Association of Depression and Survival in Patients with Cancer over 10 Years

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Purpose: This study was conducted to identify the effects of depression on the survival of patients with cancer over a 10 year period. **Methods:** A retrospective review was conducted to examine survival of 218 patients with stomach, colorectal and breast cancer, who had been treated for cancer from 2002 to 2011. Depression was assessed by using the Symptom Check List-90 Revision in 2002, and hope, fighting spirit and other potential confounders were also measured to control for their effects on the association between depression and the survival time. Data on survival were collected from the Statistics Korea and also from medical record in 2011. Kaplan-Meier survival analysis and Cox proportional hazard regression model were used to examine if depression affected survival. **Results:** The total number of death was 106, and the non-survivors scored higher on depression than survivors. Depression was found to be one of the influencing factors on survival from cancer. **Conclusion:** Depression was significantly associated with the increased risk of death in cancer patients. Further research is needed to identify in details which type of emotional interventions can extend the survival time of cancer patients in depression.

Key Words: *Neoplasms, Hope, Psychological Adjustment, Survival, Depression*

INTRODUCTION

Cancer is one of the leading causes of all deaths worldwide, and it accounted for approximately 28.2% of all deaths in Korea in 2013.[1] As of 2013 alone, the number of cancer patients was estimated at over 240,000, which has doubled in the past decade since 2003.[1] The predictors of death for patients with cancer were related to various factors such as tumor biology, cancer treatment. lifestyle factors, and depression.[2-5]

Patients with cancer experience a diversity of negative feelings caused by physical pain, frequent hospitalization and rehospitalization for treatment for cancer, financial burden of medical cost, feelings of hopelessness and isolation from normal social relationships, and fear of death.[6,7] Depression is one of the major complications of cancer.[8] As much as 38% of cancer patients showed major depressive disorders,[9] and the co-occurrence of cancer and depression had a double-faced relationship in the progression of cancer.[10,11]

There is mounting evidence that co-morbid depression predicts shorter survival in patients with cancer.[4,5] However, these studies were conducted in western countries,[12] there was no study with longitudinal data to identify effects of depression on survival of Korean patients with cancer who have different psychosocial responses about disease. In Korea, the 1st and 2nd ranking of cancer prevalence were stomach and colorectal cancer in male population and thyroid and breast cancer in female population.[13] Therefore, it needs to compare depression and survival in patients with the high prevalent cancers in Korea, excluding thyroid cancer, which is relatively mild. Through this study, we would provide useful data on the longitudinal effect of depression on prognosis in patients with stomach, colorectal, and breast cancer in Korea and on the importance of emotional intervention for those who are suffering from cancer-related depression. In addition, since psycho-social variables such as hope and fighting spirit contributed to decreasing depression and increasing survival in patients with cancer,[14,15] hope and fighting spirit were also included in the questionnaire to identify their confounding effects on the relationship between depressive symptoms and survival time.

In light of addressing this issue, this study was conducted to identify the effects of depression on cancer survival in patients with the three kinds of cancer, who underwent surgery in 2002 and had received followed-up care at a hospital in Korea since then.

METHOD

1. Study Design and Procedure

A retrospective review was conducted to examine survival of 218 patients with stomach, colorectal and breast cancer in this study. The patients had been treated for cancer from 2002 to 2011. The baseline survey of this study was performed in 2002. At that time, the study protocol adhered to the Declaration of Helsinki, and consent forms were collected from the patients. The data related to the metastasis of cancer were collected in 2003 from medical records (Three articles[16-18] based on this dataset have already been published somewhere else.). Finally, research assistant reviewed patients' hospital medical records to confirm death in 2011. If patients were not identified in the medical records, whether the death was confirmed by telephone surveys. The patients who didn't contact telephone were determined the death and survival time through linkage with mortality statistics at the Statistics Korea.

2. Participants

Participants in this study included patients who were diagnosed with, and had surgery for cancer of the stomach, colorectum, and breast from a cancer center at a university hospital in Korea. As many as 223 patients analyzed in the previous studies[16-18] were included in this study, but 5 patients were excluded from final analysis because the results of the death data of them were not found, totalling 218 participants for this study.

