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THE INFLUENCE OF NUTRITIONAL STATUS AND CANCER-RELATED FATIGUE (CRF) ON QUALITY OF LIFE IN CANCER SURVIVORS

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ABSTRACT

Background: People who live with cancer often experience malnutrition due to the disease mechanism, host response towards tumor, and side effect of anti-cancer therapy. Nutrient or energy deficiency added by some other contributing factors may result in CRF that potentially decrease quality of life (QOL). **Objectives:** This study aimed to analyze the influence of nutritional status and CRF on QOL in cancer survivors. **Methods:** This is a cross-sectional study. Population was all cancer patients in the district of Rangkah, Gading, and Pacarkeling, Surabaya. Sample size was 129. Total sampling was applied. Instrument of PG-SGA, FSI, and QOL-CS were used for data collection. Simple and multiple linear regression test was used in data analysis ($\alpha < .05$). Ethical clearance was issued. **Results:** 58 breast cancer, 47 cervical cancer, and 24 other cancer survivors participated in this study. Majority was married woman, 51-50 years old, housewife, Islam, Javanese, lives with spouse, GDP less than minimum wage, have cancer for more than four years, and already had a surgery. Most respondents were well-nourished, experienced mild CRF, and had moderate QOL. Nutritional status influenced CRF and QOL significantly by 23.80% and 9.20% respectively, while CRF influenced QOL significantly by 53.60% (@ $p = .000$). Nutritional status together with CRF could influence QOL significantly by 54% ($p = .000$). **Conclusions:** Nutritional status and CRF influence QOL significantly in cancer survivors, in which CRF has greater influence than nutritional status. Poor nutritional status along with severe CRF is highly potential for lowering QOL significantly.

Keywords: cancer, cancer-related fatigue, nutritional status, quality of life.

INTRODUCTION

Cancer is the growth of new cells that form abnormal tissue and characterized by open function. According to statistics from World Health Organization (WHO), cancer is the highest cause of death in the world, accounting for 7.6 million deaths (13% of all deaths) in 2008. In the same year, Indonesia's death rate from cancer was 245 per 100,000 inhabitants (men > women); in which lung cancer is the most frequent killer, followed by breast and colon cancer (WHO, 2008; in Tejawinata, 2012). It can be estimated that the incidence of cancer in Indonesia is 0.1% of the population, and more than 50% of cancer patients first come to seek for medication in an advanced stage (Tejawinata, 2012). In 2014, the incidence of breast cancer occupied the first position, followed by cervical cancer with the number of 20,928 cases in Indonesia (WHO, 2015). In the period of six years, we can see that more women suffered from cancer.

In general, cancer therapy includes surgery, chemotherapy, and radiation. Chemotherapy is a therapy that involves the use of chemicals or drugs that aim to kill cancer cells (Rozi, 2013). Post-chemotherapy, cancer sufferers may experience malnutrition; even before treatment they often have metabolic disorders (Trijayanti & Probosari, 2016). Malnutrition is a sub-acute or chronic condition of low nutrition at various levels and inflammatory activity resulting in changes and decline in body composition (Souters, et al., 2008). Malnutrition and weight loss in cancer patients are caused by

several mechanisms of cancer and host response to tumors and anti-cancer therapy. Also, lack of energy, protein and other nutrients, in malnourished patients can cause opposite effects on body tissue formation, body composition, body function and clinical outcome. Malnutrition is associated with decreased quality of life (QOL), decreased therapeutic response, high risk of chemotherapy-induced toxicity, and decreased survival rate (Andreoli et al., 2011).

Side effects that can result from direct chemotherapy are severe nausea and vomiting, caused by antitumor substances in the drug that can affect the hypothalamus and brain chemoreceptors in the center of nausea, thereby affecting the patient's intake of feeding after chemotherapy. Patients with cancer become susceptible to nutritional problems and changes in nutritional status. The most common nutritional problems in post-chemotherapy patients are poor protein and caloric intake, so the risk of infection increases and the healing/recovery process slows (Sutandyo, 2007; Lara et al., 2012). Cancer in the body and therapy undertaken by cancer patients make nutrition problems worsen (Sudoyo, 2006; Haryani, 2008). In cancer patients, nutrients can affect tumor biology, co-morbidity and therapeutic response (Andreoli et al., 2011). Weight loss and nutritional problems are often associated with cancer (Souters et al., 2008).

