ORIGINAL ARTICLE

Quality of Life after Haematopoietic Stem Cell Transplantation in a Multiracial Population

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SUMMARY

Haematopoietic stem cell transplantation (HSCT) was started in Malaysia since 1993 and it has improved the survival of patients with otherwise fatal haematological diseases. This study was initiated because quality of life of these survivors is an important tool in assessing the outcome of this treatment modality. The secondary objective was to identify factors that influenced their quality of life. The European Organization of Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-30) was used to assess the quality of life of eligible patients. A total of 62 patents were recruited. The mean global health score (QoL) was 71.2. The major symptoms faced by our patients were fatigue, financial difficulty and appetite loss. Appetite loss was an independent adverse factor for lower QoL.

KEY WORDS:
Quality of Life, Haematopoietic stem cell transplantation, EORCT-30, Appetite loss

INTRODUCTION

Health related quality of life (QOL) is defined as 'the extents to which one's usual or expected physical, emotional and social well-being are affected by medical condition or its treatment[1]. Subjectivity and multidimensionality are the two essential aspects when measuring QOL[2]. Subjectivity indicates that QOL must be measured from the individual's viewpoint. This is because individual patients with the same objective health status may report different QOL due to their different expectations and coping skills. It is a general consensus that QOL should comprise different dimensions of influence which include physical, functional, emotional and family well-being, social functioning, financial concerns and sexual satisfaction[3]. There are many validated and reliable QOL questionnaires for different cohorts and these questionnaires can be divided into three main types; generic health status instruments, generic illness instruments, and disease-specific instruments[4].

The impact of HSCT on QOL has received substantial attention among medical health workers since 1980's and this has resulted in many studies in this area[5-10]. This is in conjunction with huge number of survivors as a result of rapid advancement of autologous and allogeneic HSCT since their introduction in 1960's. These procedures had prolonged the survival and more importantly, provided cure for many historically fatal haematological diseases. However, cure or longer survival is not always accompanied by complete restoration of health. Long-term survivors may encounter a variety of medical problems secondary to the side effects and complications of HSCT. On the other hand, the malignant nature of the underlying disease for most HSCT patients renders them to have more emotional distress because of the uncertainty or concern about the possibility of recurrence. In addition, HSCT is an expensive procedure and it would become a life-long financial burden particularly for patients with late complications.

The first HSCT in Malaysia was done in 1993 and the role of HSCT had become more and more important as the incidence of malignancy is increasing. In year 2006, malignant neoplasm (10%) is the third leading cause of death after septicaemia and heart disease and the Age standardised Incidence Rate for all cancers was 131.3 per 100,000 populations. Haematological malignancies are the third commonest cancer among males (7.8%) and seventh commonest cancer among females (4.3%). HSCT has prolonged the survival of many of these patients. However, measurement of the QOL of these survivors is essential to assess the success of this treatment. In addition, it is useful to identify factors that are affecting the QOL of our heterogeneous population of patients so that necessary measures can be taken to improve their QOL.

MATERIALS AND METHODS

Design

This was a cross sectional study. The study was conducted between February and June 2009. EORTC QLQ-30 questionnaire was used to assess QOL.

Sample

The targets for this study were all HSCT patients whom were healthy and stable enough to be followed up at adult bone marrow transplantation clinic in University Malaya Medical Centre. They were approached during their visits. Objectives and implications of the study were explained to them and only patients that gave informed consent were recruited. The calculated sample size based on a confidence level of 95% and confidence level of 5 was 73.

Setting

University Malaya Medical Centre (UMMC) is a tertiary teaching hospital which receives referrals from the whole country. The adult haematopoietic stem cell transplantation unit started the country's first HSCT in 1993 and it is one of

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the three HSCT centers in the country. Up to June 2009, there were 120 allogeneic and 65 autologous HSCT done respectively. The overall survival and disease free survival at five years for allogeneic HSCT patients were 50% and 60%, respectively[11].

