RESEARCH ARTICLE

Health Related Quality of Life (HRQoL) among Breast Cancer Patients Receiving Chemotherapy in Hospital Melaka: Single Centre Experience

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Abstract

Objective: To investigate the impact of chemotherapy on quality of life (QoL) among breast cancer patients and to evaluate the relationship with age, cancer stage and presence of any comorbidity. **Methods:** A prospective study was conducted among breast cancer patients receiving chemotherapy in Hospital Melaka from 1st January 2014 to 31st July 2014. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) was given to patients to fill in prior chemotherapy (baseline) and after the third cycle of chemotherapy. Socio-demographic and clinical data were collected and analyzed using SPSS version 20. **Result:** Respondents were 32 female patients [mean age (SD): 49.7(9.93) years]. They reported a significant lower global health status ($P < 0.01$) and significant higher symptoms of nausea and vomiting ($P < 0.01$), loss of appetite ($P = 0.028$) and diarrhea ($P = 0.026$) after the third cycle of chemotherapy as compared to baseline. Compare to, this study showed significant better emotional functioning ($P < 0.01$) and social functioning ($P < 0.01$) than the EORTC QLQ-C30 Reference Values 2008 for breast cancer cases. Under symptom scales higher scores were noted for appetite loss ($P = 0.017$), nausea and vomiting ($P < 0.01$). Age, stage and comorbidity had no clear associations with global health status in our patients ($P > 0.05$). **Conclusion:** Chemotherapy did reduce the QoL of breast cancer patients. Management of chemotherapy-induced loss of appetite, diarrhea, nausea and vomiting should be improved for a better outcome.

Keywords: Breast cancer- chemotherapy- quality of life (QoL)- EORTC QLQ-C30

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Introduction

Breast cancer is the most frequent cancer in females and the first most common cancer among population regardless of sex in Malaysia. There were 3,242 female breast cancer cases diagnosed in 2007 and reported to Malaysia National Cancer Registry, accounted for 18.1% of all cancer cases reported and 32.1% of all female cases (Zainal, 2011) . In year 2013, 106 (18.9%) breast cancer patients treated with chemotherapy in Hospital Melaka, which is highest among all cancer patient who received chemotherapy.

Being diagnosed with breast cancer is a very stressful event, affecting all aspects of life and thus compromising the quality of life (Montazeri et al., 2008). The temporary side effects associated with the treatment may influence the patients' Health Related Quality of Life (HRQoL) during treatment (Eisenbraun et al., 2011). As a result of that, HRQoL measurement is important since the patients are offered highly toxic treatments to aid recovery or prolong their survival. Understanding quality of life from the patient's perspective especially in oncology area is a pivotal factor for clinical decisions (Montazeri et al., 2008) and patient preferences (Valderas et al., 2008). Although routine QoL assessments are generally recommended and known as a more reliable collection method for QoL data, but they are still yet to be incorporated in clinical practice, as there is a considerable incongruity between clinicians' ratings and patients' self-report (Pakhomov et al., 2008).

Quality of Life (QoL) assessment of breast cancer patient is vital for both patients as well as clinicians because the results can guide patients on treatment options and informed decision-making can be made by the clinician. Although QoL is a subjective perception of cancer patients' symptoms, function and side effects of the treatment, it may help clinicians in making treatment decisions and determine the best ways to support and improve the quality of life of breast cancer patients during the difficult times of their disease and on-going cancer treatments (Yusuf et al., 2013). In fact, self-assessed health status was proved to be more powerful predictor of mortality and morbidity (DeSalvo et al., 2006).

The objective of this study is to measure and evaluate the quality of life among breast cancer patient treated with chemotherapy treatment in Hospital Melaka, in view to provide a broader picture on how a cancer treatment especially chemotherapy impacts the breast cancer patients' life. The obtained information may be

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crucial for the development of methods to upgrading of treatment facilities, facilitate rehabilitation and palliative care to assist cancer patient to cope for a better recovery and improve their quality of life (Helena et al., 2000).

Materials and Methods

Sample and Procedure

This was a cross-sectional, descriptive study of the health-related quality of life among breast cancer patient treated with chemotherapy which was conducted at Hospital Melaka from January 2014 to July 2014. Convenient sampling was used as sampling method. Besides, this study was registered under National Medical Research Register (NMRR) (NMRR-14-335-19480) and permission to conduct this study was obtained from the Ministry of Health (MOH) Research and Ethnics Committee (MREC), Malaysia.

