

Original Articles

## Analysis of Survival in 273 Terminally Ill Cancer Patients Treated with Traditional Oriental Therapies

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**Objective :** Recently, an increasing portion of cancer patients use various therapies of complementary and alternative medicine (CAM) including traditional oriental medicine, which is believed to improve the consequence of cancer according to clinical experience and laboratory data. But the clinical-based systemic statistic validity of these therapies is lacking, so this study was aimed to validate the traditional oriental therapies (TOT) for terminally ill cancer patients.

**Patients and methods :** This retrospective study was performed on 273 patients who were diagnosed with terminally ill cancer in Korea and treated with TOT in the oriental hospital of Daejeon University, from March 1997 to June 2003. We examined the median duration of the terminal period and the correlations between 9 factors and survival of terminally ill cancer patients.

**Results :** During the study period, we could confirm 142 patients' death (52.01%) in 273 subjects. The median length of survival in terminally ill cancer patients was 16 weeks (95%CI 14.0~20.0) and 40.15% (95%CI 40.07~40.22) of patients had survived more than 24 weeks. According to Cox's proportional hazard model including gender, age, conventional therapies (chemotherapy, radiotherapy and surgery), performance status and clinical symptoms as independent variables, history of conventional therapies (RR 0.581, 95%CI 0.381~0.885), higher performance status (RR 1.855, 95%CI 1.454~2.366) and absence of ascites and pleural effusion (RR 1.631, 95%CI 1.047~2.538) showed independent prognostic value of survival.

**Conclusion :** Our findings suggest that TOT offer potential benefits for cancer patients at the terminal stage.

**Key Words:** Terminally ill cancer, Survival, Traditional oriental therapies (TOT)

### Introduction

The use of complementary and alternative medicine

(CAM) in the general population has grown considerably in recent years throughout the world. CAM is now a significant issue for those delivering cancer-patient care and management<sup>1-3)</sup>. As another conventional medicine in addition to the western medicine in Korea, traditional oriental therapies (TOT) provide elaborate and accountable theories backed by thousands of years of experience, abundant sources of herbal medicine and a variety of different clinical treatments, and exploring laboratory data to give positive views for

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the effects recently<sup>4-6</sup>. For this reason, the importance of TOT as a complement and alternative to western conventional therapy is now being acknowledged around the world.

At our hospital, we have incorporated our knowledge of TOT with western conventional methods of cancer treatment to complement each other's weaknesses mutually and also developed new cancer-fighting drugs independently. Since the establishment of the East-West Cancer Center, Daejeon Oriental Hospital, in 1991, we have been able to develop new drugs and research the mechanisms of TOT through the use of these advancements in cancer treatment. Various clinical trials and laboratory findings assured us to believe that TOT, provided to patients in the oriental hospital of Daejeon University, has significant positive effects on cancer-treatment<sup>4-12</sup>.

However, it is still needed to evaluate the effect of TOT on the basis of clinically based systemic and statistic validation with more intensive and careful procedures. The aim of this study was to examine the validity of TOT in the terminal period. In the present study, we investigated the median duration of the terminal period and the correlations between the clinical factors and the duration of survival in the terminally ill cancer patients treated with TOT.

## Patients and methods

This retrospective study was performed on 273 patients, who were diagnosed as having terminally ill cancer in Korea and treated in the Oriental Hospital of Daejeon University from March 1997 to June 2003. All the patients recruited for the study were terminally ill with solid and metastatic tumors, which were no longer treatable by specific antineoplastic therapies. For further information about the patients, we interviewed with surviving relatives by telephone, and we requested administrative help in order to get information about the date of death. We examined the relations of 9 factors with survival in patients with terminally ill cancer. It is not a common practice to perform routine blood tests on these patients unless indicated, so biochemical and molecular markers were excluded from this study.

### 1. Composition of traditional oriental therapies

TOT was defined as any treatment that had been used traditionally to treat cancer in Korea. TOT consists of well known and frequently used methods in Oriental Hospital of Daejeon University. The following methods were described in TOT: Use of oriental herbal products, acupuncture, meditation, controlled breathing therapy, herbal enema, physical exercise and diet treatment, etc.

