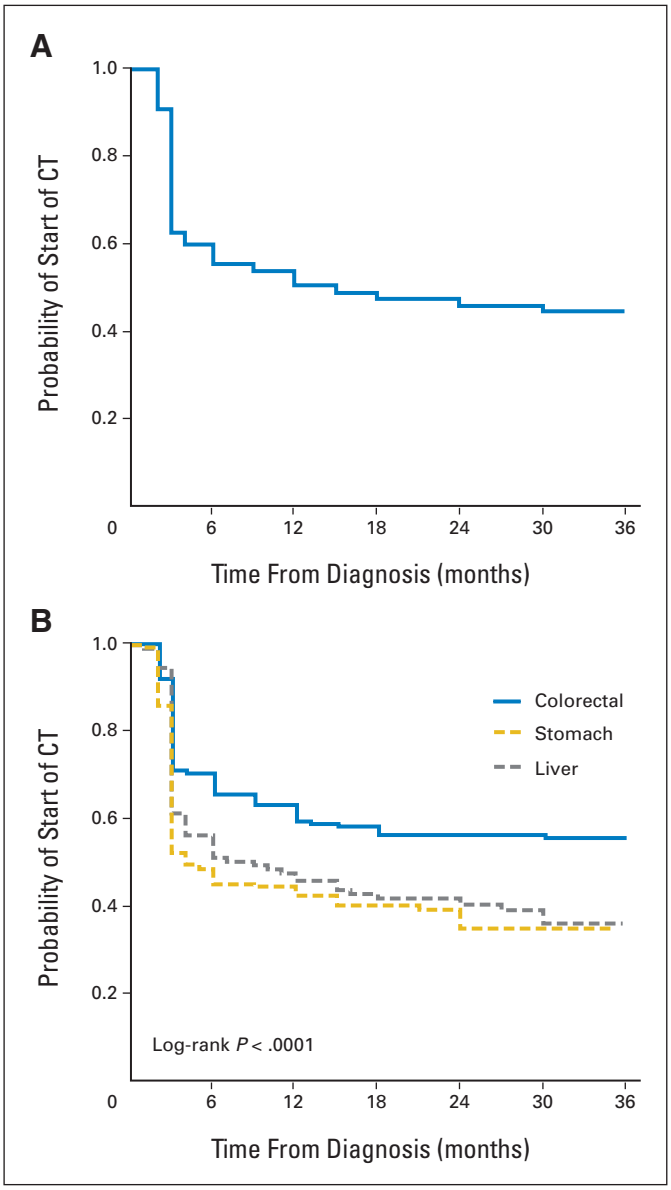

Fig 1. Kaplan-Meier curves for the probability of starting complementary therapy (CT).