Other co-morbidities that are also increasingly debilitating the condition of cancer sufferers are Cancer-Related Fatigue (CRF) which has a significant impact on health status (Andreoli et al., 2011). CRF is a symptom that is often experienced by the majority of cancer patients, especially those who underwent chemotherapy or radiation therapy (Borneman, 2013). CRF is subjective, which can affect physical and cognitive function, psychosocial, and can reduce QOL (Pierre et al., 2007). The hybrid model suggests that cancer-related stressors and cancer therapies cause a decrease in four major areas, such as cognitive function, nutrition, muscle strength, and sleep quality, affecting the ability to adapt to ill conditions; where changes in the biological, psychological, and functional aspects that result in CRF induced (Mitchell, 2010). The negative impact of CRF can even be felt before the formal diagnosis of cancer established, and continues to be experienced during the treatment process. CRF is not affected by the type of cancer nor the type of therapy that is undertaken (Jean-Pierre et al., 2007).

Quality of life is a broad concept and a complex variable. Its value is perceived solely by individuals based on self-defined life standards, which include several aspects/domains: physical, psychological, social, and environmental. The determination of individual life standards differs across gender, age, and developmental groups, and is also strongly influenced by social/demographic determinants, such as education, employment, income, social environment, socio-economic status, marital status, housing status, etc. Nutritional status and CRF are related to the physical domain of QOL, but they potentially have impacts on other domains of QOL. This study aimed to analyze the influence of nutritional status and CRF on QOL in cancer survivors.

2 METHODS

This is a cross-sectional study. The population was all cancer patients in the district of Rangkah, Gading, and Pacar Keling, Surabaya. Sample criteria were divided into inclusion and exclusion criteria. Inclusion criteria were adult (> 18 years old), a cancer diagnosis has been confirmed, and regularly home-visited by a palliative volunteer under the supervision of Rangkah Public Health Center, Surabaya. Exclusion criteria were rejection on filling out the consent form. Total sampling was applied, and sample size of 129 was obtained. Independent variable was nutritional status, the moderating variable was CRF, and the dependent variable was QOL. The instrument of PG-SGA (Ottery, 2014), FSI (Moffitt Cancer Center and University of South Florida, 1998; in Jacobsen, 2004), and QOL-CS (Ferrel et al., 1995) were used for collecting data of nutritional status, CRF, and QOL respectively. Data were collected from February until March 2018. Simple and multiple linear regression test was used in data analysis ($\alpha < .05$). Ethical clearance was issued by Faculty of Nursing, Airlangga University, Surabaya, Indonesia, with certificate number of 681-KEPK.

RESULTS

There were 58 patients with breast cancer, 47 patients with cervical cancer, and 24 patients of other types of cancer compiled from the working area of Rangkah, Gading, and Pacar Keling Public Health Centers. Table 1 below explains the demography characteristics of study respondents.

Table 1. Demography Characteristic

CHARACTERISTIC	FREQUENCY	%
1. Age (years old)		
a. < 21	2	1.55
b. 21-30	5	3.88
c. 31-40	15	11.63
d. 41-50	30	23.26
e. 51-60	46	35.66
f. 61-70	25	19.38
g. > 70	6	4.65
2. Gender		
a. Male	7	5.43
b. Female	122	94.57
3. Religion		
a. Catholic	1	0.78
b. Christian	19	14.73
c. Islam	109	84.50
4. Ethnic		
a. Javanese	121	93.80
b. Maduranese	6	4.65
c. Chinese	2	1.55
5. Educational background		
a. Primary school	30	2.33
b. Secondary school	26	20.16
c. High school	50	38.76
d. Diploma / Bachelor degree	18	13.95
e. Uneducated	5	3.88
6. Marital status		
a. Single	12	9.30
b. Married	94	72.87
c. Widow	22	17.05
d. Divorce	1	0.78
7. Living at home with		
a. Spouse	83	64.34
b. Children	67	51.94
c. Alone	5	3.88
d. Parents	14	10.85
e. Sibling	3	2.33
8. Occupational status		
a. Full-timer	15	11.63
b. Part-timer	6	4.65
c. Retired	8	6.20
d. Housewife	92	71.32
e. Student	1	0.78
f. Seeking a job	1	0.78
g. Unemployed	6	4.65
9. GDP per month		
a. Less than minimum wage	92	71.32
b. Minimum wage - IDR 5 million	27	20.93
c. More than IDR 5 million	8	6.20
d. No income	2	1.55

Table 1 showed that most of the respondents are a married woman, 51-50 years old, housewife, Islam, Javanese, high school graduates, lives with a spouse, and Gross Domestic Product

(GDP) less than the minimum wage of Surabaya. These results indicate that majority of cancer suffered by late adult women with lower middle socioeconomic status.