3. Study instruments

A questionnaire used in this study included demographic characteristics (age, gender, education, and occupation), clinical characteristics (type and stage of cancer at diagnosis, recurrence of cancer, tumor size, and adjuvant therapy), and psycho-spiritual variables (hope, fighting spirit and depression). The explanation of the instrument for depression, hope and fighting spirit was in the previous study.[16] Only whether the death and survival time were included in this study.

4. Data analysis

Using PAWS 20.0 program (SPSS INC., Chicago, IL, USA), data were analyzed by descriptive statistics, χ^2-test, and independent t-test to compare demographic and clinical characteristics with depression between survivors and non-survivors of cancer. Kaplan-Meier survival analysis was used to compare survival for more depressed and less depressed patients who were stratified according to the mean depression score in the SCL-90R. The associations of the independent variables, including age, gender, cancer types, stage at diagnosis, tumor size, cancer recurrence or metastasis, adjuvant therapies, fighting spirit, hope, and depression, with the dependent variable of cancer survival were analyzed using the Cox proportional hazard regression model to assess the influential power of depression on cancer survival.

RESULTS

1. Demographic, clinical and psychosocial characteristics

Table 1 shows the demographic, clinical and psycho-social characteristics. Of 218 participants in this study, 48.6% (n = 106) had died during the period of 10 years between 2002 and 2011. The characteristics of non-survivors of cancer differed significantly from those of survivors in the following respects: They were less employed (χ^2 = 15.15, $p < .001$), were at more advanced stages of cancer (χ^2 = 32.14, $p < .001$), showed more recurrence or metastasis of cancer before and after the survey (χ^2 = 32.15, $p < .001$; χ^2 = 60.71, $p < .001$), took less adjuvant chemotherapies (χ^2 = 10.27, $p = .001$), and scored higher on depression (t = -2.77, $p < .006$) than survivors. On the other hand, there were no significant differences in age, gender, education, types of cancer, tumor size, the score of hope and fighting spirit between survivors and non-survivors from cancer (all $p > .005$). The mean length of cancer survival was 35.4 (SD = 28.8) months for non-survivors from the time of conducting this survey (Table1).

2. Influence of Depression on survival in patients with cancer

Table 2 presents the result of cox proportional hazard regression analysis. The results showed that gender, age, and cancer type did not affect on survival. However, the mortality in patients at stage 4, patients who had the recurrence or metastasis, and patients who had taken adjuvant therapies were higher than those who did not.

The participants who scored higher on depression (HR 1.03, 95% CI = 1.01~1.06, $p = .008$) appeared to have 1.03 times higher mortality than their counterparts controlling covariates (Table2).

Kaplan-Meier analysis revealed that time to death was longer in pa-

Table 1. Demographic, Clinical and Psychological Characteristics   (N = 218)

Characteristics	Categories	Total n	Survivors (n = 112) n (%)	Non-survivors (n = 106) n (%)	χ^2	p
Gender	Male	89	47 (42.0)	42 (39.6)	0.12	.725
	Female	129	65 (58.0)	64 (60.4)		
Age (at the time of survey)	20~39	38	19 (17.0)	19 (17.9)	2.53	.282
	40~59	110	62 (55.4)	48 (45.3)		
	≥60	70	31 (27.6)	39 (36.8)		
Education	≤High school	132	64 (59.8)	68 (65.4)	1.22	.543
	College graduate	63	33 (30.8)	30 (28.8)		
	≥Graduate	16	10 (9.4)	6 (5.8)		
Present occupation	No	146	62 (58.5)	84 (83.2)	15.15	<.001
	Yes	61	44 (41.5)	17 (16.8)		
Type of cancer	Stomach	65	33 (29.5)	32 (30.2)	0.38	.945
	Colorectum	83	41 (36.6)	42 (39.6)		
	Breast	70	38 (33.9)	32 (30.2)		
Stage	1	9	4 (3.6)	5 (4.7)	32.14	<.001
	2	74	56 (50.5)	18 (17.0)		
	3	101	44 (39.6)	57 (53.8)		
	4	33	7 (6.3)	26 (24.5)		
Tumor size	≤4 cm	100	60 (53.6)	40 (37.7)	2.02	.155
	≥4.1 cm	100	50 (44.6)	50 (47.2)		
	Unknown	18	2 (1.8)	16 (15.1)		
Adjunctive chemotherapy	No	32	8 (7.2)	24 (22.6)	10.27	.001
	Yes	185	103 (92.8)	82 (77.4)		
Recurrence or metastasis (before survey)	No	179	108 (96.4)	71 (67.0)	32.15	<.001
	Yes	39	4 (3.6)	35 (33.0)		
Recurrence or metastasis (after survey)	No	130	95 (84.8)	35 (33.0)	60.71	<.001
	Yes	88	17 (15.2)	71 (67.0)		
Hope (M±SD)			16.8±4.05	17.3±4.18	0.92	.359
Fighting spirit (M±SD)			48.8±5.17	48.0±5.50	-1.22	.224
Depression (M±SD)			15.4±9.04	18.9±9.52	-2.77	.006
Survival time (M±SD)			-	35.4±28.8		

