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Report

Patients' understanding of their own disease and survival potential in patients with metastatic breast cancer

Hitoshi Okamura[1], Noboru Yamamoto[2], Toru Watanabe[2], Noriyuki Katsumata[2], Shigemitsu Takashima[3], Isamu Adachi[2], Akira Kugaya[1], Tatsuo Akechi[4], and Yosuke Uchitomi[1]
[1]*Psycho-Oncology Division, National Cancer Center Research Institute East;* [2]*Department of Medical Oncology, National Cancer Center Hospital;* [3]*Department of Surgery, National Shikoku Cancer Center Hospital; Chairman of the Breast Cancer Study Group of the Japan Clinical Oncology Group (JCOG);* [4]*Psychiatry Division, National Cancer Center Hospital*

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Summary

Purpose: To investigate the effect of understanding their own disease by patients with metastatic breast cancer on their survival potential after being informed by their physician.

Patients and methods: Two hundred and fourteen women with metastatic breast cancer who participated in a multi-institutional, randomized phase III trial (Japan Clinical Oncology Group (JCOG) Study 8808) were asked whether they understood their own disease after being given information about the clinical trial. They were classified into two groups on the basis of whether they understood or not. We estimated their survival after the time of registration and derived relative hazard ratios from Cox's proportional hazards model.

Results: There were 190 patients in the 'better understanding' group and 24 in the 'poor understanding' group. Median survival times after registration were 28.3 and 16.1 months, respectively. The 'better understanding' group showed a significant difference from the 'poor understanding' group ($p = 0.016$). In multivariate regression analysis, patients who did not understand still showed poorer survival than those who understood (hazard ratio $= 2.09$; 95% confidence interval (CI) 1.16–3.78; $p = 0.014$).

Conclusion: These results support the supposition that patients' understanding of information about their disease may influence their survival. Thus, it is important to evaluate patients' recognition about information even after obtaining their consent. However, further investigation is needed to clarify the exact nature of this relationship.

Introduction

Why is informed consent important for cancer patients? It has been emphasized that all cancer research demands fully informed consent from all patients [1–3], but an explicit answer to this question has not yet been provided. In randomized clinical trials, patients should know about the potential randomization, all the treatment options, and their own disease through the information they are given. However, some reports show that patients are not always given full information [4] and that they do not always give their consent after they have understood the information [5].

Psycho-oncology research has shown that some psychosocial and behavioral factors such as social support [6], coping strategies [7], and psychiatric group interventions [8, 9] can contribute to cancer patients' quality of life or length of survival. Social or emotional support is thought to promote biological or behavioral adaptation in the face of stress [10] and result in better compliance with treatment [11]. Richardson et al. [12] found that improving patient compliance with treatment was associated with significant prolongation of patient survival. Furthermore, support from the physician is reported to be the most important source of support [13] and a significant predictor of

coping response [14]. This means that support from the physician help patients cope better with cancer [15]. Better support from the physician leads to an attitude of fighting spirit in patients [7, 16] or active behavioral coping [9], which is associated with better survival. Psychiatric interventions are suggested to foster improved health habits such as better nutrition and exercise regimens, and enhance effective and active behavioral coping, resulting in improved physician–patient relationships, positive mental attitudes, and greater compliance with treatment [12]. However, no published data are available concerning the relationship between informed consent and quality of life or length of survival.

In this study, we tried to answer the initial question from the viewpoint of psycho-oncology. We used data from a multi-institutional, prospective, randomized phase III trial conducted by the Japan cooperative oncology group (JCOG). Our objective was to investigate the effect of patients' understanding of their disease on their survival after being informed by their physician. All the patients had metastatic breast cancer and participated in the clinical trial.

Patients and methods

Women with metastatic breast cancer who participated in a multi-institutional, randomized clinical trial (JCOG study 8808) were studied. This trial consisted of two therapy regimens to allow comparison of hormonal agents: ACT (doxorubicin, cyclophosphamide, tamoxifen) and ACM (doxorubicin, cyclophosphamide, medroxyprogesterone) [17]. Patients were randomly assigned to receive either of the regimens, and were recruited between December 1988 and December 1991; 218 patients agreed to participate. Patients with severe mental disorders or cognitive impairment were excluded.