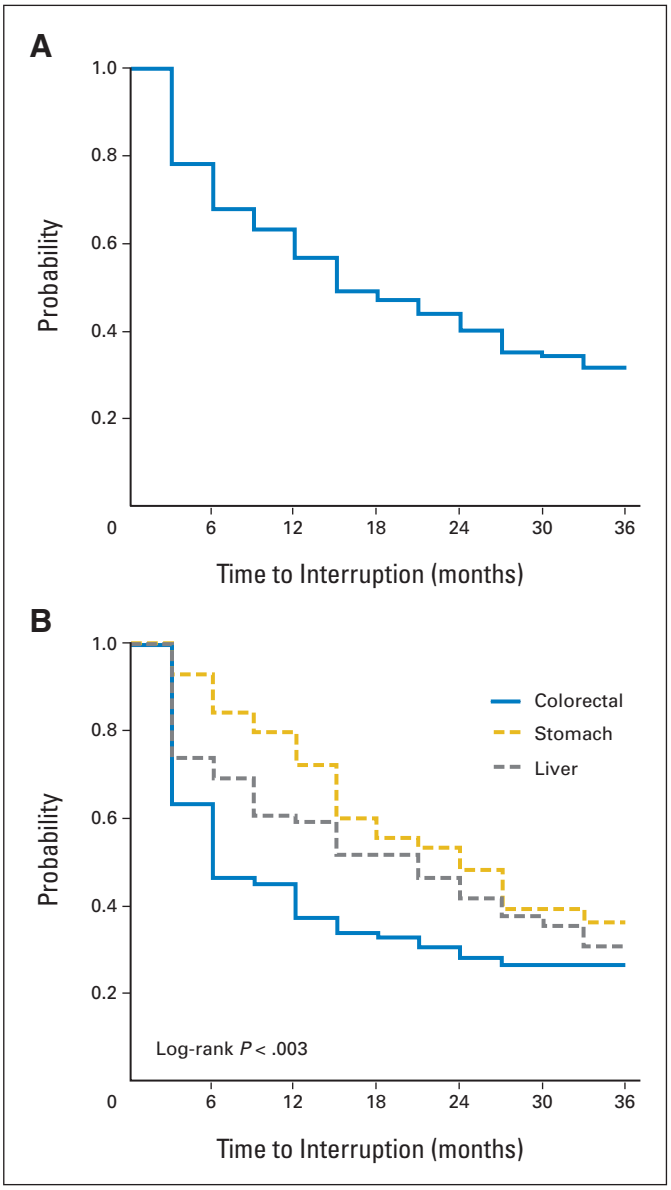

Fig 2. Kaplan-Meier curves for the probability of discontinuing complementary therapy (CT).

Accordingly, sufficient and honest discussion during the first 6 months may bring several benefits to both the patient and the physician. If necessary, patients with cancer can be referred to appropriate mental health therapists or a support group to deal with anxiety or depression, one of the causes of CT use.[15,16] In addition, physicians can assist patients to minimize adverse interactions with conventional treatment so that they can definitively evaluate the outcomes of conventional therapy for all cancer patients, particularly those participating in clinical trials.

In another aspect of patient-provider communication, physicians should systematically record and monitor information on CT use so that they can attempt to document observed effects. Given insufficient clinical research about the safety and efficacy of CT, well-maintained records may facilitate the conduct of a best-case series, which is often the first step in clinical research on the efficacy of a CT.[11] Oncologists should also arm themselves with more information on CT and monitor the medical literature for new reports about CT. Moreover, it is important for physicians to show an open and nonjudgmental attitude toward CT, which may avoid disrupting the patient-provider relationship and encourage compliance with conventional treatment.[9,49]

In the multivariate analysis, women were more likely than men to start CT use. According to previous studies, the effect of sex on CT use is controversial, with no association[8,47,50,51] or greater use by women.[1,6,9,14,17,20,48,52] To clarify the influence of sex on CT use, further studies that include psychological factors and use qualitative methodologies should be conducted. Higher economic status was also associated with the use of CT, which has been confirmed by other studies.[1,20,53] Because the volume of medical services provided at the initial treatment phase leads to high

Table 3. Cox Multiple Regression Model for the Initiation of CT

Variable	Adjusted HR	95% CI	Unadjusted HR	95% CI	*P*
Sex					
Male	1.00		1.00		
Female	1.30	1.01 to 1.68	1.19	0.94 to 1.51	.16
Age, years					
≤ 60	1.00		1.00		
> 60	1.01	0.74 to 1.38	0.75	0.59 to 0.96	.02
Education					
High school or less	1.00		1.00		
Post-high school	1.23	0.90 to 1.69	1.28	0.97 to 1.69	.08
Occupation					
No	1.00		1.00		
Yes	0.88	0.64 to 1.22	1.21	0.90 to 1.61	.21
Place of residence					
Metropolitan	1.00		1.00		
Other	0.81	0.64 to 1.04	0.84	0.66 to 1.06	.14
Private insurance					
No	1.00		1.00		
Yes	1.22	0.92 to 1.61	1.41	1.12 to 1.78	.004
Household income, US $/month					
≤ 1,000	1.00		1.00		
1,001-3,000	1.52	1.10 to 2.10	1.53	1.14 to 2.06	< .001
> 3,000	1.86	1.26 to 2.76	2.02	1.46 to 2.81	< .001
Diagnosis site					
Colorectal	1.00		1.00		
Stomach	1.91	1.41 to 2.60	1.71	1.30 to 2.24	< .001
Liver	1.58	1.01 to 2.46	1.51	1.11 to 2.06	.01
Stage at diagnosis					
I	0.85	0.54 to 1.33	1.05	0.72 to 1.54	.79
II	1.16	0.80 to 1.69	1.14	0.81 to 1.60	.45
III	1.03	0.72 to 1.47	1.02	0.73 to 1.43	.92
IV	1.00		1.00		
Surgery*					
No	1.00		1.00		
Yes	0.91	0.62 to 1.32	1.05	0.77 to 1.43	.76
Radiation therapy*					
No	1.00		1.00		
Yes	0.93	0.58 to 1.50	1.20	0.78 to 1.85	.40
Chemotherapy*					
No	1.00		1.00		
Yes	1.10	0.78 to 1.54	1.14	0.89 to 1.45	.30

Abbreviations: CT, complementary therapy; HR, hazard ratio.
*Time-dependent covariate.

medical expenditure, and health insurance does not generally cover the cost of CT, individuals with high income may be more likely to start CT. The stage at diagnosis was not associated with the likelihood of starting CT, which is consistent with results from previous studies.[9,17] Moreover, treatment-related variables defined as time-dependent covariates were not associated with the likelihood of starting CT.