Instruments
A disease specific questionnaire, the European Organization of Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) was used in this study[12]. Permission was obtained from the organization. The EORTC QLQ-C30 is composed of both multi-item scales and single-item measures. These include five functional scales, three symptom scales, a global health status / QoL scale, and six single items (dyspnoea, loss of appetite, insomnia, constipation, diarrhoea and perceived financial impact of the disease)[12]. The questionnaires were available in English, Malay and Chinese languages to accommodate our multi-racial and multi-linguistic society. The translation of the core questionnaire and modules into other languages follows a procedure that has been documented in detail in the EORTC Quality of Life Group manual: *Translation Procedure, Cull et al., 1998.*

Data collection procedure
Patients were allowed to choose their preferred or most familiar language in order to ensure the accuracy and reliability of the results. They were asked to answer the questionnaires either after their consultation session or while waiting for their turns to see a doctor. They answered the questionnaire on their own and no assistance was allowed. There was no time limit but they had to finish it within the clinic session which was approximately three hours. Patients' characteristics such as age, ethnicity, gender, diagnosis, type of transplantation, co-morbidity, duration after transplantation and graft-versus-host disease (GVHD) were recorded from their case notes.

Data analysis
Data was organized and processed using SPSS version 17. The individual score was calculated based on the formula given by EORTC[13]. All of the scales and single-item measures range in a score from 0 to 100. A high scale score represents a higher response level. Thus a high score for a functional scale represents a high / healthy level of functioning; a high score for the global health status / QoL represents a high QOL, but a high score for a symptom scale / item represents a high level of symptomatology / problems[13].

Independent t-test and one way Anova were used to compare the mean of continuous data for two and more than two independent groups respectively. Linear regression was used to analyze the relationship between symptoms and QoL. Multinomial Logistic Regression test was used for multivariate analysis.

Missing items were analyzed as suggested by EORTC scoring manual: For single-item measures, un-answered item will be set to missing score; for scale items, if at least half of the items from the scale had been answered, all the items that were completed were used for calculating the scales scores with the standard equations; any items with missing values were ignored when making the calculations. There were three missing items from three separate patients, two on emotional scale and one on social function scale. All three patients missed only one item in the scales and the scores were calculated as mentioned.

RESULTS

There were 62 patients recruited; 21 patients (33.9%) had autologous and 41 patients (66.1%) had allogeneic HSCT done respectively. The duration after transplantation ranged from 7 to 181 months (median duration was 48 months). Characteristics of patients are shown in Table I. On statistical analysis, the QoL was not influenced by age, gender, race, type of transplantation, presence of GVHD, comorbidity or post transplantation duration.

There were 10 (16.1%) and 11 (17.7%) patients who rated excellent for their overall quality of life and overall health status respectively (Table II). The mean global health (QoL) score was 71.2 and other functional scores ranged from 73.9 to 83.1 (Table III). GVHD was found to be a contributor to lower cognitive function score, the mean score for patients with and without GVHD were 66.7and 83.7 respectively (P=0.001) (Table IV). On the other hand, females were found to have higher mean social function scores compared to male (87.1 VS 68.6, P=0.011). Patients who had allogeneic HSCT had more severe nausea and vomiting if compared to patients who underwent autologous HSCT (mean score 11.8 vs 2.4, P=0.048).

Financial difficulty had the highest mean score (50.0) among the problems/symptoms whereas nausea and vomiting had the lowest score (Table III). There were only 12 patients (19.4%) who did not have financial difficulty at all while 14 (22.6%), 16 (25.8%) and 20 (32.3%) patients had very much, quite a bit and a little financial difficulty, respectively. The other major symptoms faced by our patients were fatigue, pain and insomnia. Indian patients were found to have highest mean score for fatigue (53.1 vs 36.5 vs 31.0, P=0.035) and pain (42.6 vs 28.6 vs 17.9, P=0.039) if compared to Malay and Chinese patients. In addition, 50% of Malay and 46.2% of Chinese did not have pain at all and only 11.1% of Indian was not disturbed by any pain.