**Table 1.** Grade of ECOG

Grade	Performance status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house chore, office work
2	Ambulatory and capable of selfcare but unable to carry out any work activities. 50% or more of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

**Table 2.** Grade of Pain

Grade	Pain status
0	none
1(mild)	Pain that can be relieved by drugs like aspirin, acetaminophen or an NSAID.
2(moderate)	Pain that can be relieved by drugs like codeine or pentazocine.
3(severe)	Pain that can be relieved by drugs like morphine or fentanyl.

**Table 3.** Demographic and Clinical Characteristics of 273 Evaluable Patients

Variable		No(%)
Sex	Male	177(64.84)
	Female	96(35.16)
Age	20~29	2(0.73)
	30~39	30(10.99)
	40~49	40(14.65)
	50~59	53(19.41)
	60~69	93(34.07)
	70~79	48(17.58)
	79~	7(2.56)
Primary Site	Lung	41(15.02)
	Stomach	74(27.11)
	Colon	30(10.99)
	Head & Neck	1(0.37)
	Pancreas	23(8.42)
	Uterine Cervix	5(1.83)
	Liver	60(21.98)
	Other	39(14.29)
	None	166(61.48)
Previous treatment	Conventional Tx*	104(38.52)

\*Conventional Tx : chemotherapy, radiotherapy, surgery

**Table 4.** Median Survival by Demographic and Clinical Characteristics of 273 Evaluable Patients

		Total	Death	Median (wk)	95% CI	p-value*
Sex	Male	177	100	15.0	[11.0, 18.0]	0.0773
	Female	96	42	24.0	[14.0, 86.0]	
Age	≤65	181	101	14.0	[11.0, 18.0]	0.0861
	>65	92	41	21.0	[15.0, 26.0]	
Previous treatment	Yes	104	48	19.0	[14.0, 56.0]	0.0505
	No	166	93	15.0	[11.0, 20.0]	
Anorexia	Yes	162	88	15.0	[11.0, 19.0]	<0.05
	No	61	32	20.0	[14.0, 87.0]	
Dyspnea	Yes	39	28	12.0	[10.0, 20.0]	NS
	No	178	86	18.0	[14.0, 26.0]	
Ascites or Pleural effusion	Yes	69	47	10.0	[ 7.0, 15.0]	<0.001
	No	153	70	21.0	[16.0, 41.0]	
Performance** (ECOG)	1	51	19	86.0	[22.0, 123.0]	<0.001
	2	99	60	16.0	[14.0, 19.0]	
	3	51	29	10.0	[7.0, 14.0]	
	4	16	10	6.0	[3.0, 10.0]	
	0	95	47	20.0	[14.0, 79.0]	
Severity	0	95	47	20.0	[14.0, 79.0]	NS
	1	70	43	16.0	[10.0, 24.0]	

of pain***	2	23	11	11.0	[8.0, 19.0]
	3	32	13	14.0	[ 8.0, 41.0]

\*Log-Rank test

\*\*The results of ECOG=0 is not reported because only 2 patients of 11 patients (in ECOG=0) failed

\*\*\*0-none, 1-mild, 2-moderate, 3-severe

**Table 5. Median Survival by Diagnoses of Cancer**

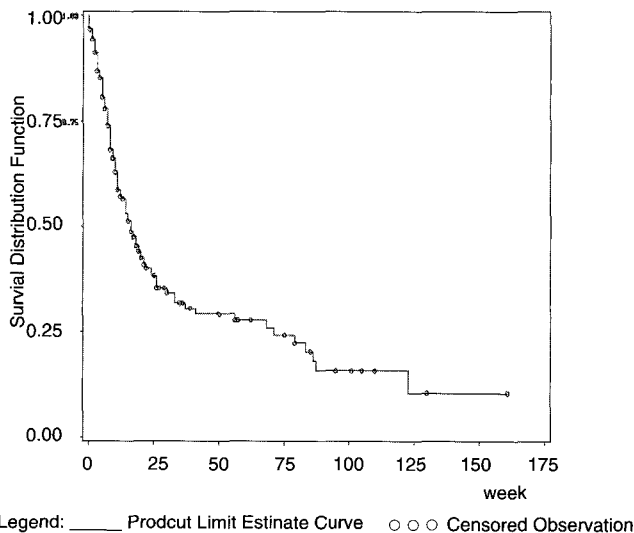
cancer site	Total	Death	Median (wk)	95% CI	p-value*
Lung	41	22	16.0	[10.0, 83.0]	0.1271
Stomach	74	38	14.0	[10.0, 18.0]	
Colon	30	10	22.0	[16.0, * ]	
Head & Neck	1	0	**	[ ** ]	
Pancreas	23	10	16.0	[11.0, 37.0]	
Uterine Cervix	5	1	**	[ ** ]	
Liver	60	40	12.0	[8.0, 15.0]	
Other	39	21	21.0	[14.0, 87.0]	

