Survival Prediction for Terminal Cancer Patients A preliminary Study

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Abstract

Background and purpose **: In order to provide appropriate care for terminal cancer patients, palliative care professionals require reliable prognostic criteria. The purpose of this study was to identify significant prognostic factors for survival in terminal cancer patients.**

Methods: Chart review was conducted for the 214 consecutive terminal cancer patients (108males, 106 females; age range: 8~97 years old) admitted to the palliative care unit at National Taiwan University Hospital between June 1995 and May 1996. Univariate log-rank test and multiple Cox regression analysis were used to examine the relationship among demographic data, initial symptoms/signs and the survival of patients.

Results: The median survival for all patients was 18 days. Significant predictors for survial were confusion (hazard ratio HR: 2.04, 95% CI: 1.36-3.05), anorexia (HR: 1.90, 95% CI: 1.30-2.77), dyspnea (HR: 1.74, 95% CI: 1.28-2.36), ascites (HR: 1.49, 95% CI: 1.08-2.07), ulcerated wounds (HR: 1.48, 95% CI: 1.01-2.17), and dysphagia (HR: 1.46, 95% CI: 1.01-2.15), which were independent of patient characteristics, primary cancer sites, and metastatic sites.

Conclusions **: A combination of initial symptoms/signs might be used for survival prediction in terminal cancer patients.**

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Key Words : prediction, survival, terminal cancer patients, palliative care

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Introduction

Several studies have shown that the survival predictions of physicians or nurses for terminal cancer patients may be often not accurate [1-4]. For palliative care professionals, reliable prognostic criteria to estimate the survival is not only helpful in answering the inquiry of patients and their families, but also useful in the following aspects: 1) for the decisions of appropriate management and vigorous planning of home care such as the appropriateness for a patient who has only days to live; 2) in distributing the palliative care to patients, the prediction of survival will be an important consideration or criteria in enrolling a patient into the palliative care program; 3) when allocating the health resources, predictions of survival could help us to assess the need of palliative services in the community [5-7].

The purpose of this study was to identify those factors predictive of a very poor prognosis and relevant in the planning of management and the preparation for death. Several studies have tried to develope a prognostic model to increase the accuracy of clinical estimate [8-12]. We also hope the findings in this study can be helpful to find a practical model useful to develop prognostic criteria for the terminal cancer patients in Taiwan.

Patients and Methods

Two hundred fourteen consecutive patients admitted to the palliative care unit at National Taiwan University Hospital between June 1995 and the end of May 1996 were enrolled in the study. The palliative care unit at National Taiwan University Hospital takes care of incurable cancer patients referred from other wards in the same hospital as well as from other hospitals or home. The admission is decided, through an initial assessment, according to the governmental regulations for hospice and palliative care. About 30 percent of admitted patients could be discharged with stable condition after intensive inpatient care. Considerable time is invested by members of the multidisciplinary team in restoring the best possible functional status and in planning the discharge for those patients considered to be possiblely discharged from the hospital.

Medical records of each patient were reviewed by experienced staffs, comprising physicians and senior nurses, who took care of the patients during the study period. All the data were analyzed and determined in the weekly team meeting, which helped to confirm the data as complete and correct as possible. The information collected in the study included: 1) demographic characteristics (gender, age, referral from hospital or home, primary cancer sites, metastatic sites), 2) initial symptoms on admission: pain, dyspnea, and other common symptoms. The study also assessed some common problems encountered in terminal care including ulcerated wounds, ascites, edema, pleural effusion (which, though basically signs, can be accompanied by symptoms). All the variables in the recording form were designed after a careful scrutiny of the literature by investigators. The recording form was tested for content validity with a panel and used pilotly for ten patients to confirm the ease of application.

