ORIGINAL ARTICLE

Functional Status and Health-Related Quality of Life in Patients with Primary Intracranial Tumour

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SUMMARY

This study aimed to evaluate the functional status and HRQoL in patients with primary intracranial tumours in Malaysia. Karnofsky Performance Scale (KPS) and Modified Barthel Index (MBI) were used to assess the functional status whereas EORTC core Quality of Life Questionnaire (QLQ-C30) and Brain Cancer Module (BN-20) questionnaires were used to assess the HRQoL. Thirty-eight patients with primary intracranial tumours admitted for surgery in University Malaya Medical Center were recruited. These assessments were administered before surgery (baseline) and six months after surgery (follow-up). All patients received some form of rehabilitation interventions after surgery. The global HRQoL and functional status of these patients showed improvement at six months after surgery. Emotional Functioning score showed the greatest improvement among the functional domains (63 vs 86, p=0.003). Reduction in symptom burden such as fatigue, nausea, vomiting, pain and headache were also noted at follow-up together with less future uncertainty (p<0.05). Pearson correlation revealed statistically significant positive correlation between functional status and HRQoL at baseline and follow-up, in particular, global health status (r=0.50 and r=0.67), physical functioning (r=0.53 and r=0.90) and role functioning (r=0.34 and r=0.77). Thus, from the correlation found, improving a patient's function and independence level throughout all stages of care, even before any surgical intervention is offered would improve the HRQoL concurrently.

KEY WORDS:
Primary Intracranial Tumour, Functional Status, Quality Of Life, Rehabilitation

INTRODUCTION

Functional impairment of patients with primary intracranial tumours can occur at any point in the diagnostic and therapeutic continuum. It is usually a direct result of the disease at the time of diagnosis although it is frequently associated with treatment-related sequelae during therapy. They are caused, amongst others, by focal neurological deficits, cognitive dysfunctions, poor emotional well-being and high symptom burden although these factors are well-documented to have varying effects on patients' overall wellbeing and health-related quality of life (HRQoL)[1-5].

Improving the functional status of patients with intracranial tumours may benefit the overall HRQoL. Earlier studies measured functional status, especially the physical functioning, as a surrogate to HRQoL outcome in patients with intracranial tumours[5]. However, quality of life is a far greater issue than is reflected in the physical performance status. The effects of tumour on a patient's HRQoL were not fully reflected when the cognitive, emotional and social components are excluded[6]. Therefore, current studies incorporate multidimensional HRQoL outcome in addition to functional status measured.

For patients requiring surgical interventions, the relationship between functional status and HRQoL can be assessed at different levels of care. Often, the relationship between function and HRQoL is examined after surgical intervention and patients with poor functional status are noted to have a significantly lower global HRQoL than those with better functional status[5]. It is not widely known if correlation exists between functional status and HRQoL throughout the whole spectrum of patient care, especially before any surgical procedure is performed.

The purpose of the current study was to document the functional status and describe the HRQoL in patients with primary intracranial tumours. The instruments used were European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30), together with a supplemented brain tumour specific questionnaire, Brain Cancer Module (BN-20)[7]. We also examined the correlation between functional status and HRQoL at two levels of care, before surgery and six months after surgery. In addition, since there is limited published data on HRQoL in patients with primary intracranial tumour in Malaysia, understanding the HRQoL from a local perspective can assist us in future treatment planning and rehabilitation strategies of the patients during pre-operative and post-operative care.

MATERIALS AND METHODS

This is a prospective study conducted in University Malaya Medical Centre (UMMC), a tertiary hospital situated in an urban area in Malaysia. All adult patients, aged 18 years and older, were selected when they were admitted for surgery in UMMC's neurosurgical unit from June 2009 to May 2010. The patients were included in the study if they were diagnosed

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pre-operatively to have primary intracranial tumour based on imaging, had no previous surgical intervention for the tumour, were able to provide informed consent and were able to complete the HRQoL questionnaires or have a proxy available if they were unable to complete the HRQoL questionnaires themselves. Patients with metastases, recurrent tumour or whose final histological diagnosis was not tumours were excluded from the study.