\*The result is not reported because only 10 patients out of 30 failed.

\*\*The result is not reported because the sample is too small.

**Table 6. Multivariate Analysis of Survival with Cox's Proportional Hazards Model**

	Multivariate		
	RR	95%CI	p-value
Age	0.778	[0.498, 1.216]	0.2706
Sex	0.779	[0.509, 1.191]	0.2489
Previous conventional treatment	0.581	[0.381, 0.885]	0.0115
Performance group	1.855	[1.454, 2.366]	<0.001
Anorexia	0.904	[0.548, 1.491]	0.6930
Dyspnea	1.149	[0.701, 1.884]	0.5806
Ascites and pleural effusion	1.631	[1.047, 2.538]	0.0304



**Fig. 1.** Survival curve of 273 terminally ill cancer patients

## 2. Statistical method

The survival in terminally ill cancer patients treated with TOT was estimated by the Kaplan-Meier method. To examine the association between the survival and the clinical factors in predicting survival; gender, age, history of conventional therapies (chemotherapy, radiotherapy and surgery), performance (Eastern Cooperative Oncology Group; ECOG status) and clinical symptoms (severity of pain, dyspnea, pleural effusion and ascites), we carried out univariate analysis using a log-rank test (Table 1-5). To investigate the adjusted effects of the factors with  $p$ -value $<0.1$  in the univariate analysis, multiple regression analysis was carried out using Cox proportional hazards models. For these analyses SAS V8.01 for windows (SAS Institute Inc., Cary, N.C., U.S.A) was used and statistical significance was decided by  $p$ -value $<0.05$ .

## Results

### 1. Demographic and clinical characteristics

During the study periods, we could confirm 142 patients' death (52.01%) in 273 subjects. The patients had a mean age of 58.3 (SD 12.9) years and 177 patients (64.84%) were men. 273 patients were stratified by diagnosis: 74 stomach, 60 liver and 139 patients with various other cancers. Of the 273 patients, 104 patients (38.52%) reported having a history of conventional therapies and 3 patients did not answer this question. In this study, breast cancer was excluded due to their expected survival was longer than others. In our opinion, the inclusion of patients with breast cancer might have yielded less valid results<sup>23</sup>. Table 3 shows demographic and clinical characteristics of the patients.

### 2. Analyses of association between survival and clinical factors

#### (1) Univariate analysis

The median duration of the terminal period was 16 weeks (95%CI 14.0~20.0) and 40.15% (95%CI 40.07~40.22) of patients survived more than 24 weeks. Median survival duration by demographic and clinical characteristics of 273 evaluable patients are shown in Table 4 and Fig. 1.

By univariate analysis of survival stratified for single clinical factors showed that anorexia ( $p<0.05$ ), ascites and pleural effusion ( $p<0.001$ ) and performance ( $p<0.001$ ) were predictor variables.

In the analysis of survival by cancer site, the survival of colon cancer (median survival 22 weeks) was longer than others (Table 5). However, this result and other parameters did not show significance in a statistically manner.

#### (2) Multivariate analysis

The univariate analysis of single parameters is not sufficient to clarify the true independent prognostic factors. Multiple regression using the Cox proportional hazards model is likely to be more accurate. With the clinical variables which are proved to be significant by the univariate analysis ( $p$ -value $<0.1$ ), multiple regression analysis was carried out.