Table 2. Cox Regression Analysis on Survival in Patients with Cancer over 10 Years

Variable	Categories	HR	95.0% CI	p
Gender		0.91	0.56~1.49	.713
Age (year)	20~39	1.00		
	40~59	0.73	0.41~1.33	.311
	≥60	1.18	0.60~2.31	.631
Diagnosis	Colorectal Ca	1.00		
	Gastric Ca	0.87	0.49~1.57	.648
	Breast Ca	1.07	0.51~2.28	.853
Stage	1	1.00		
	2	0.97	0.24~3.89	.960
	3	2.86	0.80~10.20	.105
	4	6.74	1.71~26.50	.006
Recurrence or metastasis (before survey)		3.71	2.22~6.20	<.001
Recurrence or metastasis (after survey)		3.28	2.01~5.38	<.001
Tumor size		0.96	0.86~1.06	.369
Adjuvant therapy (yes)		1.44	1.01~2.05	.046
Fighting Spirit (low)		1.36	0.87~2.13	.180
Hope (low)		1.44	0.94~2.21	.098
Depression		1.03	1.01~1.06	.008

CI=Confidence interval.

tients with low depression score (log rank test: $\chi^2 = 9.24$, $p = .002$). The survival curve, depicted according to the levels of depression, displayed that 82 (75.2%) out of 109 participants who scored low on depression survived from cancer at the time of 40 months after the study, and 66 (60.6%) of 109 participants at 111 months, while 63 (57.8%) of 109 participants who scored high on depression survived from cancer at the time of 40 months, and 47 (43.1%) of 109 participants at 111 months, indicating that patients with the high level of depression were less likely to survive from cancer (Fig. 1).

DISCUSSION

This study was conducted to assess a longitudinal effect of depression on survival in patients with cancer over the period of 10 years, controlling for other confounding factors. The participants in this study included 218 patients diagnosed with cancer of the stomach, colorectal, and breast, who took part in the baseline study conducted in 2002. After 10 years, approx-
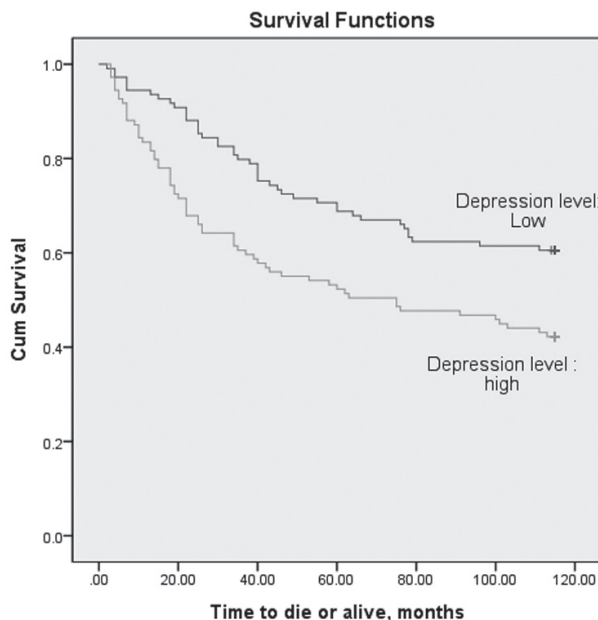
Fig. 1. Kaplan-Meier Pots of Survival in Patients with Cancer by Severity of Depression

imately half of the patients, or 51.4% of them, survived from cancer.

As a result, depression appeared to affect survival from cancer after other confounding variables were controlled. The reason why the psychospiritual variables controlled was that fighting spirit was most commonly used adjustment response,[15] and hope was related to decrease in depression[19] when people were suffering from loss and uncertainty.