The inclusion criteria included respondent that was diagnosed with breast cancer and enrolled in Hospital Melaka to receive FEC regimen (5-Fluorouracil, Epirubicin, Cyclophosphamide) as chemotherapy treatment. Besides, the respondent should be 18 years old and above who was agreed to participate with written consent and could either communicate in English, Malay or Chinese language and understood the study procedure. Those patients with inability to give full cooperation due to severity of the illness will be excluded in this study.

An assessment instrument in form of questionnaires were given to respondents to fill in before initiation of the first cycle chemotherapy, and again after the third cycle of chemotherapy. Informed consent to participate in the study was obtained from patients prior to the guided, face to face interview. The subject demographic and medical information to ensure validity of diagnosis, stages of breast cancer and treatment were obtained from medical records. The data was collected personally by the researcher and time to complete the questionnaire was approximately 15-30 minutes.

Assessment Instrument

The health-related quality of life of respondents were measured using Malay, English or Chinese version of EORTC QLQ-C30. These questionnaires were copyright instruments and permission to use them was obtained from the EORTC Quality of Life Study Group in Brussels, Belgium. The validity and reliability of the EORTC QLQ-C30 in measuring the HRQoL of cancer patients in multi-cultural clinical research settings have been reported by Aaronson and colleagues (1993). The translated Malay and Chinese version was validated and have well documented psychometric properties (Yusoff et al., 2010; Magaji et al., 2012). In EORTC-QLQ C-30, there are 30 questions that assess three main domains which are global health status, functional status, symptoms and financial status. A raw score of the participants' responses were transformed according to EORTC scoring manual (Fayers et al., 2001). The score ranges from zero to 100, with higher score representing better quality of life for the functioning and global quality of life but representing poorer quality of life if higher level of symptoms.

Statistical Methods

Sociodemographic data of respondent were gathered which include gender, age, ethnicity, marital status, number of children, educational level, employment status, household income, house locality, stage of breast cancer, previous breast cancer treatment and comorbidity. The data was entered and analysed by using the Statistical Package for the Social Science (SPSS, version 20.0). Descriptive analysis was used to analyse overall QoL, level of functioning and level of symptomatology among subject. All continuous variables were checked for their normality through Kolmogorov-Smirnov analysis. Wilcoxon test was used to identify significant difference of QoL between pre and post chemotherapy for data that was not normally distributed. For the correlation between patient's age with global health status, Pearson's correlation test was used. Independent T-test was used to test whether there are relationship of cancer stages and presence of comorbidity with global health status. A p-value of equal or less than 0.05 was considered significant. Comparisons of the medians (IQRs) were made between the current research group and the reference value reported in a study by Scott (2008) for all the elements tested for health related quality of life among the breast cancer patient in the current study.

Results

Patients' Demographic

A total of 32 respondents were participated in the study. All respondents were female. Majority of the patients were from age group between 40 to 60 years old (65.6%, n=21). They were more Malays (78.1%, n=25) followed by Chinese (18.8%, n=6) and Indian (3.1%, n=1). Almost all respondents were married (93.8%, n=30) and more than half respondents have 3 or less children (62.5%, n=20). In term of education level, more than half (53.1%, n=17) were reported to have secondary school level of education, followed by primary school (25%, n=8) and tertiary school which having diploma or degree (21.9%, n=7). In term of employment status, more than half respondents were unemployed (56.3%, n=18) and were housewife. Other respondents were working (31.2%, n=10), retired (9.4%, n=3) and self-employed (3.1%, n=1). Most respondents had a household income ranging from RM1001 to RM3000 per month (53.1%, n=17) followed by income ranging from RM0 to RM 1000 (28.1%, n=9). 18 of the respondents live in rural areas (56.3%) while others reside in urban. About 47% of respondent came with breast cancer at early stage and the remaining respondents were diagnosed late stage of breast cancer with 46.8% Stage III and 6.3% Stage IV respectively. About 81% of the respondents underwent surgery (n=26) either lumpectomy or mastectomy and majority of them had comorbidity (53.1%, n=17). Details on socio-demographic information are presented in Table 1.