According to Cox's proportional hazards model given gender, age, history of conventional therapies, performance status and clinical symptoms as variables, history of conventional therapies (RR 0.581, 95%CI 0.381~0.885), higher performance status (RR 1.855, 95%CI 1.454~2.366) and absence of ascites and pleural effusion (RR 1.631, 95%CI 1.047~2.538) showed independent prognostic value (Table 6).

## Discussion

Various factors in relation to survival of terminally ill cancer patients have been investigated more and more in the last two decades<sup>23-26</sup>. In our study, performance

status has been found to be the most strongly correlated variable with the duration of survival, followed by the 'terminal syndrome' which includes ascites and pleural effusion. According to Risberg and colleagues, the use of CAM seems to be related with shorter survival from cancer. The negative effect appeared predominantly in patients with good performance status<sup>27</sup>. Contrary to their observations, our results show that patients treated with TOT in a good functional status exhibited significantly longer survival times.

The history of conventional therapies seems to predict a longer survival from terminal cancer. The result implies that even if conventional therapies fails to reduce the tumor progression, these have positive effect on survival of cancer patients. We believe that TOT is effective in symptom control and in noninvasive palliation with minimal side effects thus improving patients' well-being and having positive synergistic effect of cancer medicine. The conventional western therapies in combination with TOT will be able to give balance to sophisticated cancer care technically<sup>28</sup>.

Opinions vary as to correlation between the survival and the site of cancer. According to Forster and Lynn, patients with pancreatic, prostate, brain, skin, and breast cancer had longer survival times, and patients with breast cancer survived the longest. It was for this reason that breast cancer was excluded in our study. Nevertheless, the survival of terminally ill cancer patients has no relevance to cancer site in general, as can be seen in the previous studies<sup>16, 22</sup>. Though our results show that the survival of colon cancer (median survival 22 weeks) was longer than others, this result did not show significance in a statistical manner as well.

It is interesting to note that the survival of elderly patients was longer than others (>65; median 21.0 95%CI 15.0~26.0, ≤65; median 14.0 95%CI 11.0~18.0). Generally, we expect that patients aged over 65 years would exhibit shorter survival times because of

debilitation and various complications. Although it has no significant impact statistically, this discrepancy could be explained that the use of TOT is more effective in elderly patients than in younger. We hope that other groups would perform further studies on the relationship between age and the use of TOT.

The clinical symptoms related with terminal syndrome have been investigated as factors capable of identifying survival of terminally ill cancer patients. Bruera and colleagues prospectively studied 47 terminally ill cancer patients admitted to an inpatient palliative care unit to determine whether specific clinical symptoms of functional status was associated with the length of survival. The combined presence of dysphagia, cognitive failure and weight loss was found to be highly correlated with a shorter survival (less than 4 weeks)<sup>29</sup>. In our study, the presence of ascites and pleural effusion was found to be correlated strongly with a shorter survival. Other variables, such as anorexia and severity of pain were not found to have a relationship to the length of survival.

Some previous studies have documented that the use of CAM does not influence observed survival among cancer patients. In fact, estimation of CAM's validity in terminally ill cancer patients is controversial. CAM is now a hot issue in cancer-patient care and management<sup>27, 30-33</sup>. In this study, to examine the validity of TOT in terminally ill cancer patients, we analysed survival by the Kaplan Meier method. In general, the median survival of most terminally ill cancer patients was less than 8 weeks and approximately 10% of patients survived more than 24 weeks<sup>15-17</sup>. In our survey, the median length of survival in terminally ill cancer patients treated with TOT was 16 weeks (95%CI 14.0~20.0) and 40.15% of patients survived more than 24 weeks.

The most commonly accepted definition of the 'terminal period' includes life expectancy of less than 6

months in recent decades. Many oncologists defined the onset of the terminal period as: "The moment in the natural history of the cancer in which there is little likelihood that specialized oncological treatment will extend survival time, induce an objective response, or halt the progress of the disease; continuous use of health resource is required to alleviate the patient's symptoms; and any treatment is administered solely for palliative purposes"<sup>14)</sup>.