Depression has been known as one of the most devastating mental problems in cancer patients, which not only contributes to the progression of cancer to a more advanced stage, but also makes the disease condition worsened directly or indirectly.[12] When other variables were controlled, the patients at stage 4 cancer, those having cancer recurred or metastatic, and those with a high level of depression had shorter survival from cancer. This result was supported by other studies, showing that as the course of the disease in cancer patients progressed to a more advanced stage, the consequences of chronic stress caused by prolonged physical ailments and pain contributed to the physiological change in the immune system, which, in turn, increased the negative psychological state such as depression.[9] This study result could also be elucidated in the same context with another study,[20] showing that the more advanced the stages of breast cancer and the longer the period of depression, the higher the mortality rate for breast cancer.

However, though depression affected mortality, the hazard ratio of mortality in this study showed very low (HR = 1.03), compared to other study.[20] Mol et al's study[21] used only 7 items of the Hospital Anxiety and Depression Scale to measure depression. Although the hazard ratio of mortality was 2.07 in their study when they entered depression as a dichotomous variable in analysis, such as those who were diagnosed as being depressed or not, the hazard ratio of mortality was 1.12 when they entered depression as a continuous variable into analysis, which is consistent with the result of this study.

In this study, the differences between the survival rates and the levels of depression (low versus high) were estimated about 17% from the time of 30 months since the diagnosis of cancer. Patients with cancer suffer from a wide range of physical and psychological symptoms. Since depression occurs in association with the co-existing symptoms of fatigue, weakness, and pain,[22] it is important for nurses to provide care for relieving depression to control these kind of symptom clusters. Accordingly, there must be preventive measures that should be taken into consideration by health care providers to assess the intensity of depression and to prevent depression from being exacerbated. Depression in cancer patients was caused either by physical conditions[7,23,24] or behavioral patterns related to non-compliance with treatment regimens for cancer,[25,26] both of which led to more depression and more serious progression of cancer. Therefore, there must be an educational approach to stop the vicious circle among physical conditions, behavioral non-compliance, and depression,[7] and enhance motivation of patients with cancer for treatment regimens by improving a therapeutic relationship with health care providers more effectively.[27]

For cancer patients, cancer can be taken as a matter of life and death, but a more important issue remains how to best maintain quality of life as long as they struggle against the life-threatening disease. Therefore, based on the result[28] that a sense of self-esteem and a feeling of hope acted as mediating factors to decrease depression, educational programs that can improve positive and healthy emotional feelings of their own worths as well as hope for best should be developed with an urgent priority. In addition, a periodic assessment of emotional state in cancer patients is needed to detect psycho-social risk factors such as fighting spirit and hope for depression as early as possible.

The limitations of this study were as follows: First, in as much as any studies on human psychology suggesting statistical limitations,[29] this study carefully attempted to control some biological and psychosocial variables for analyzing cancer survival, but not all the potential confounders, which may affect the study results. Therefore, the findings of this study need to be carefully interpreted, because the study results may show a general direction of the association between depressive symp-

toms and the survival time for the study patients. It can also be argued that the death observed in this study occurred by any other possible causes of death, not just by cancer, although such possibility is rare, in that all the study patients have been observed through the hospital record systems. Thus the generalizability of the study results may be limited to a certain degree. Nonetheless, through this study with a longitudinal review, the effect of depression on the cancer patients came to appear as significant and continuous as to lessen their survival time. It is our understanding that this study has also contributed to providing a better understanding of the importance of continuous follow-up care for chronically ill patients with cancer.

CONCLUSION

Depression was found to be related to the shorter duration of survival after demographic, disease-related, and psychological variables were controlled. Based on these findings, this study suggests more comprehensive long-term follow-up care and interventions tailored for the particular needs of cancer patients to sustain and improve psychological strength and survival, rather than merely treating and caring physical symptoms. Periodic monitoring of any changes in emotional status and depressive symptoms on a regular basis may be of practical significance and high priority for the quality of life and survival of all the patients suffering from various types of cancer. Finally, the examination of the effects of other psychospiritual factors such as fighting spirit and hope on the survival of cancer patients may be needed in other studies related to cancer in more details. That examination will help to diversify the intervention strategies for cancer patients to prolong their survival time.

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