Table 2. Primary Data

CHARACTERISTIC	FREQUENCY	%
1. Type of cancer		
a. Breast cancer	58	44.96
b. Cervical cancer	47	36.43
c. Others	24	18.61
2. Another type of cancer (n = 24)		
a. Skin cancer	1	0.78
b. Hepaton ¹⁶	1	0.78
c. Thyroid cancer	2	1.55
d. Colon cancer	2	1.55
e. Lung cancer	4	3.10
f. Leukemia	1	0.78
g. Cavum uteri cancer	3	2.33
h. Ovarium cancer	1	0.78
i. Willm's tumor	1	0.78
j. Nasopharyngeal cancer	1	0.78
k. Prostate cancer	2	1.55
l. Hemangioma	2	1.55
m. Limfoma	3	2.33
3. Firstly diagnosed in (year)		
a. 2018	6	4.65
b. 2017	29	22.48
c. 2016	22	17.05
d. 2015	18	13.95
e. 2014	12	9.30
f. < 2014	42	32.56
4. Type of therapy		
a. Surgery	38	29.46
b. Chemotherapy	26	20.16
c. Surgery + chemotherapy	19	14.73
d. Surgery + radiotherapy	3	2.33
e. Chemotherapy + radiotherapy	9	6.98
f. Surgery + chemotherapy + radiotherapy	22	17.05
g. Surgery + chemotherapy + radiotherapy + analgesic	1	0.78
h. Surgery + chemotherapy + radiotherapy + medicine	1	0.78
i. Chemotherapy + analgesic	1	0.78
j. Oral medicine (various types)	3	2.33
k. Untreated	6	4.65

Table 2 showed that most cases were breast cancer (44.96%), followed by cervical cancer (36.43%), and some other type of cancer (majority was lung cancer). This data shows a dramatical change in the situation of 2008, in which lung cancer being the most frequent killer; and the same situation in 2014 ¹⁰ which breast cancer being the most frequent cases then followed by cervical cancer. Since 014, breast cancer and cervical cancer are being the two most frequent cancer cases in Indonesia. The majority of respondents were diagnosed before 2014 (more than four years ago). This indicates that the survival rate of breast cancer and cervical cancer is particularly long, which makes both types of cancer a chronic disease with high burden and requires long-term supportive care.

The majority of therapy undertaken by respondents was surgery (only), both for curative and palliative purposes. The most common combination therapy was surgery followed by chemoradiotherapy (17.05%). The surprising fact was 4.65% of respondents prefer not to undergo any therapy; they possibly use alternative therapy. Regardless of the lack of information, lack of

knowledge, financial problems, or personal beliefs, these 4.65% respondents feel their condition was quite good despite not getting any therapy.

Table 3. Variables Measured

CHARACTERISTIC	FREQUENCY	%
1. Nutritional status		
a. Well-nourished (stage A)	111	86.05
b. Moderately malnourished (stage B)	18	13.95
c. Severely malnourished (stage C)	0	0
2. CRF		
a. Mild	87	67.44
b. Moderate	30	23.26
c. Severe	5	3.88
d. None	7	5.43
3. QOL		
a. High	17	13.18
b. Moderate	110	85.27
c. Low	2	1.55

*The category presented above was aimed to ease the data presentation, not for statistical analysis purposes.

Table 3 showed that the majority of respondents had well-nourished nutritional status (86.05%). This fact is really surprising and relieving because under challenging circumstances (serious illness, various therapy, weakness, fatigue, nausea, vomiting, diarrhea, stress, etc.) most study respondents could maintain their intake resulted in maximum energy. This also potentially correlated with the majority of surgical therapy undertaken by respondents which had no side effects of gastrointestinal symptom.

There were 5.43% of respondents who did not experience fatigue in the past week, but fatigue remains one of the cancer symptoms ever experienced before. From 122 respondents, most of them reported mild fatigue (67.44%) in the past week. This fact potentially correlated with the well-nourished nutritional status also in the majority. It could be assumed that most respondents had sufficient energy for doing daily activities.