Before the initial treatment, the patients were asked in writing 'To what extent do you understand your own disease after being informed by your physician during the explanation of the clinical trial?' Two hundred and fourteen women (98.2%) replied. Responses were graded 1 (understand well), 2 (understand to some extent), 3 (understand only a little), 4 (do not understand well), or 5 (do not understand at all). After the first cycle of treatment, we asked the question again.

For all patients, with permission of the JCOG data center, we gathered data from case report forms on age, marital status, Eastern Cooperative Oncology Group performance status (PS), menopausal status, disease-free interval (DFI), assigned therapy, recurrent or advanced disease, estrogen receptors (ER) and progesterone receptors (PgR), axillary nodal status, history of adjuvant therapy, sites and number of metastases, blood counts, biochemical data, and serum tumor markers. Age, marital status, PS, and menopausal status were determined at the time of registration. ER, PgR, and axillary nodal status were determined at the time of primary diagnosis. Mean patient age at registration was 54.5 years (SD 9.7; range 24–72). We estimated the duration of survival from the time of registration to either death or the date of the last follow-up.

Statistical analysis

The chi-square test, Fisher's exact probability test, or *t*-test was used for comparing the characteristics of patients and tumors. Survival rates were calculated using the Kaplan–Meier method [18]. All deaths were counted, regardless of their cause. Each patient was considered alive at the time of her last evaluation unless death had been documented. The stratified log-rank test was used for comparison of survival curves, and censored data were taken into account [19]. Both univariate and multivariate analyses were used for the analysis of potential prognostic factors. All factors other than age were dichotomized and coded as 0 (reference level) or 1. Age was evaluated as a continuous variable. For determination of the most significant variables contributing to survival, the Cox proportional hazards model was applied [20]. Differences with a P value of less than 0.05 were considered significant. All P values were two-sided. Analyses of prognostic factors in this patient population are reported in detail elsewhere [21]. All data analyses used SPSS Version 6.1 statistical software (SPSS Inc., Chicago, IL, USA).

Results

Patients' classification and characteristics

Ninety-five patients (44.4%) understood well, 95 understood to some extent, 18 (8.4%) understood only a little, 3 (1.4%) did not understand well, and 3 did not understand at all. Their median survival times were 28.3, 28.5, 20.9, 10.5 and 10.0 months, respectively. From this result, we thought it was appropriate to

Table 1. Distribution of selected characteristics in patients among 'better understanding' group and 'poor understanding' group

	'Better understanding' group ($N = 190$)	'Poor understanding' group ($N = 24$)	P value*
Age (years)			
Mean (SD)	54.2 (9.8)	57.4 (9.1)	0.12
Range (SD)	24–72	36–72	
Marital status			
Unmarried	19 (24%)	2 (24%)	0.79
Married	60 (76%)	5 (76%)	
Unknown	111	17	
Performance status			
2–4	43 (23%)	6 (25%)	0.79
0 or 1	147 (77%)	18 (75%)	
Menopausal status			
Pre-	57 (30%)	6 (25%)	0.31
Post-	133 (70%)	18 (75%)	
Therapy regimen			
ACT	96 (51%)	13 (54%)	0.61
ACM	94 (49%)	11 (46%)	
Estrogen-receptor status			
Negative	52 (51%)	6 (55%)	0.82
Positive	50 (49%)	5 (45%)	
Unknown	88	13	
Progesterone-receptor status			
Negative	43 (61%)	8 (89%)	0.10
Positive	28 (39%)	1 (11%)	
Unknown	119	15	
Axillary lymph node status			
$\geqq 10$	30 (19%)	4 (17%)	0.88
<10	130 (81%)	19 (83%)	
Unknown	30	1	
Disease status			
Advanced disease	43 (23%)	3 (13%)	0.25
Recurrent disease	147 (77%)	21 (87%)	
Adjuvant chemotherapy			
Received	110 (58%)	13 (54%)	0.73
Not received	80 (42%)	11 (46%)	
Number of metastatic sites			
$\geqq 2$	83 (44%)	10 (42%)	0.85
1	107 (56%)	14 (58%)	
Disease-free interval (months)			
<24	73 (38%)	12 (50%)	0.35
$\geqq 24$	117 (62%)	12 (50%)	

*Chi-square test, Fisher's exact probability test, or t-test (age).