Health-related quality of life and global health status

Table 2 presents the health-related quality of life before and after chemotherapy as well as patient's global quality of life and patient's functioning as compared to reference value for all cancer patients provided by EORTC Quality of Life Group Members and other users of the QLQ-C30. Comparison of global health status score, functional scale score and symptoms scale/item score before and after chemotherapy indicated that breast cancer patient who received chemotherapy showed a significant lower degree of global health status (p=0.001), significant increase of certain symptoms of chemotherapy side effects which are nausea and vomiting (p=0.000), appetite loss (p=0.028), and diarrhea (p=0.026). There were no significant between before and after chemotherapy in term of functional scale.

Global health status score was same with reference group. Under functional scales, physical functioning and role functioning were lower than reference value whereas emotional, cognitive and social functioning of this study were higher than reference value. For symptoms scales, nausea, vomiting and appetite loss were found to be higher than reference value while other symptoms scale except insomnia showed similar result with reference value. For insomnia symptom, it was lower than reference value. Breast cancer staging had no significant correlation with global health status patient underwent chemotherapy (p=0.22). In addition, there were no significant relationship found between comorbidity and global health status (p=0.872) (Table 3). Age patient was not significantly correlated with global health status of patient receive chemotherapy as well (r = -0.194, p=0.286).

Table 1. Socio-Demographic Data of Patients

Variables	n	Percentage (%)
Gender		
Female	32	100
Male	0	0
Age		
18-40	6	18.8
40-60	21	65.6
>60	5	15.6
Ethnicity		
Malay	25	78.1
Chinese	6	18.8
Indian	1	3.1
Others	0	0
Marital status		
Single	1	3.1
Married	30	93.8
Divorced/separated	1	3.1
No. of children		
0-3	20	62.5
>3	12	37.5
Educational level		
Never schooled	0	0
Primary school	8	25.0
Secondary school	17	53.1
Tertiary school	7	21.9
Employment status		
Employee	10	31.2
Studying	0	0
Unemployed	18	56.3
Retired	3	9.4
Self-employed	1	3.1
Monthly income (myr)		
RM0- RM 1,000	9	28.1
RM 1,001-RM 3,000	17	53.1
RM 3,001-RM 5,000	3	9.4
> RM 5,000	3	9.4
House location		
Rural	18	56.3
Urban	14	43.7
Tumour stage		
Stage I	2	6.3
Stage II	13	40.6
Stage III	15	46.8
Stage IV	2	6.3
Previous treatment		
Chemotherapy	0	0
Radiotherapy	0	0
Surgery	26	81.2
Hormonal therapy	0	0
None	6	18.8
Chronic health condition		
With comorbidity	17	53.1
Without comorbidity	15	46.9

Discussion

The results of this study demonstrated that patients who were currently receiving chemotherapy had significantly lower global health status. Symptoms such as nausea, vomiting, loss of appetite and diarrhea are significantly higher after the chemotherapy. In parallel with our findings, a study done by Watters (2003) on 65 women with breast cancer receiving anthracycline- based adjuvant chemotherapy using European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-Module (QLQ-C30) determined that patients had a decrease in global health status after adjuvant chemotherapy compared to patients' baseline status before chemotherapy. According to the comments leaved by patients in study done by Palmer (1980) on what extent the chemotherapy affect quality of life, some stated that "treatment was unbearable" or "never again" and some stated that the experience had been "most unpleasant" or they had "dreaded" the treatment "but would have it again if it were recommended for their health's sake." This showed that they experienced poor quality of life following chemotherapy.

Chemotherapy-induced nausea and vomiting have been commonly rated as the most unpleasant and distressing side effect (Cohen et al., 2007). Consistent with a previous study done by Lua (2012) that involving larger number of patients (n=41), there is a significant proportion of patients remain to suffer nausea and vomiting after receiving chemotherapy even after usual antiemetics management. In that study, patients who experienced vomiting exhibited lower quality of life than those who did not suggesting possible close association between the occurrence of vomiting and quality of life. Besides, in a

Table 2. Comparison Health Related Quality of Life Pre-Chemotherapy, Post-Chemotherapy and European Organisation for the Research and Treatment of Cancer (EORTC) QLQ C-30 Reference Values 2008