Most of the respondents perceived that they had moderate QOL (85.27%). In most cases, cancer survivor felt very difficult to perceived high QOL, thus making the variable of QOL as a very interesting aspect to be studied continuously in cancer patients to develop the most effective method/intervention to increase its value. One of the basic principles of palliative care also aims to improve or optimize the individual QOL, especially for the patients.

The data of nutritional status, CRF, and QOL then analyzed by simple and multiple linear regression test, but priorly the test of normality and linearity were performed to meet the test assumption. The result of normality test showed that only QOL data were normally distributed ($p = .664$). This happened potentially due to the existence of some extreme values in nutritional status and CRF data. The result of linearity test showed that nutritional status and CRF were not linear. This happened potentially due to abnormal distribution of nutritional status and CRF. Nutritional status and CRF were linear with QOL ($p > \alpha$). The multicollinearity test showed that all eigenvalue values were more than .01 and the condition index value was less than 30, which meant no multicollinearity symptoms was found in the regression model.

Descriptive statistical test results showed that nutritional status data was less varied than other variables ($SD = 4.72$). This potentially occurred as the majority of respondents had well-nourished nutritional status (86.05%), so the data became relatively homogeneous. The highest mean was found in the QOL data (244.00). This happened due to the large intervals (0-10), and a considerable number of items (46) on the QOL-CS instrument. Mean of nutritional status and CRF was 5.46 and 34.93 respectively.

Simple linear regression test result showed that nutritional status significantly influenced CRF and QOL by 23.8% and 9.2% respectively (@ $p = .000$); while CRF influenced QOL

significantly by 53.6% ($p = .000$). Three simple linear regression test results indicated that nutritional status has the weakest effect on QOL. Even the effect of CRF on QOL was greater than the effect of nutritional status on CRF (direct correlation). These results indicated the possibility for more factors affecting CRF than the factors affecting QOL in cancer survivors, as more than 50% of the effect on QOL came from CRF.

The result of multiple linear regression test showed that nutritional status and CRF simultaneously influenced QOL significantly by 54% ($p = .000$); this value was slightly higher than the influence of CRF on QOL. This result indicated that poor nutritional status along with severe CRF could more likely decrease QOL significantly in cancer survivors.

DISCUSSION

Results showed that nutritional status influenced CRF significantly by 23.8% ($p = .000$). This effect was considered as weak (< 40%).

Nutritional status is a balance between food intake by organisms and the use in the process of growth, reproduction, and health maintenance. Although there are many factors that can affect the health status of cancer patients, nutrients can affect tumor biology, comorbidity and response to therapy. Also, other morbidities that further weaken the conditions, such as depression, weakness, CRF could have a significant impact on the health status of cancer patients (Andreoli et al., 2011).

CRF is a frequent symptom which able to weaken the majority of cancer patients, both during and after therapy. CRF differs from acute fatigue because CRF occurs prolonged, debilitating, persistent, and does not improve with rest. CRF's pathobiology is complicated and is caused by a cascade of events that results in the production of pro-inflammatory cytokines, HPA activation dysfunction, endocrine and metabolic dysregulation, circadian rhythm disturbance, and neuromuscular function abnormalities (Saligan et al., 2015). The negative impact of CRF is often experienced even before a formal diagnosis of cancer is established and continues until therapy is completed, regardless of the type of therapy. CRF potentially affect cognitive function, the physical and emotional condition of cancer patients. The difficulty of measuring CRF is when a cancer patient finds it difficult to distinguish severity and time of appearance or loss of CRF. As a result, CRF is often undiagnosed, so it is not addressed, thus negatively impacting the adherence to treatment, disease control, and outcomes (Jean-Pierre, 2007).

There has not been much study on the influence of nutritional status on CRF specifically, especially in cancer survivors. Nutritional status is more associated with tumor biology, comorbidity and response to therapy, whereas CRF is more associated with the disease mechanism, anti-cancer therapy, daily functioning, and QOL. Physiologically, the fulfillment of adequate nutritional needs can help the production of enough energy for daily activity and support the body's metabolism resulting in perceptions of physical strength and weakness. Nutrition and energy are essential for acute fatigue management, but the characteristic of CRF has made its management relatively more difficult.