The factors associated with the discontinuation of CT were the primary cancer site and tumor stage at diagnosis. Compared with advanced disease, patients with regional or local disease used CT for longer periods before discontinuation. Patients who were diagnosed with advanced-stage cancer might have a short survival time, and therefore they had less time to use CT than those with regional or local disease.

Patients with stomach or liver cancer used CT about four times longer than did those with colorectal cancer. Directly comparing these results with other studies is difficult because of differences in the study design, but an association between CT use and the primary cancer site can be explained in part by differences in the type of CT used.[8,9] Indeed, Patterson et al[9] reported that the disease site is associated with the use of dietary supplements, but not with mental or emotional therapies. We did not consider mental or spiritual practices, and except for acupuncture and moxibustion, most CT involved only the use of dietary supplements.

Another possible explanation for this result is the difference in adverse effects and complications caused by cancer. In particular, nutritional problems that impede oral intake, including anorexia, nausea, vomiting, diarrhea, constipation, mouth sores, trouble swallowing, and pain, are common in cancer patients.[54,55] However, some complications, such as weight loss or cachexia, commonly occur in patients with tumors of the upper gastrointestinal tract, but occur less often in patients with lower gastrointestinal cancer.[56,57] In fact,

Table 4. Cox Multiple Regression Model for the Discontinuation of CT

Variable	Adjusted HR	95% CI	*P*
Sex			
Male	1.00		
Female	1.10	0.80 to 1.52	.56
Age, years			
≤ 60	1.00		
> 60	1.31	0.95 to 1.82	.11
Diagnosis site			
Colorectal	1.00		
Stomach	0.49	0.33 to 0.75	.001
Liver	0.65	0.37 to 1.15	.14
Stage at diagnosis			
I	0.49	0.27 to 0.92	.03
II	0.40	0.24 to 0.66	< .001
III	0.58	0.37 to 0.91	.02
IV	1.00		
Surgery*			
No	1.00		
Yes	1.10	0.75 to 1.63	.63
Chemotherapy*			
No	1.00		
Yes	1.18	0.75 to 1.86	.48
Radiation therapy*			
No	1.00		
Yes	1.00	0.56 to 1.81	.99
Time to start of CT, months			
≤ 6	1.00		
> 6	1.26	0.76 to 2.09	.37

Abbreviations: CT, complementary therapy; HR, hazard ratio.
*Time-dependent covariate.

patients who are experiencing cancer-related symptoms are more likely to use CAM.[6,12]

The limitations of this study must be acknowledged. First, the sample was restricted to outpatients attending the NCC. These patients therefore may not be representative of the Korean population with cancer. Second, we examined only patients with colorectal, stomach, and liver cancer, so the results are not fully generalizable to all cancer patients. Finally, we did not ask the patients about why they started or discontinued CT. The CT use of cancer patients can be influenced by the patient's belief about CT or psychological factors, in addition to sex, type of cancer, and cancer stage, which we investigated. These reasons need to be investigated in further studies using various qualitative methodologies.

Based on the 3-year follow-up survey, our findings indicated that a significant number of cancer patients started to use CT during the intensive initial treatment period, which suggests that oncologists should initiate a discussion with their patients at this time. In addition, information on factors associated with the beginning and end of CT use could contribute to educating physicians about CT.

Despite advances in conventional medicine, interest in CT continues to grow at an exponential rate. Moreover, there is no definite evidence that the positive effects experienced by CT users are a result of the CT, and a great deal of scientifically untested information about CT is disseminated among cancer patients. Therefore, we recommend that future research should be conducted to assess associations between CT and quality of life, and interactions between CT and conventional treatment. Finally, a few oncologists have begun to incorporate CT into their medical practices, and numerous hospitals and medical centers have developed research and clinical service programs in CT.[1,11] In the future, these working relationships with CT practitioners should be maintained to allow the potential extension and enhancement of the quality of life of cancer patients.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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Manuscript writing: Sung-Gyeong Kim, Jae-Hyun Park
Final approval of manuscript: Jae-Hyun Park

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