Survival time was calculated from the date of admission to the date of death or from admission to the end of study period for those still alive. Fifteen patients who died within the first 24 hours were assigned a one-day survival time. Those patients who were still alive at the end of study period were treated as censoring data and also included into the following analyses. First, we examined the influence of the following factors on survival prediction in univariate analysis, which included: gender, age (<40; 40-64; 64+ years), referral from home or hospital, primary cancer sites, metastatic sites, and the initial symptoms, by using the log rank test. Then, the factors with significant effect on survival prediction in univariate analysis or the symptoms with p value less than 0.05 were used to enter the multivariate analysis. This study also examined the plot of ln-ln(S(t)), where the S(t) is the Kaplan-Meier estimate of the survival curves, against the logrithm of the time for each level of the factors in the study, suggested that the Cox regression model might serve for a parametric modeling of the data [13,14]. Hence the final model in the study was built using the Cox regression model fitted with the forward procedure. All the analyses were done using SPSS 8.0 statistical software.

Results

There were 214 consecutive patients admitted during this 12-month period. Thirty-five patients (16.4%) were still alive at the end of the study period and treated as censoring data. The median survival from the first admission was 18 days (range 1-216), which was similar to other palliative care units in Taiwan [15]. The characteristics of patients in the study and their corresponding survival data were showed in Table 1.

In univariate analysis of characteristics of patients, the survival was shorter for male (Hazard ratio: 1.45, 95% CI: 1.08-1.95) and for patients referred from hospital (Hazard ratio: 1.56, 95% CI: 1.07-2.28). There was no significant influence on the survival for the following factors: age, primary cancer sites, and metastatic sites. However, in comparing the survival among the three most common cancers furtherly (Table 2), a significant difference was observed between liver and lung (Hazard ratios: 1 vs 0.52, 95% CI: 0.30-0.89) as well as between liver and colorectal cancer (Hazard ratios: 1 vs 0.48, 95% CI: 0.27-0.86).

Weakness, pain and anorexia were the most common symptoms on admission. Table 3 showed that among the initial common symptoms, confusion, anorexia and dyspnea were the most significant factors ($p < 0.01$) for survival prediction; weakness, xerostomia, ascites, stomatitis, dysphagia and ulcerated wound carried weaker predictive significance (p value <0.05). In the final model only confusion (Hazard ratio: 2.04, 95% CI: 1.36-3.05), anorexia (Hazard ratio: 1.90, 95% CI: 1.30-2.77), dyspnea (Hazard ratio: 1.74, 95% CI: 1.28-2.36), ascites (Hazard ratio: 1.49, 95% CI: 1.08-2.07), ulcerated wounds (Hazard ratio: 1.48, 95% CI: 1.01-2.17), and dysphagia (Hazard ratio: 1.46, 95% CI: 1.01-2.15) were included, but sex and reference have been excluded after adjusting for the above symptoms. That is, only the symptom predictors were included in the final model (Table 4).

Discussion

Some studies have been conducted and several factors or indicators were examined to reduce prognostic uncertainty in terminally ill cancer patients. In a previous study,

Table 1. The survival and the hazard ratios by the characteristics of patients

Characteristic	No. of patients(%)	Median survival in days	Hazard ratios (95% CI)
All patients	214 (100.0)	18	
Sex			
Female	106 (49.5)	24	1.00
Male	108 (50.5)	13	1.45(1.08-1.95)*
Age in years			
<40	32 (14.9)	22	1.00
40-64	92 (43.0)	21	0.93(0.61-1.43)
≧65	90 (42.1)	16	0.98(0.64-1.50)
Referral places			
Home	45 (21.0)	24	1.00
Hospital	169 (79.0)	16	1.56(1.07-2.28)*
Metastatic sites #			
Bone	86 (40.2)	18	1.03(0.89-1.21)##
Lung	62 (29.0)	10	0.88(0.75-1.03)##
Liver	48 (22.4)	16	0.98(0.82-1.17)##
Brain	23 (10.7)	24	1.18(0.91-1.53)##

For those who had records on the chart

Hazard ratio compared with no corresponding metastasis

*P<0.05

CI: confidence interval

Table 2. Survival and hazard ratios of patients with liver, lung and colorectal cancer adjusted for sex and age

Primary cancer site	No. of patients (%)	Median survival in days	Hazard ratios (95% CI)
Liver	38 (17.8)	13	1
Lung	32 (15.0)	24	0.52(0.30-0.89)*
Colorectal	25 (11.7)	28	0.48(0.27-0.86)*
Breast	14 (6.5)	7	0.86(0.34-2.13)

*p<0.05

Table 3. Initial symptoms on admission and p value by univariate log-rank analysis