Table 2. Comparison os survival classified into two groups according to their understanding of their disease: 'better understanding group' and 'poor understanding group'

Group	Patients No. (%)	MST (months)	95% confidence interval	*P* value*	Survival rate (%) 1-year	2-year	5-year
Better understanding	190 (88.8)	28.3	22.3–34.3		81	55	23
Poor understanding	23 (11.2)	16.1	9.1–24.0	0.0016	71	33	8

Abbreviation: MST, median survival time.
*Log-rank test.

consider patients in the first two groups together, and compare them with the patients in the last three groups combined. Therefore, 190 patients (89%) formed the 'better understanding' group and 24 patients (11%) formed the 'poor understanding' group.

Table 1 summarizes the characteristics of patients and tumors. There were no significant differences in any factors between the two groups. At the time of analysis, the median follow-up time was 25.5 months (range 0.9–97.1). For the 30 censored patients still alive, the median follow-up time was 79.9 months (range 61.4–97.1).

Follow-up data regarding patients' understanding

When the question was repeated after the first cycle of treatment, only 10 patients (4.6%) gave answers that were different to those before treatment: four from poor understanding to better understanding, and six from better understanding to poor understanding.

Comparison of survival between the two groups

Table 2 lists survival rates from 1 to 5 years and the median survival times. The median survival times were 28.3 months for the 'better understanding' group (95% CI 22.3–34.3), and 16.1 months for the 'poor understanding' group (95% CI, 8.1–24.0). The 'poor understanding' group also showed a significantly different overall survival from the 'better understanding' group ($p = 0.016$) (Figure 1).

Univariate and multivariate analyses

Univariate analysis of pretreatment characteristics of patients and tumors revealed significant prognostic influences for DFI ($p < 0.01$), PS ($p < 0.01$), distant lymph nodes metastasis ($p = 0.032$), liver metastasis ($p < 0.01$), number of metastatic sites ($p = 0.029$), hemoglobin (Hb) ($p = 0.025$), serum lactic dehydrogenase (LDH) ($p < 0.01$), serum total protein (TP)

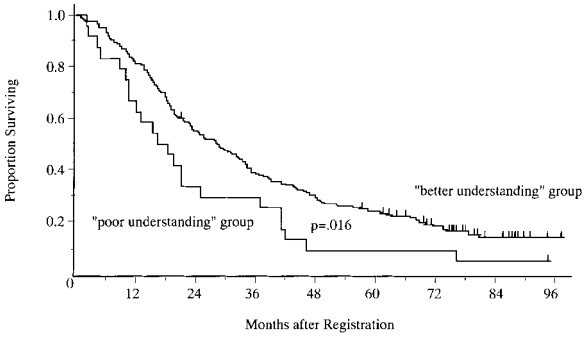

Figure 1. Comparative survival curves of patients classified according to their understanding of their disease: 'better understanding' group and 'poor understanding' group. *P* values were calculated by the log-rank test.

($p = 0.033$), serum aspartate aminotransferase (AST) ($p < 0.01$), serum alanine aminotransferase (ALT) ($p < 0.01$), serum alkaline phosphatase (ALP) ($p < 0.01$), serum carcinoembryonic antigen (CEA) ($p = 0.02$), and serum CA15-3 ($p < 0.01$), as well as patient understanding. Based on these significant factors and on adjuvant chemotherapy, which is an important prognostic factor for patients with metastatic breast cancer, multivariate regression analyses using the Cox proportional hazard model were conducted to identify factors that independently had the most important prognostic influence on survival. Stepwise regression procedures were applied to calculate the values of the beta-coefficients of the Cox model. After adjustment for age, which is suggested to be associated with patients' understanding, patients who did not understand still had poorer survival than those who understood (hazard ratio = 2.09; 95% CI, 1.16–3.78; $p = 0.014$) (Table 3).