Data for socio-demographic characteristics, tumour histological types and types of treatment were recorded. Histological grading of the tumour was based on the World Health Organization classification system[8]. All patients with primary intracranial tumours regardless of the histological diagnoses were assessed together due to the time constraint of the study duration. There was also a relatively low incidence of primary intracranial tumours at our centre during the study period thus categorizing the patients into different histological diagnoses may further reduce the number of patients in each group. Assessments of HRQoL and functional status were carried out at two intervals, at baseline (before surgery) and at six months after surgery. All patients were referred for rehabilitation and received some form of rehabilitation intervention and multidisciplinary care immediately after surgery.

Study instruments

Two HRQoL questionnaires and two functional status assessment scales were used in this study. The questionnaires used were QLQ-C30 version 3.0 and BN-20. Both questionnaires have been validated by the EORTC group to have adequate reliability and validity when used in assessing HRQoL of brain cancer patients in international studies[7, 9]. However, there is limited data on the reliability and validity of the instruments in the Asian context[10]. The functional assessment scales used were Modified Barthel Index (MBI), a generic functional assessment and Karnofsky Performance Scale (KPS), a specific functional assessment for patients with cancer[11-13].

QLQ-C30 is a 30-items questionnaire developed for assessing the HRQoL of cancer patients. The instrument has multidimensional coverage and being available in 81 translated and validated languages, it is fast becoming the commonly used assessment worldwide[7]. QLQ-C30 consists of both single-item and multiple item scales. The questionnaire is composed of global health status (2 items), 5 functional scales: physical functioning (5 items), role functioning (2 items), emotional functioning (4 items), cognitive function (2 items) and social functioning (2 items); and 9 symptoms scales: fatigue (3 items), nausea and vomiting (2 items), pain (2 items), and 1 item each of dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties[14].

BN-20 is a 20-items questionnaire specifically supplemented for patients with brain tumour[15]. It is grouped into 4 domains and 7 single items assessing disease symptoms, side effects of radiation and chemotherapy and specific psychosocial issues of relevance to patient with brain cancer. The domains assessed are future uncertainty (4 items), visual disorder (3 items), motor dysfunction (3 items) and communication deficits (3 items). The 7 single item assessments are headaches, seizures, drowsiness, hair loss, itchy skin, weakness of legs and bladder control.

Assessment methods and analysis

Two designated clinicians were assigned to assess patients' functional status and HRQoL.

All items in both QLQ-C30 and BN-20 were scored on a linear scale of 0 – 100 with higher scores representing higher response levels. For QLQ-C30, a high score for global health status represents a high QoL, a high score for functional scale represents a high level of functioning but a high score for symptom scale or item represents a high level of problem or symptomatology. In BN-20 the scoring algorithm is similar to QLQ-C30. A higher score of the scales and single items represents worse QoL. The details of the study instrument and scoring algorithm are explained in the EORTC QLQ-C30 scoring manual[7].

MBI and KPS are both ordinal scales from 0 to 100. MBI measures 10 aspects of personal activities of daily living including feeding, dressing, toileting and mobility[11,12]. KPS measures a patient's ability to carry on his daily activities and degree of dependency on nursing care which is used specifically for patient with cancer. It is scored at 10 unit intervals[13]. A higher score represents a lower dependency level and a lower score represents a higher dependency level in both MBI and KPS.

For the purpose of comparing HRQoL, patients were divided into two groups. Patients with MBI score of 100 or KPS score of 80-100 were grouped as "independent" representing patients who were independent in performing activities of daily living. Patients with MBI score of less than 100 or KPS score of less than 80 were grouped as "dependent" representing those who needed assistance in activities of daily living. This study has been approved by the UMMC medical ethical committee and the BN-20 user's agreement was completed and returned to the co-ordinator of the EORTC Quality of Life group prior to the start of this study.