Constructed scales	Pre	Post	Z statistic a	*P value	EORTC QLQ-C30 References Values 2008
	Median (IQR)	Median (IQR)			Median (IQR)
Global Health Status	75 (22.9)	66.7 (8.3)	-3.2	0.001	66.7 (50.0-83.3)
Functional scale					
Physical Functioning	93.3 (23.3)	80.0 (20.0)	-1.6	0.11	86.7 (66.7-93.3)
Role Functioning	100.0 (16.7)	75.0 (33.3)	-1.8	0.076	83.3 (50.0-100.0)
Emotional Functioning	83.3 (33.3)	91.7 (33.3)	-0.9	0.342	75.0 (50.0-83.3)
Cognitive Functioning	100.0 (33.3)	100.0 (33.3)	-0.6	0.526	83.3 (66.7-100.0)
Social Functioning	100.0 (16.7)	100.0 (12.5)	-0.2	0.823	83.3 (66.7-100.0)
Symptoms scale/ items					
Fatigue	27.8 (33.3)	33.3 (33.3)	-1.6	0.105	33.3 (11.1-44.4)
Nausea & Vomiting	0.0 (0.0)	33.3 (50.0)	-3.7	0	0.0 (0.0-0.0)
Pain	16.7 (33.3)	16.7 (33.3)	-0.7	0.459	16.7 (0.0-50.0)
Dyspnea	0.0 (0.0)	0.0 (0.0)	-0.9	0.334	0.0 (0.0-33.3)
Insomnia	0.0 (33.3)	0 (33.3)	-1.3	0.196	33.0 (0.0-33.3)
Appetite Loss	0.0 (33.3)	33.3 (66.7)	-2.2	0.028	0.0 (0.0-33.3)
Constipation	0.0 (25.0)	0 (33.3)	-0.9	0.357	0.0 (0.0-33.3)
Diarrhea	0.0 (0.0)	0.0 (0.0)	-2.2	0.026	0.0 (0.0-0.0)
Financial Difficulty	0.0 (33.3)	0.0 (33.3)	-0.4	0.67	0.0 (0-33.3)

*Wilcoxon test, P value < 0.05

Table 3. Relationship of Comorbidity and Cancer Staging with Global Health Status Post Chemotherapy

Measures	Global Health Status post chemotherapy Mean (SD)	Mean differenceb (95% confidence Interval)	P value†
Comorbidity			
Without comorbidity	68.9 (13.9)	-0.9(-12.3, 10.5)	0.872
With comorbidity	64.8(13.8)		
Staging			
Stage I and II cancer	68.9 (13.9)	6.8(-4.3, 18.0)	0.22
Stage III and IV cancer	62.1 (16.6)		

† Independent t-test, P value < 0.05

study done by Gozzo and colleagues (2013) by using EORTC QLQ-C30 on 79 women receiving chemotherapy revealed that 93% had nausea and 87% had vomited at least once during the treatment. Cytotoxic drugs used by the participants in this study may become the reason of statistically significant higher nausea and vomiting after chemotherapy as cyclophosphamide and epirubicin present an emetic potential of level 4 which has higher risk (>90%) to cause emesis (MOH, Malaysia, 2011).

Diarrhea is one of the most common chemotherapy side effects and different mechanisms may be involved in its pathogenesis (Sharma et al., 2005; Melicher and Zezulova, 2011). Cytotoxic drugs impair the turn-over of intestinal epithelia and induce flattening of the villi and an increased exposure of luminal contents to crypts (Keefe et al., 2000). These alterations could be involved in the frequent recurrence of diarrhea in patients undergoing chemotherapy (Kadowaki and Yamaguchi, 2011). In this study, it was found that there is a significant increase in diarrhea in patients after undergoing chemotherapy. This finding is parallel to the study result done by Russo (2013). From their study result, it could be supposed that in patients with extra GI neoplasms, such as breast cancer, the FEC regimen induces alteration in the intestinal permeability, which was associated with modifications in the levels of hormones regulating the growth and physiology of intestinal membranes that resulted in diarrhea. In fact, Palmer (1980) reported patient who had received the single or multiple chemotherapy agent in their study complained of diarrhea which occurred within 12 hours after starting the treatment and most of them experienced reduction of appetite which is in line with our study.

The effect of chemotherapy on functional status of breast cancer patients is not significant in this study. This may due to adequate pain and symptoms management, achieving a sense of control and strengthening relationship with family member (Singer et al., 1999). Although the results found in this study point to a stable functional status during chemotherapy, most of the published studies evidence a significantly negative interference of the chemotherapy in the functional status of women with breast cancer. Watters (2003) reported moderate decline in physical function by patients receiving chemotherapy in their study. Emotional and social function had improved by the completion of chemotherapy and there was no significant change in role and cognitive function from baseline to completion of therapy. Other than that, this study was in contrast with a study which stated that the worsening physical and psychological function of women with breast cancer was associated with chemotherapy (Ogce and Ozkan, 2008). The differences may be due to different patients' population (sample size or patient age).