Symptoms on admission	No. of patients(%)	Median survival in days (yes/no)	Hazard ratios (95% CI)
Weakness	181(84.6)	16/31	1.59(1.03-2.50)*
Pain	172(80.4)	14/18	0.88(0.63-1.27)
Anorexia	159(74.3)	13/32	1.92(1.35-2.70)**
Weight loss	124(57.9)	17/19	1.14(0.84-1.54)
Constipation	101(47.2)	24/13	0.78(0.58-1.05)
Edema	90(42.1)	13/24	1.20(0.90-1.11)
Dyspnea	84(39.3)	8/24	1.56(1.16-2.13)**
Ascites	64(29.9)	10/24	1.45(1.05-2.00)*
Xerostomia	64(29.9)	17/19	1.39(1.01-1.91)*
Depression	58(27.1)	24/16	0.92(0.66-1.28)
Insomnia	58(27.1)	19/17	1.22(0.88-1.69)
Nausea/vomiting	50(23.4)	23/17	0.94(0.67-1.33)
Bleeding	45(21.0)	16/18	1.03(0.72-1.47)
Ulcerated wound	41(19.2)	9/22	1.39(1.05-2.00)*
Stomatitis	40(18.7)	12/20	1.47(1.02-2.12)*
Dysphagia	38(17.8)	12/19	1.56(1.08-2.27)*
Pleural effusion	38(17.8)	16/19	1.03(0.70-1.49)
Fever	37(17.3)	28/16	0.71(0.48-1.06)
Confusion	35(16.4)	7/23	2.27(1.54-3.33)**
Bowel obstruction	27(12.6)	24/17	1.15(0.75-1.75)
Hypercalcemia	18(8.4)	8/20	1.85(1.09-3.12)*
Dizziness	14(6.4)	13/19	1.37(0.79-2.38)

* P-value < 0.05 **P-value <0.01

Table 4. Significant predictors for the survival in the final model by using multiple Cox regression analysis.

	Hazard ratios(95% CI)	P-value
Confusion	2.04 (1.36-3.05)	< 0.001
Anorexia	1.90 (1.30-2.77)	< 0.001
Dyspnea	1.74 (1.28-2.36)	< 0.001
Ascites	1.49 (1.08-2.07)	0.015
Ulcerated wound	1.48 (1.01-2.17)	0.044
Dysphagia	1.46 (1.01-2.15)	0.049

the Karnofsky scale was found to predict survival more accurately than the physician's estimate [2]. The National Hospice Study found that in addition to performance status, assessment of clinical symptoms (shortness of breath, problem in eating, recent weight loss, and trouble swallowing) help to improve the ability to predict survival [8]. In the study of Bruera et al [9], the symptom combination (dysphagia, cognitive failure, and weight loss) was shown to be a useful predictive factor and better than clinical prediction of physicians. Hardy *et al* [10] found that dyspnea, decubitus ulcers, predicted outcome, interventions and a diagnosis of lung cancer were the most significant survival predictors. When symptoms alone were analyzed, they found dyspnea and immobility carried the highest relative risk of death. Rosenthal *et al* [11] studied the performance status as well as objective clinical data to predict survival of patients admitted to the hospice unit. Hypotension and hyperbilirubinemia were the most significant objective clinical data. The comparison and summary of the above studies was listed in Table 5.

This study reviewed the characteristics and initial symptoms of patients admitted over a 12-month period. Primary sites were generally thought to relate with the length of survival [10]. Although there was no significant difference in survival across primary cancer sites in this study, we found that patients with hepatocellular carcinoma had a shorter survival than lung cancer and colorectal cancer. This finding was different from previous studies by Hardy *et al* [10] and Allard *et al* [16] in which patients with lung cancer had a shorter survival than patients with other cancers. The reason of this difference might be caused from that, hepatocellular carcinoma is more prevalent in Taiwan; and the patients with hepatocelluar carcinoma were admitted to palliative care unit in a more terminal stage than lung cancer and colorectal cancer. The problem of late referral to hospice care was more common in patients with hepatocellular carcinoma, which may be due to some factors such as rapid progressive course, frequent use of alternative treatments,...etc [17,18]. Therefore, patients with different cancers may require in-hospital palliative care at different times when their cancers are considered to be