Data were analysed using SPSS 17.0. The internal consistency (reliability) of the QLQ-C30 and BN-20 were assessed using Cronbach's coeficient α. Non parametric tests were used with Wilcoxon Signed Rank test for comparing baseline and follow up data and Mann-Whitney U test to compare different functional groups. Pearson correlation was used to identify if any correlations exist between the functional and HRQoL scales. p values <0.05 were considered to be statistically significant.

RESULTS

Patient population and tumour characteristics

Thirty-eight patients (74.5%) were recruited into this study from the initial 51 eligible patients. Thirteen patients did not participate due to patient refusal (three patients), inability to give consent in the severe cognitively impaired patients due to no proxy (four patients) and failure of administrative staff to inform admission (six patients). The patients' characteristics are shown in Table I.

Seven patients (18.4%) completed the baseline questionnaires with the help of a proxy. At six months, 32 patients (84.2%) completed the follow-up questionnaires. Five patients died and one patient refused to participate, stating that he had fully recovered. Three patients (9.4%) completed the follow-up questionnaires with the help of a proxy.

Psychometric properties of the QLQ-C30 and BN-20

The mean values and internal consistency estimates (Cronbach's α) of QLQ-C30 and BN-20 for all the patients were reasonable (α > 0.70) at baseline and at follow up after six months, except for cognitive functioning. (Table II)

HRQoL and functional status

There were statistically significant improvements in the patients' emotional and cognitive functioning, future certainty, symptoms of fatigue, nausea, vomiting, pain and headache in the HRQoL score from baseline to six months follow-up. However, there was no statistically significant change in median scores between baseline and follow up in functional status measured by the KPS and MBI (Table III). Despite no significant change in median scores, analysis of individual patient's KPS and MBI score showed that the majority of patients improved their functional status at six months (Figure 1).

KPS and MBI correlated well with the majority of the QLQ-C30 scales and some items in BN-20 at baseline and follow-up. There were statistically significant positive correlations for global health status, physical, cognitive, social and role functioning; whereas motor dysfunction, leg weakness, constipation, drowsiness and bladder control exhibited inverse correlation when measured at both instances. Other symptoms with significant correlations only at baseline were diarrhoea and seizure. Symptoms of fatigue, pain and appetite loss showed significant correlations only at six months follow-up.

Patients who were dependent had a lower global quality of life at both baseline and at six months follow-up compared to independent patients. They also reported worse physical, role and social functioning. Both groups of patients reported fatigue at six months follow-up on the QLQ-C30 symptom scale. Using the BN-20, the most commonly reported domains at baseline were motor dysfunction by dependent patients and headache in independent patients. At six months follow up, visual disorder and drowsiness were common in both groups of patients.

Table I: Socio-demographic and clinical characteristics of the patients with primary intracranial tumours (n=38)

Sociodemographic	**No. (%)**
Gender	
Male	15 (40%)
Female	23 (60%)
Age in years	
≤ 45	19 (50%)
> 45	19 (50%)
Ethnicity:	
Malay	16 (42%)
Chinese	18 (47%)
Indian	4 (11%)
Marital status:	
Single	9 (24%)
Married	29 (76%)
Occupation:	
Employed	21 (55%)
Unemployed	17 (45%)
Clinical characteristics	**No. (%)**
Tumour types	
Glioma	3 (8%)
Meningioma	12 (32%)
Schwannoma	4 (10%)
Adenoma	8 (21%)
Others	11 (29%)
Surgical intervention:	
Biopsy	6 (16%)
Total resection	17 (45%)
Subtotal resection	15 (39%)
Adjuvant therapy:	
Chemotherapy	3 (8%)
Radiotherapy	1 (3%)
Combination	2 (5%)
Nil	32 (84%)
Baseline functional status	
According to KPS:	
Independent	18 (47%)
Dependent	20 (53%)
According to MBI:	
Independent	15 (39%)
Dependent	23 (61%)