Discussion

Informed consent is the basic component of all cancer care and is considered an essential psychosocial, be-

Table 3. Multivaliate survival analysis using Cox's proportional hazard model

Variable	Coefficient (β)	Standard error	Hazard ratio*	93% confidence interval	*P* value
Disease-free interval					
<24	0.970	0.196	2.639	1.796–3.879	<0.001
≧24			1.000		
Distant lymph nodes metastasis					
Present	0.565	0.247	1.760	1.083–2.860	0.022
Absent			1.000		
Liver metastasis					
Present	0.581	0.238	1.789	1.121–2.854	0.014
Absent			1.000		
LDH					
>1 × normal	0.574	0.180	1.776	1.247–2.529	0.001
≦1 × normal			1.000		
Adjuvant chemotherapy					
Received	0.623	0.196	1.865	1.269–2.739	0.001
Not received			1.000		
Understanding					
Poor	0.740	0.301	2.097	1.162–3.785	0.014
Better			1.000		

*The lower range of each category is the reference category.

havioral, and ethical aspect of cancer treatment. The present study showed that patients who reported that they did not understand their disease after being informed by their physician during the explanation of the clinical trial had poorer survival than patients who reported that they understood. As there were no differences in medical factors between the two groups classified according to patients' understanding, some other factor such as psychosocial or behavioral factor might have contributed to their survival.

Considering the previous reports on the relationship between psychosocial or behavioral factors and survival, there are a number of possible reasons why patients who do not understand their disease have higher mortality from cancer. One possibility is related to social support from physicians [7, 9, 16]. Patients who do not understand their disease may not be able to talk honestly with their physician in order to solve problems, develop an attitude of partnership with the physician, and consequently receive better support.

Another possibility is related to patients' coping or behavior [7, 12]. Understanding the nature and course of the disease may change patients' behavior, that is, patients who understand their disease may acquire better health habits and self-care and regularly consult the hospital, resulting in greater treatment compliance. However, treatment compliance with the clinical trial was not apparent in this study. The relative dose intensity of doxorubicin (intravenous) was approximately 90% in both treatment arms, and the patients were asked at each clinic visit whether they had swallowed the prescribed drugs. However, no records were available. Therefore, although these explanations are still highly speculative and further studies are needed, our findings support the supposition that it is important to evaluate patients' understanding of information, even after their consent has been obtained.

The major limitations of this study were the use of only a single item for measuring patients' understanding of their disease and the lack of measurement of other variables that might have helped to explain the link between understanding and survival. It is unclear why 24 patients (11%) reported that they did not understand their disease, although they were all able to read, speak, and communicate in Japanese. It is unlikely that these patients were unable to understand due to mental problems, because the eligibility criteria for this clinical trial excluded patients with severe mental disorders or cognitive impairment. Education level, which was not evaluated in this study, may be

an important factor in explaining the reason for differences in patients' understanding of their disease [22, 23]. However, there were no illiterate patients, among whom the survival rate was reported to be lower than that among patients who had more than 12 years of education [24]. It is possible that the patients may not have wanted to understand the bad news. Furthermore, the patients may not have understood on only one occasion, or sufficient information may not have been provided by the physician.

In conclusion, this study had some limitations due to the retrospective analysis employed. However, it seems that the present results include important findings regarding the relationship between patients' understanding of their disease after giving their informed consent and length of survival. Therefore, it would be worthwhile to investigate this relationship further.

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Address for offprints and correspondence: Yosuke Uchitomi, Psycho-Oncology Division, National Cancer Center Research Institute East, 6-5-1 Kashiwanoha, Kashiwa 277-8577, Japan; *Tel.:* +81-471-34-7013; *Fax:* +81-471-34-7026; *E-mail:* yuchitom @east.ncc.go.jp