Real survival time of many patients often come short of the date on which the patients would die. Because they enter palliative and hospice care so late in the course of their terminal illness. Doctors are inaccurate in their prognoses for terminally ill patients and make mistakes by being too optimistic. These phenomena may be adversely affecting the quality of care given to patients near the end of life<sup>34)</sup>. Timely and appropriate treatment for the dying person would provide the potential benefits such as; to participate directly in the process of recalling the past and planning for the future and to give the family the chance to relish or repair bonds with the dying person<sup>35)</sup>.

In comparing survival in our study with that in the other's, we observed that survival of TOT users is longer than that of the non-users. However, some *methodological limitations* of the study should be exhibited.

1) These results are out of place as for being generalized because the sample under investigation is too small, and results might apply only to Korea.

2) Terminally ill cancer patients in our study represent a heterogeneous group. Moreover, our study is a small one of retrospective series, thus making comparison across studies difficult. This study is needed for more accurate estimation of the duration of the terminal period treated with TOT compared with untreated control group. Despite the lack of accuracy, the value of the estimation of survival time after TOT

use can not be discounted, since it has a certain validity by itself.

Taken together, we suggest that TOT offers potential benefits (from an approach aimed at halting the progress of the disease and extending survival to palliative care) for patients with terminal cancer.

## References

1. Sibbritt D, Adams J, Easthope G, Young A. Complementary and alternative medicine (CAM) use among elderly Australian women who have cancer. *Support Care Cancer*. 2003;11:548-550.
2. Risberg T, Kaasa S, Wist E, Melsom H. Why are cancer patients using non-proven complementary therapies A cross-sectional multicentre study in Norway. *Eur J Cancer*. 1997;33:575-580.
3. Astin JA. Why patients use alternative medicine: results of a national study. *JAMA*. 1998;279: 1548-1553.
4. Choi WJ, Song KC, Choi BR, Lee YY, Seo SH, Yoo HW, Cho JH, Lee YW, Son CG, Cho CK. Study on the anti-angiogenic therapy to cancer disease with oriental medicine. *Korean J Orient Int Med*. 2001;22(4):639-645.
5. Yoo HS, Lee YY, Cho JH, Lee YW, Son CG, Cho CK, Hwang KJ. A study on recent tendency of anti-tumor herbal acupuncture. *KIHA*. 2001;4:23-37.
6. Lee YW, Son CG, Cho CK. A study on cancer therapy of activating blood circulation and congestion. *Proceeding of 2002 international symposium of Traditional Korean Med*. 2002: 109-115.
7. Son CG, Cho CK. Effect of hangambujeongtang on the reticuloendothelial system blocking by silica and the immune depression induced by 5-FU in mice. *The thesis collection of the 19th annual convention of Korean Orient Med*. 1997; 19:203-228.
8. Son CG, Han SH, Cho JH, Shin JW, Cho CH, Lee YW, Cho CK. Introduction of hemopoiesis by Saenghyuldan a mixture of Ginseng Radix, Paeoniae Radix Alba, and Hominis Placenta extracts. *Acta Pharmacol Sin*. 2003;24(2):120-126.
9. Seo SH, Son CK, Cho CK. Clinical study in 67 cases of