Footnote: KPS: Karnofsky Performance Scale, MBI: Modified Barthel Index

DISCUSSION

In this study, the global HRQoL and functional status of patients with primary intracranial tumours showed improvement at six months after surgery. There was also improvement in majority of the symptom burden previously reported by the patients at baseline. The most prominent improvements were for fatigue, nausea, vomiting, pain and headache. These symptoms have been associated with poor HRQoL in previous related studies involving patients with primary intracranial tumours[16]. In particular, fatigue has been one of the leading symptoms for decreasing quality of life[17-19]. Identifying the symptom burden in patients with primary intracranial tumour especially symptoms of fatigue, nausea, vomiting and headache should be initiated at the early stage of management even before surgical intervention. As evidenced from this study, the symptoms do not appear in isolation and they can improve significantly with surgical intervention and a comprehensive management, thus improving the overall HRQoL.

All patients in this study were referred for rehabilitation and received some form of rehabilitation intervention post-surgery either as inpatient or outpatient therapy. Although we did not specifically look into the intensity and duration of rehabilitation the patients received, functional and HRQoL gains could be partly contributed from the coordinated multidisciplinary care post-surgery. Evidence for effectiveness of rehabilitation after primary brain tumours are favourable in previous studies[20,21]. Patients received inpatient rehabilitation care after surgery showed significant functional gains and symptoms such as fatigue, pain and headache are better managed[21].

Table II: Mean and internal consistency estimates (Cronbach's α) of both QLQ-C30 and BN-20 at baseline and follow up

	Baseline (n=38)		Follow up (n=32)	
	Mean (SD)	α	Mean (SD)	α
QLQ-C30				
Global health status	47.1 (22.9)	0.87	56.5 (26.8)	0.91
Functional scales:				
Physical	63.2 (28.2)	0.82	66.0 (30.9)	0.89
Role	52.6 (34.1)	0.70	66.7 (36.9)	0.86
Emotional	57.5 (32.5)	0.88	80.5 (25.5)	0.91
Cognitive	52.2 (32.5)	0.62	62.5 (29.0)	0.32
Social	62.3 (33.3)	0.80	60.4 (35.9)	0.76
Symptoms scales:				
Fatigue	52.0 (25.7)	0.59	38.9 (31.4)	0.88
Nausea and vomiting	19.3 (31.4)	0.85	4.2 (13.4)	0.91
Pain	45.6 (34.2)	0.71	21.9 (25.9)	0.65
BN-20				
Future uncertainty	40.8 (27.3)	0.69	28.6 (29.0)	0.89
Visual disorder	30.1 (28.9)	0.78	35.4 (36.2)	0.91
Motor dysfunction	37.7 (31.4)	0.81	26.4 (31.4)	0.87
Communication deficit	14.0 (18.2)	0.65	19.4 (34.0)	0.95

Footnote: For QLQ-C30: Higher score for global health status and functional scales indicates a better level of functioning and higher scores for symptoms scales indicates a higher level of symptoms. For BN-20: Higher score indicates worse quality of life.

Table III: Functional status and health-related quality of life (HRQoL) of patients with primary intracranial tumours (n=32) measured before surgery (baseline) and six months after surgery (follow up)

	Baseline Median (IQR)	Follow up Median (IQR)	p
Functional status			
KPS	75 (53-80)	80 (60-80)	0.088
MBI	98 (59-100)	100 (85-100)	0.122
HRQoL			
1) QLQ-C30			
Global health status	50 (35-67)	58 (42-75)	0.095
Functional scales:			
Emotional	63 (27-90)	86 (75-100)	0.003**
Cognitive	50 (22-83)	67 (50-83)	0.030*
Symptoms scales:			
Fatigue	56 (36-75)	29 (14-56)	0.030*
Nausea and vomiting	0 (0-33)	0 (0)	0.007**
Pain	50 (4-79)	16 (0-33)	0.002**
2) BN-20			
Future uncertainty	42 (17-65)	17 (8-46)	0.033*
Headaches	33 (0-67)	0 (0-33)	0.007**

Footnote: Only statistically significant results of the Functional and Symptom scales in QLQ-C30 and BN-20 are shown in Table III.
IQR: Interquartile range; *0.01≤p≤0.05, **p<0.01.
KPS: Karnofsky Performance Scale
MBI: Modified Barthel Index