On linear regression analysis, pain, fatigue, insomnia, financial difficulty, appetite loss and constipation were significantly affecting the global health score inversely (Table IV). However, appetite loss was the only independent adverse factor after multinomial logistic regression analysis (Table V).

DISCUSSION

It has now been generally agreed that the outcome of a disease or a treatment should be assessed by both aspects of quantity and quality. In parallel with this insight, the United States Food & Drug Administration has included quality of life (QOL) as one of the two potential benefits when approving new anti-cancer drugs[14].

The results of this study showed that our post HSCT patients had good quality of life. The high mean QoL score among our patients is consistent with other studies[10, 15]. Furthermore, there were more than 10% of patients who reported their

Table I: Patients' Characteristics

Characteristics	Number	Percentage (%) (mean scores)	QoL deviation	Standard	P value
Sex					
Male	35	56.5	71.0	19.21	0.891
Female	27	43.5	71.6	17.64	
Ethnicity					
Chinese	39	62.9	72.2	19.89	0.533
Malay	14	22.6	72.6	17.42	
Indian	9	14.5	64.8	12.34	
Diagnosis					
AML	22	35.5			
ALL	3	4.8	-	-	-
CML	11	17.7			
NHL/HD	13	21.0			
Multiple myeloma	7	11.3			
Others	6	9.7			
Transplant					
Allogeneic					
Autologous					
Duration of transplant					
< 1 year	41	66.1	68.9	19.27	0.165
≥ 1 year	21	33.9	75.8	16.00	
GVHD					
Acute	5	8.1	69.7*	15.76	0.673
Chronic	14	22.6			
None	43	69.4	71.9	19.58	
Co-morbidity					
Diabetes mellitus	4	6.5	76**	19.69	0.228
Hypertension	8	12.9			
IHD	1	1.6			
Others	3	4.8			
None	46	74.2	69.6	17.84	
Age					
≤ 40 year old	31	50	73.4	20.00	0.362
> 40 year old	31	50	69.1	16.69	

Age ranged from 17 to 61 years old, mean and median age were 40 years old
* Acute + chronic ** All comorbidity AML Acute myeloid leukaemia ALL Acute lymphoblastic leukaemia CML Chronic myeloid leukaemia NHL Non-Hodgkin's lymphoma HD Hodgkin disease

Table II: Scores of overall health and quality of life

Scores	Overall health status		Overall Quality of life	
	Number	Percentage (%)	Number	Percentage (%)
1*	0	0	0	0
2	1	1.6	1	1.6
3	2	3.2	1	1.6
4	13	21.0	10	16.1
5	22	35.5	20	32.3
6	13	21.0	20	32.3
7**	11	17.7	10	16.1

*very poor
**Excellent

overall quality of life and health status as excellent and more than 70% of them rated at least 5 (score scale from 1 to 7) for these two categories. Therefore, it is clear that majority of our patients considered themselves as having good QOL.

Two separate studies found that younger[10] and male patients[16] had better QOL. In addition, Christopher *et al*[17] noted that active GVHD significantly influenced QOL of their post HSCT patients. However, the QOL of our patients was not affected by any of the seven independent variables which include GVHD, age, gender, ethnicity, type of transplantation, comorbidity and duration post transplantation. Another study found that QOL for autologous and allogeneic patients was equalized 12 months post transplantation[18]. This observation may explain our results where 88.7% of our patients had post HSCT duration of more than 12 months at the time of recruitment. Moreover, the activity of GVHD was not assessed in this study and therefore, the effect of GVHD on our patients' QOL might be underestimated. Nevertheless, we found that patients who had GVHD had statistically significant lower cognitive function score if compared to their counterparts. This could be due to the effect of GVHD as well as the side effect of immunosuppressant.