- hepatoma patients by Oriental medicine. *KJOMPP*. 2001;15(3):507-512.
10. Song KC, Choi BL, Lee YY, Yoo HS, Seo SH, Choi WJ, Cho JH, Lee YW, Son CK, Cho CK. The clinical study in 60 cases for breast cancer patients on the effects by Hangamadan. *Korean J. Orient. Int. Med*. 2001;22(4):669-674.
  11. Choi WJ, Son CG, Cho CK. The clinical report of PSM about 121 cancer patients. *KJOMPP*. 2001;15(2):361-366.
  12. Lee YY, Seo SH, Yoo HS, Choi WJ, Cho JH, Lee YW, Son CK, Cho CK. The clinical study in 83 cases for colorectal cancer patients on the effects by Hangamdan. *J. of Kor. Oriental Onco logy*. 2000;6(1):165-180.
  13. Berkman P, Heinik J, Michal R. Social worker estimations of life span in terminal cancer patients. *Arch. Gerontol. Geriatr*. 2001;33:227-235.
  14. Llobera J, Esteva M, Rifa J, Benito E, Terrasa J, Rojas C, Pons O, Catalan G, Avella A. Terminal cancer: duration and prediction of survival time. *Eur J Cancer*. 2000;36:2036-2043.
  15. Christakis NA, Escarce JJ. Survival of Medicare patients after enrollment in hospice programs. *N Engl J Med*. 1996;335:172-178.
  16. Yun YH, Heo DS, Bae JM, Im SA, Yoo TW, Huh BY, Kim NK. Retrospective cohort study of survival and prognostic factors in patients with terminal cancer. *J Korean Cancer Assoc* . 1998;30(2):384-393.
  17. Tamburini M, Brunelli C, Rosso S, Ventafriida V. Prognostic value of quality of life scores in terminal cancer patients. *J Pain Symptom Manage*. 1996;1:32-41.
  18. Yates JW, Chalmer B, McKegney FP. Evaluation of patients with advanced cancer using the Karnofsky performance status scale: an examination of its reliability and validity in a research setting. *Cancer*. 1980;45:2220-2224.
  19. Reuben D, Mor V, Hiris J. Clinical symptoms and length of survival in patients with terminal cancer. *Arch Intern Med*. 1988;148:1586-1591.
  20. Watson PG. The optimal functioning plan: a key element in cancer rehabilitation. *Cancer Nurs* . 1992;15:254-263.
  21. Maltoni M, Pirovano M, Nanni O, Marinari Mauro, Indelli M, Gramazio A, Terzoli E, Luzzani M, Marinis FD, Caraceni A, Labianca R. Biological indices predictive of survival in 519 Italian terminally ill cancer patients. *J Pain Symptom Manage*. 1997;13:1-9.
  22. Daas ND. Estimating length of survival in end-stage cancer: A review of the literature. *J Pain Symptom Manage*. 1995;10:548-555.
  23. Chow E, Harth T, Hruba G, Finkelstein J, Wu J, Danjoux C. How accurate are physicians' clinical predictions of survival and the available prognostic tools in estimating survival times in terminally ill cancer patients A systemic review. *J Clin Oncol*. 2001;13:209-218.
  24. Oxenham D, Cornbleet MA. Accuracy of prediction of survival by different professional groups in a hospice. *Palliat Med*. 1998;12:117-118.
  25. Viganò A, Dorgan M, Bruera E. The relative accuracy of the clinical estimation of the duration of life for patients with end of life cancer. *Cancer*. 1999;86:170-176.
  26. Maltoni M, Nanni O, Pirovano M. Successful validation of the patient' prognostic score in terminally ill cancer patients. Italian Multicentre Study Group on Palliative Care. *J Pain Symptom Manage*. 1999;17:240-247.
  27. Risberg T, Vickers A, Bremnes RM, Wist EA, Kaasa S, Cassileth BR. Dose use of alternative medicine predict survival from cancer *Eur J Cancer*. 2003;39:372-377.
  28. Cassileth BR. Alternative and complementary cancer treatments. *J. Oncol*. 1996;3:173-179.
  29. Bruera E, Miller MJ, Kuehn N, Maceachern T, Hanson J. Estimate of survival of patients admitted to a palliative care unit: a prospective study. *J Pain Symptom Manage*. 1992;7:82-86.
  30. Stoll BA. Can unorthodox cancer therapy improve quality of life *Ann Oncol*. 1993;4:121-123.
  31. Risberg T, Lund E, Wist E, Kaasa S, Wilsgaard T. Cancer patients use of nonproven therapy: a 5-year follow-up study. *J. Clin Oncol*. 1998; 16(1):6-12.
  32. Sollner W, Maislinger S, Devries A, Steixner E, Rumpold G, Lukas P. Use of complementary and alternative medicine by cancer patients is not associated with perceived distress or poor compliance with



- standard treatment but with active coping behavior. *Cancer*.2000;89:873-880.
33. Strenli RA. Use of alternative medicine by patients with cancer in a rural area of Switzerland. *SWISS MED WKLY*.2003;133: 233-240.
34. Christakis NA, Lamont EB. Extent and determinant of error in doctor' prognoses in terminally ill patients: prospective cohort study. *BMJ* 2000;320:469-473.
35. Smith JL. Commentary: Why do doctors overestimate *BMJ*. 2000;320:472-473.