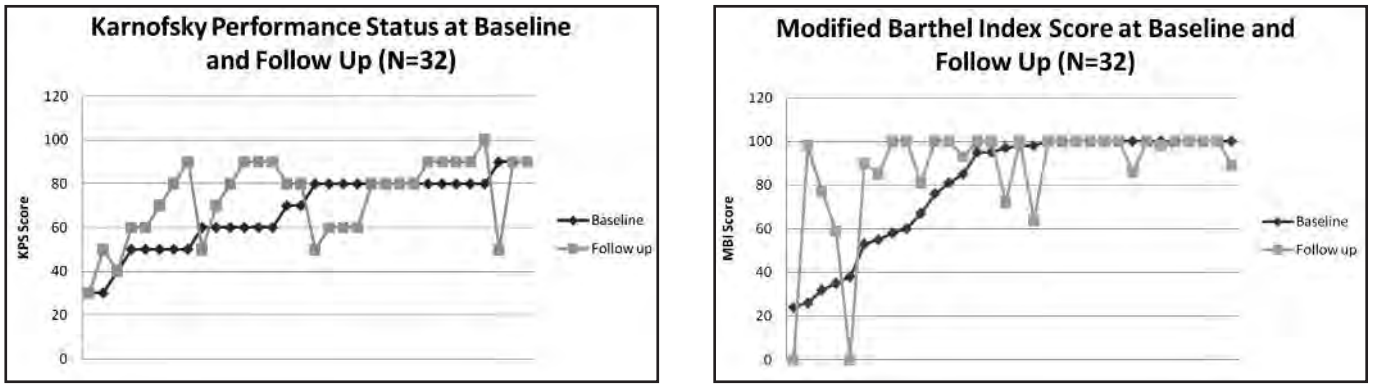

Fig. 1 : Karnofsky Performance Scale (KPS) and Modified Barthel Index (MBI) score for each patient who completed the study.

The domains in the functional scales that were severely compromised when measured at baseline were components of the Role Functioning, Cognitive Functioning and Emotional Functioning. These components showed improvement at six months after surgery with Emotional Functioning scores showed the greatest improvement. However, we found that dependent patients have greater emotional gains compared to the independent patients. This observation is in contrast with the finding by Osoba *et al.*[5], which showed better emotional functioning improvement for the independent group. The authors believe one of the reasons for the finding in this study could be due to the different functional and social expectations of the independent patients who are largely young and employed before the surgery compared to the dependent patients. As psychological issues are often overlooked in independent patients, future studies need to look into the emotional component of this group of patients.

Majority of the patients reported better functional status at follow-up, nevertheless, this improvement was not statistically significant when we analyzed using the mean scores of both KPS and MBI. The mean MBI baseline score was already near the upper limit and thus, potential of a ceiling effect to the MBI score improvement at follow-up could not be ruled out. Despite the lack of statistically significant improvement in the mean MBI score, the significant correlation noted between functional status and HRQoL can emphasize the importance of having good functional status in order to have better HRQoL. Thus, improving a patient's function and independence level before any surgical intervention is offered and throughout all stages of care should be emphasized in the management of patients with primary intracranial tumours.

The limitation of this study includes a small number of respondents due to time constraint, however the compliance rate in this study (84% at follow-up) was in keeping with the experience in other cancer studies[5,22]. Although the number is small, we believe this study adds to the information on this subject to those involved in the care of patients with intracranial tumors requiring surgery in Malaysia.

Future studies with a larger sample size should be conducted to ascertain a better understanding of the HRQoL in dependent and independent patients with different types of primary intracranial tumours. Apart from recruiting a larger number of patients, future studies should also focus on confounding factors which could affect either the functional status or the HRQoL such as the patient's cultural beliefs, socioeconomic backgrounds, premorbid comorbidities and the availability of a structured multidisciplinary care after surgery. In conclusion, patients with primary intracranial tumours have an improved functional status and HRQoL when assessed at six months after surgery and a coordinated rehabilitation care.

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