CRF is associated with oxidative stress, and during cancer therapy, an excess of oxidative stress induced by anti-cancer drugs can limit the effectiveness of therapy and cause some serious side effects, such as fatigue, nausea, vomiting, etc. (Nicolson, 2010). A systematic review conducted by Marx et al. (2017) states that carnitine deficiency is one of the causes of CRF. Of the 12 articles analyzed, eight articles concluded that carnitine supplementation was useful for CRF, while the other four articles showed no significant benefit. Meta-analysis of 3 articles with sufficient data suggests that carnitine supplementation did not significantly reduce CRF.

Borneman (2013) proposed that there are several stronger factors affecting CRF in cancer patients compared to nutritional status alone. These factors can be seen in Table 4.

Table 4. The Factors Affecting CRF in Cancer Survivors

ASPECT	CONTRIBUTING FACTOR
1. Reported cancer symptoms	
a. Physical symptoms	Pain, dyspnea, general fatigue, inability to perform daily task, palpitation, insomnia, low appetite, immobility
b. Psychological symptoms	Depressive mood, anxiety, emotional distress

2. Co-morbidity:	Organ failure: heart, kidney, lung, nerve, hear, GI tract, endocrine
3. Treatment	
a. Therapy	Chemotherapy, including targetted therapy, radiotherapy, surgery
b. Medication	A side effect of taste changes, polypharmacy
4. Another factor:	Abnormal laboratorium value because of cancer, anti-cancer therapy, or infection

Minton et al. (2012) conducted a study in 278 women with breast cancer, and the results showed that 37.77% respondents had CRF. Of the 11 variables analyzed, five variables were independently able to influence CRF, namely: anxiety and depression, pain and insomnia, systemic therapy side effects, and plasma sodium. No correlation was found between demographic variables and therapy with CRF. CRF of post-cancer therapy is associated with subclinical mood pain and subjective sleep disorders, as well as systemic therapy side effects.

Results showed that nutritional status influenced QOL significantly by 9.2% ($p = .000$). This effect was considered as very weak ($< 20\%$).

Nutritional status is related to QOL, the psychosocial, functional, and social/spiritual domain of an individual. People with cancer whose nutritional status are poor have consequences of low QOL. It is important to educate and provide them with information/suggestions on how to maintain optimal food intake to keep the optimum nutritional status (Ebling et al., 2014).

For example in patients with prostate cancer, the results of a systematic review conducted by Baguley, et al. (2017) about the impact of nutrition and exercise therapy on CRF and quality of life shows that soybean supplementation can improve QOL, but it has some side effects. Recommending a healthy food eating guide combined with aerobic exercise and resistance training can address CRF, but its impact on QOL remains unclear. Dietary interventions can change the condition of CRF and improve QOL, but the efficacy of nutritional management with or without physical exercise on improving the QOL of cancer patient needs to be explored further.

Another example of head-neck cancer patients in the study of Capuano et al. (2010) in 61 untreated late-stage head-neck cancer patients (undertaken radiotherapy or chemo-radiotherapy) in an outpatient clinic showed that unintended weight loss and decreased Hb levels could independently influence QOL in the domain of physical, functional, and social functions. There were 36% respondents experienced malnutrition before cancer therapy, and they had lower physical, role, and social function score than the group of good nutritional status. Fatigue, loss of appetite, and nausea were also found to be worse in these 36% respondents who were malnourished.

Parmar et al. (2013) analyzed the medical records of 306 cancer patients who have experienced paralysis. They found that weight changes during the first, second, and third visits, are related to appearance status, physical strength, and QOL. In the subsequent (short-term) Cohort study it was found that weight changes were positively correlated with appearance status, physical strength, and QOL. The correlation between changes in physical strength and QOL was found to be consistent across all groups of respondents. Weight gain was related to the subjective improvement of physical function variables, and changes in physical strength were consistently related to QOL.

Results showed that CRF influenced QOL significantly by 53.6% ($p = .000$). This effect was considered as strong ($> 50\%$).

It was found that there are several types of cancer therapy that potentially affect the incidence of CRF. CRF is found more frequently in cancer patients receiving chemotherapy and radiotherapy. CRF is highly subjective, so the assessment of the impact of the disorder on functional status and QOL is very important. Educating patients on how to deal with other cancer symptoms, such as pain, along with adequate nutritional support & hydration and energy conservation will be able to reinforce better cope with CRF (Borneman, 2013).