A comparison between the quality of life of breast cancer patients in Hospital Melaka and general population by using EORTC QLQ-C30 reference value 2008 was also carried out in the current study. The reference data is important to provide information about the distribution of quality of life scores for specific cancer populations with certain characteristics to explain differences in clinical outcomes. They provide one potential reference point against which future populations may be compared (Scott et al., 2008). In this comparison, the patients in Hospital Melaka presented with higher event of appetite loss, nausea and vomiting symptoms compare with the reference value based on the result obtained. The difference in result can be due to the sample population difference, as reference data was collected from different countries in the world which include non-Asian country, while sample of this study is only obtained from Malaysian. In another study, Bourdeanu and colleagues (2012) revealed that ethnicity influences nausea and vomiting in patient receiving chemotherapy. The sample of that study consisted of Caucasians, Hispanics, Asians, and African Americans. In parallel to the current study, the published results indicate that Asian women with breast cancer undergoing anthracycline- based chemotherapy experienced statistically significantly more clinically important nausea and vomiting than non-Asian counterparts.

It was postulated that older women with breast cancer would experience declines in global health status during chemotherapy compare to younger women. The postulation is based on the fact that body composition tends to change in a predictable manner during adult life for example, age-related differences in muscle fibre types, numbers of functioning motor units and changes in muscle energetic with the most substantial decline in muscle mass of as much as 40 to 50% by the eight decade of life relative to young adulthood (Cohn et al., 1980; Kallman et al., 1990). In spite of the postulation, this study found that there was no correlation between age and quality of life. This finding is in agreement to Watters (2003), who reported quality of life of young (<65 years old) and older (≥65 years old) patients similar decline in global health status. Similar results also have been reported by Mols (2005) which concluded that age is not a predictor of quality of life. On contrary, Akin and co-workers reported a study that showed relationship between quality of life and age. In that study, the overall quality of life and its dimension (emotional wellness, functional wellness and additional concerns) were more negatively affected in younger patients (Akin et al., 2008). However, the age range of patients in this study are not normally distributed which may contribute to the different result obtained in comparison to Watters (2003) and Mols (2005).

Interestingly, the current study shows no correlation between extend of disease and quality of life. Similar results have been reported by Dehkordi (2009), that quality of life was not affected by stage of cancer. In contrast, Rustoen (1995) and Holzner (2001) in two separate studies found that the extent to which quality of life of cancer patients depends on the time elapsed since initial treatment; with an increase in extent of disease, a decrease in the quality of life was observed. The difference may be due to different in cancer types in each study. Also, uneven distribution of patients in each tumor stages in the current study that may cause differences in study result. Similar deduction is obtained for comorbid condition whereby no significant correlation was found between comorbid condition and quality of life of the patient. Influence of a given comorbid condition will vary depending on where a patient is located within the cancer care trajectory. According to a study done by Wolf (2005), patients with comorbidity such as diabetes mellitus did not appear to worsen breast-cancer specific outcome which was in line with this study result. However, Mao (2007) observed that symptom burden among cancer survivors in their study is substantial and impacted by other comorbidities.

In conclusion, this study showed chemotherapy increase in nausea, vomiting, diarrhea and loss of appetite as well as reducing global health status among breast cancer patients in Hospital Melaka. Although the quality of life among breast cancer patients is comparable with general population (from EORTC reference value), result showed that age, staging and comorbidity have no association with global health status in breast cancer patient. Deterioration in quality of life is caused by pain, insomnia, fatigue, physical difficulties, emotional, and cognitive distress. From this study, we can see that symptoms presented before chemotherapy may be an important variable in finding risk factors for the development of the symptoms over the course of treatment (Ogce and Ozkan, 2008). Royer (2009) noticed that women do not communicate with their healthcare providers about symptoms. Thus, results from this study may be useful for pharmacist so that pharmacist interventions related to symptom management can be carry out to assist women in understanding the possible cause of symptoms, which may lead to more effective coping with their symptoms. The incidence of chemotherapy induced-nausea and vomiting among this sample population indicate that there is still room for improvement towards better control of nausea and vomiting, perhaps through the introduction of complementary medicine or combination of antiemetic medication. Other than that, planned education programs addressing patients' needs, help patients by providing verbal encouragement and introducing patients to positive role are crucial towards improving quality of life among breast cancer patients.

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