Table III: Mean scores for global health, five functional scales, three symptom scales and six single items

	Mean scores
Financial difficulty*	50.0
Fatigue*	35.5
Pain*	23.9
Insomnia*	23.7
Dyspnoea*	20.4
Appetite loss*	17.2
Constipation*	12.4
Diarrhoea*	10.2
Nausea & Vomiting*	8.6
Global heath**	71.2
Physical function**	83.1
Role function**	73.9
Emotional function**	76.9
Cognitive function**	78.5
Social function**	76.6

Mean score ranged from 0 to 100
* The higher score represents higher level of symptom
**The higher score represents higher level of function

Fatigue was demonstrated in a few studies as one of the most common problems that affects daily activities of patients after HSCT[16, 18-19]. So *et al* identified that fatigue was more common among older, married, unemployed, and lower income patients16. In our study, financial difficulties, fatigue and pain were the three most severe problems/symptoms that were faced by our patients. These three symptoms together with appetite loss, constipation and insomnia were correlated with lower QoL scores. Even though only appetite loss stayed as an independent risk factor for poorer QoL score after multivariate analysis, prompt measures should be taken for each problem in order to further improve the QOL of these patients.

Table IV: Linear Regression test between symptoms and QoL

	Unstandardized coefficients		Standardized coefficients	t	Sig.	95% CI	
	B	Std Error	Beta			Lower bound	Upper bound
Fatigue	-.332	.092	-.422	-3.607	0.001	-.517	-.148
Nausea & Vomiting	-.234	.130	-.226	-1.801	0.077	-.494	.026
Pain	-.233	.081	-.394	-2.884	0.005	-.394	-.071
Dyspnoea	-.069	.112	-.080	-.620	0.538	-.292	.154
Insomnia	-.293	.077	-.306	-2.493	0.015	-.348	-.038
Appetite loss	-.329	.075	-.491	-4.367	0.000	-.479	-.178
Constipation	-.207	.101	-.257	-2.057	0.044	-.409	-.178
Diarrhoea	-.254	.139	-.229	-1.826	0.073	-.532	.024
Financial difficulty	-.149	.064	-.287	-2.320	0.024	-.277	-.020

Table V: Multinomial Logistic Regression test

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
Model	B	Std. Error	Beta		
(Constant)	86.005	4.461		19.279	.000
Fatigue	-.101	.121	-.129	-.838	.406
Nausea	.227	.163	.219	-.838	.406
Pain	-.091	.105	-.137	-.869	.389
Dyspnoea	.054	.108	.062	.500	.619
Insomnia	-.026	.101	-.041	-.256	.799
Appetite loss	-.345	.110	-.516	-3.147	.003
Constipation	-.063	.117	-.078	-.537	.593
Diarrhoea	.025	.139	.023	.183	.855
Financial difficulty	-.099	.062	-.192	-1.604	.115

The influence of ethnicity on symptoms/problems is another interesting and important finding that we indentified in our multiracial cohort. Indian patients were found to have more severe fatigue and pain if compared to Chinese and Malay patients. There are many studies showing that pain thresholds are different among different ethnic groups; some authors attribute it to different socio-cultural background[20-21] whereas others proposed that the difference is due to physiological variations[22]. Nevertheless, the perception is real and it should be encountered individually so that patients' QOL can be improved.

CONCLUSION

In conclusion, majority of our patients had good QOL which is comparable to other studies. Nevertheless, QOL of a small group of patients is still not optimum. Active participation and contribution from dietitians as part of the multi-disciplinary team during HSCT should be extended to post HSCT patient care since appetite loss is an independent risk factor for QOL among our patients.

LIMITATION

The sample size in this study is small even though two third of the total estimated survivors were recruited. Therefore, collaboration with other HSCT canters in Malaysia is essential in future study.

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