In patients with cancer undergoing radiotherapy, there is a change of CRF magnitude that affects the QOL. After two weeks of radiotherapy there has been a decline in social function, and patients begin to experience financial difficulties. Decreased physical activity, role function and emotional function happen at the end of the first month after radiotherapy. Global health status decreased significantly at week 5, whereas cognitive function decline occurred only at the end of week 7 (Janaki et al., 2010).

In cancer patients undergoing chemotherapy, the physical and psychological domains are the most altered domain score, while the environmental domain score is fixed. There was no significant difference in QOL between gender, marital status, tumor type, and cycle/series of chemotherapy. QOL is not related to age and survival rate. Physical domains appear to be varied between education level groups, where the value was lower in the uneducated group. Physical and psychological domains have the strongest correlations when compared to other domains, which also greatly affects the overall QOL (Mansano-Schloss³ & Ceolim, 2012).

Kluthcovsky, et al. (2011) conducted a study in 202 women with breast cancer of in-situ until third stage cancer, located in an outpatient unit in two hospitals. After 1-2 years of diagnosis, it was showed that younger age, experiencing cancer pain, shortness of breath, insomnia, and nausea-vomiting become a predictive factor of CRF. Respondents who experienced CRF (37.6%) had a lower QOL in all domains. Many breast cancer patients who experience CRF of post-cancer therapy perceived lower QOL.

A cross-sectional study of Wang, et al. (2010) in Shanghai, China, towards 201 patients with advanced cancer showed that Karnofsky's appearance status, the location of cancer, and home hygiene had 46.9% influence on the variation of functional assessment value. The most severe symptom experienced was CRF. Psychological symptoms such as distress and sadness were the most significant factors related to QOL. They suggested providing interventions that can overcome emotional distress for improving QOL in advanced stage cancer patients.

Other cross-sectional study of Hagelin, et al. (2009) towards 228 advanced stage cancer patients who have a median of survival duration of 63 days showed that CRF increases as it approaches death, both in multidimensional and global aspects, along with more frequent drowsiness. Marital status affects the experience of CRF in both multidimensional and global ratings. The correlation between feeling fatigue, tense, anxious, irritable, depressed and perceived a lower QOL were not predictors of the acceleration of death. The correlation between CRF with QOL and negative emotions faded during the last days/weeks of remaining life.

Results showed that nutritional status and CRF simultaneously influenced QOL significantly by 54% ($p = .000$). This effect was considered as strong ($> 50\%$).

The results of this study are supported by Baguley, et al. (2017) in his systematic review about the impact of nutritional and exercise therapy on CRF and QOL in patients with prostate cancer, for example. Diet and nutritional status are essential to reduce the risk of prostate cancer mortality and regulate other clinical outcomes such as CRF and QOL. CRF in patients with prostate cancer is caused by cancer therapy, in particular the use of Androgen Deprivation Therapy (ADT), where large degenerative effects can be seen in changes in body composition (decreased muscle mass, increased fat mass, and total body mass) and systemic inflammation (IL-6, IL-8, CRP, and TNF). This impact can at least explain the causes of CRF, targeting criteria for the outcome of dietary interventions to reduce CRF and improve QOL in men with prostate cancer. With the discovery of nearly 70% men with prostate cancer who are overweight or obese, and 15.1% men who do not adhere to the guidelines for consumption of vegetables and fruits, the lifestyle choices of men can be a predisposing factor of CRF. Specific modifications to dietary intake can lead to decreased body mass and composition, inflammation and response to therapy. It is important to understand the role of isolated diets and nutrients to address CRF and improve QOL to support scientific evidence-based practices related to nutritional management in CRF incident.

Symptoms of cancer (especially pain), comorbidity, side effects of therapy, certain nutrient deficiencies, psychological disorders, sleep disturbances, and several other contributing factors could lead to CRF incidence in cancer survivors. Based on this study result, nutritional status also contributes to the incidence of CRF, although the effect is weak. Physiologically, the human body needs sufficient nutrient intake to support growth, development, cell regeneration, activity, and functioning in everyday life. In the specific case of CRF incidents in cancer patients, the needs of nutritional support increase to support the function of the immune system of preventing other comorbidities (infection), and to increase the energy use for supporting daily activity and life functioning. The dilemma inadequate nutritional support in cancer patients is that cancer cells are more dominant to absorb nutrients from the normal cells so that the size of the tumor is greater and exacerbate the appeared symptoms, especially pain. But inadequate nutritional support may result in

worse CRF, the slow healing process, increased comorbidity, and the occurrence of other complications that tend to be more harmful. All result in the decreased QOL in cancer survivors.