Table 5. Comparisons of results of previous studies

Authors	Patients and Methods	Median survival (days)	Significant survival predictors
Reuben DB	1592 cancer patients from National hospice study sample; accelerated time survival function model	35 days	performance status (Karnofsky Index), shortness of breath, problems of eating or anorexia, trouble swallowing, dry mouth and weight loss
Bruera E	61 cancer patients admitted to palliative care unit; univariate and logistic regression	28 days (mean)	dysphagia, cognitive failure and weight loss
Hardy JR	107 cancer patients admitted to hospital based palliative care unit; univariate log-rank test and Cox proportional hazard model	42 days	dyspnea, decubitus ulcers, predictive outcome, interventions and a diagnosis of lung cancer
Rosenthal MA	148 cancer patients admitted to two hospice units; ordinal regression analysis	14 days	performance status (ECOG), requirement for admission at first referral, elevated serum bilirubin and hypotension
Allard P	1081 cancer patients admitted for terminal care; univariate Kaplan-Meier analyses and multivariate time-dependent Cox regression analysis	11days	performance status (ECOG), sex, marital status and a diagnosis of lung cancer
Chuang RB	214 cancer patients admitted to palliative care unit; Cox proportinal hazard model	18 days	confusion, dyspnea, anorexia, ascites, dysphagia, and ulcerated wound

incurable. Such information could help us in allocating palliative care resources to the terminal cancer patients at the most appropriate place and time.

Among the common symptoms studied, we found that anorexia, confusion, dyspnea, ascites, dysphagia, and ulcerated wounds significantly predicted the survival in the univariate analysis. Confusion, anorexia, and dyspnea carried the most significant reduction of survival, however, ascites, dysphagia and ulcerated wounds carried borderline significance. These findings were similar to previous studies and

further confirmed that clinical symptoms in Taiwanese patients could help to predict survival independent of characteristics of patients such as: sex, age, primary cancer sites, referral places and the metastatic sites. The results also supported the concept of a "terminal cancer pathway" that spans across histologic tumor types and specific metastatic patterns [8, 19, 20].

Some clinical variables that may have prognostic importance in previous studies have been not included in our model, such as functional performance score or some measurable objective data. However, we found some difficulties to confirm the validity of recordings about the performance status in the process of chart review. It is a limitation in this study and further studies will be deserved to do. Functional performance score was found to have lower predictive power in a study population of shorter median survival (28±17 days) [9]. Our study population had even shorter median survival (18 days) and the majority of patients had severe health condition and very poor performance status. Some data from blood test might be the significant predictors, but ethically collecting these data in the very short survival time of the patients was very difficult. Another limitation is that the severity and persistence of symptoms have not been taken into analysis, which is due to inadequate case number for analysis in this study.

To develop a more applicable prognostic criteria of survival estimation for incurable cancer patients, further efforts should be invested in: 1) larger scale and multicenter studies to investigate other potential prognostic factors, such as interventions (chemotherapy or radiation therapy), objective measurable data and comorbid conditions [12]; 2) enrolling patients to the study at the time when palliative care, instead of curative treatment, become the main component of therapeutic plan. Thus, the survival prediction could actually be used in estimating the need of palliative care services, therefore allocating reasonable expenditure in palliative care and improving the quality of care for the end of life.

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【原　著】

緩和醫療病房癌末病人之存活預估－初步研究

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摘　要

爲了改善對癌末病人存活期預估之準確性，並提供末期病人妥適的醫療照顧，從事安寧緩和醫療的醫師需要較可靠的存活預估依據。本研究希望從病人之基本資料，癌症原發部位及轉移部位，入院之主要問題中，找出可供預估病人存活期之因子。本研究針對民國八十四年六月至民國八十五年五月間住院之癌末病人以病歷回顧方式進行研究。以單變數及多變數迴歸來檢驗各因子與存活期之關係。多變數迴歸之最後模式中顯示可供預估存活之因子爲呼吸困難、昏迷、厭食、吞嚥困難、腹水及潰瘍傷口。性別、年齡、癌症原發部位及轉移部位在此最後模式中顯示與癌末病人之存活期無明顯之關係。

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