CONCLUSION

Cancer survivors who have been diagnosed for more than four years and already received various anti-cancer therapy have well-nourished nutritional status, experience mild fatigue, and perceive moderate QOL. Nutritional status and CRF alone could influence QOL of cancer survivors significantly, in which CRF influences QOL stronger than nutritional status. Nutritional status and CRF simultaneously also could influence QOL significantly, slightly stronger than the influence of CRF alone. Poor nutritional status along with severe CRF have a great chance to lower QOL in cancer survivors.

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Appendix 1.

RESULT OF STATISTICAL ANALYSIS

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	Nutrition, CRF	.	Enter

a. All requested variables entered.
 b. Dependent Variable: QOL

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.735 ^a	.540	.532	35.84814

a. Predictors: (Constant), Nutrition, CRF

ANOVA^b

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	189804.753	2	94902.377	73.849	.000 ^a
	Residual	161921.247	126	1285.089		
	Total	351726.000	128			

a. Predictors: (Constant), Nutrition, CRF
 b. Dependent Variable: QOL

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B		Collinearity Statistics	
		B	Std. Error	Beta			Lower Bound	Upper Bound	Tolerance	VIF
1	(Constant)	195.752	5.537		35.353	.000	184.794	206.709		
	CRF	1.504	.136	.766	11.070	.000	1.235	1.772	.762	1.312
	Nutrition	-.783	.769	-.071	-1.019	.310	-2.304	.738	.762	1.312

a. Dependent Variable: QOL

Kesimpulan: Status nutrisi dan CRF secara bersamaan mampu mempengaruhi kualitas hidup secara signifikan ($p = 0,000$) dengan besar pengaruh 54% ($R^2 = 0,540$).

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	Nutrition ^a	.	Enter

a. All requested variables entered.
 b. Dependent Variable: CRF

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.488 ^a	.238	.232	23.41822

a. Predictors: (Constant), Nutrition

ANOVA^b

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	21729.895	1	21729.895	39.623	.000 ^a
	Residual	69648.477	127	548.413		
	Total	91378.372	128			

a. Predictors: (Constant), Nutrition

b. Dependent Variable: CRF

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	19.872	3.158		6.292	.000
	Nutrition	2.759	.438	.488	6.295	.000

a. Dependent Variable: CRF

Kesimpulan: Status nutrisi mempengaruhi CRF secara signifikan ($p = 0,000$) dengan besar pengaruh 23,8% ($R^2 = 0,238$).

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	CRF ^a		Enter

a. All requested variables entered.

b. Dependent Variable: QOL

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.732 ^a	.536	.532	35.85357

a. Predictors: (Constant), CRF

ANOVA^b

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	188470.202	1	188470.202	146.615	.000 ^a
	Residual	163255.798	127	1285.479		
	Total	351726.000	128			

a. Predictors: (Constant), CRF

b. Dependent Variable: QOL

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	193.835	5.209		37.215	.000
	CRF	1.436	.119	.732	12.108	.000

a. Dependent Variable: QOL

Kesimpulan: CRF mempengaruhi kualitas hidup secara signifikan ($p = 0,000$) dengan besar pengaruh 53,6% ($R^2 = 0,536$).

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	Nutrition ^a		Enter

a. All requested variables entered.

b. Dependent Variable: QOL

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.303 ^a	.092	.085	50.14893

a. Predictors: (Constant), Nutrition

ANOVA^b

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	32331.722	1	32331.722	12.856	.000 ^a
	Residual	319394.278	127	2514.916		
	Total	351726.000	128			

a. Predictors: (Constant), Nutrition

b. Dependent Variable: QOL

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	225.632	6.763		33.362	.000
	Nutrition	3.366	.939	.303	3.586	.000

a. Dependent Variable: QOL

Kesimpulan: Status nutrisi mempengaruhi kualitas hidup secara signifikan ($p = 0,000$) dengan besar pengaruh 9,2% ($R^2 = 0,092$).

THE INFLUENCE OF NUTRITIONAL STATUS AND CANCER-RELATED FATIGUE (CRF) ON QUALITY OF LIFE IN CANCER SURVIVORS

ORIGINALITY REPORT

%**9**

SIMILARITY INDEX

%**3**

INTERNET SOURCES

%**7**

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