

Gender Difference in Quality of Life among Brain Tumor Survivors

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Abstract

Background: Gender differences and long-term consequences of brain tumor on quality of life (QOL) have been sparsely studied.

Methods: QOL measures were assessed in 81 consecutive brain tumor patients who had survived for 5-7 years after surgical treatment. Of these patients, 22 % had gliomas, 51 % had meningiomas, 16 % had acoustic neurinomas and 11 % had pituitary adenomas. The QOL measures were the Karnofsky Performance Scale (KPS) and the Health Measurement Questionnaire (HMQ).

Results: Female patients with gliomas had significantly more distress as measured by the HMQ and significantly worse functional state in terms of the KPS compared to patients with other tumors, while among male patients there were no differences between tumor groups. Significant gender differences between the genders were found in the feeling of sadness and depression, anxiety and worry, and dependence on others, and furthermore among the female patients, those with gliomas differed strongly from those with other types of tumors.

Conclusions: Females tend to report worse QOL and more distress compared to males. Worse QOL in females with brain tumors can be a sign of more profound suffering.

Introduction

Many earlier studies have documented worse quality of life (QOL) in female patients compared to male patients. Gender differences have been found for instance in cardiac patients and cancer patients, as well as among stroke survivors [1-3].

There are some investigations on quality of life among brain tumor patients but gender difference has been sparsely studied [4-9]. Weitzner and coworkers (1996) evaluated a group of 50 patients with primary brain tumors and found that five factors adversely affected QOL, among other things, female gender and poor performance status [10]. Further, long-term quality of life studies among brain tumor patients are mainly lacking [8].

Our research group has also reported gender differences in QOL among brain tumor patients in another prospective study of 101 patients with primary brain tumors. Females had lower QOL in Sintonen's 15D measure [11] at three measurement points (before operation, at 3 months and at 12 months) compared to males. Worse QOL among female patients was associated with depression [12].

The aim of the present study was to evaluate long-term consequences of brain tumors and to examine gender differences in QOL in long-term brain tumor survivors. By using the present database we had the possibility of studying gender difference at 5-8 years after surgery. Our aim was also to validate our earlier findings of gender differences by using a separate database and other QOL measures.

Material and Methods

Patients

The basic series consisted of a geographical cohort of 191 consecutive patients (age ≥ 16 years) operated for brain tumor at the Department of Neurosurgery of Oulu University Hospital during the years 1983-1986. Survival rates were confirmed by checking the date and cause of death from official death certificates.

Of operated patients 118 patients were still alive at follow-up. All of them received a postal inquiry that included questionnaires concerning QOL and socio-demographic background. The Health Measurement Questionnaire HMQ [13] was properly filled out by 91 patients (77%). The Karnofsky Performance Scale could be assessed in 88 patients (75%) [14,15]. The follow-up was done 5-8 years after operation (median 6.00 years, range 5.01-7.96 years).

All tumor diagnoses were dated from biopsy or resection and then histologically reconfirmed by the same neuropathologist (R.H.). Tumors were classified and graded according to the WHO classification [16]. For statistical purposes tumors were gathered into larger groups according to the tumor type. We focused our study on 1) Gliomas Grades I-IV, 2) Meningiomas, 3) Acoustic neurinomas, and 4) Pituitary adenomas. The group of other tumors consisted of histologically single tumors and has been left out from further analysis (7 tumors).

In the final series there were 81 patients: 18 patients (22%) had gliomas (56% females), 41 patients (51%) had meningiomas (73% females), 13 patients (16%) had acoustic neurinomas (62% females) and 9 patients (11%) had pituitary adenomas (33% females). There were no statistically significant gender differences between males and females in any of the tumor groups.

The sample of the present study (81 patients) did not differ

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Received March 28, 2011; Accepted July 20, 2011; Published July 28, 2011

Citation: Niemelä A, Koivukangas J, Herva R, Hakko H, Räsänen P (2011) Gender Difference in Quality of Life among Brain Tumor Survivors. J Neurol Neurophysiol 2:116. doi:10.4172/2155-9562.1000116

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statistically significantly from the rest of the sample (37 patients), which were excluded from this study, in respect to gender (present study vs. attrition: males, 37% vs. 46%, $p = 0.0359$), employment status (employed, 36% vs. 25%, $p=0.405$), marital status (married, 73% vs. 50%, $p=0.083$) and age (46.1 years vs. 46.2 years, $p=0.959$). The type of tumor did not also differ between the study sample and attrition group ($p=0.001$). In the attrition group the type of tumor was distributed as follows: 8 (28%) gliomas (38% females), 15 (52%) meningiomas (60% females), 2 (7%) acoustic neurinomas (all females) and 4 (11%) pituitary adenomas (50% females).

Outcome measures

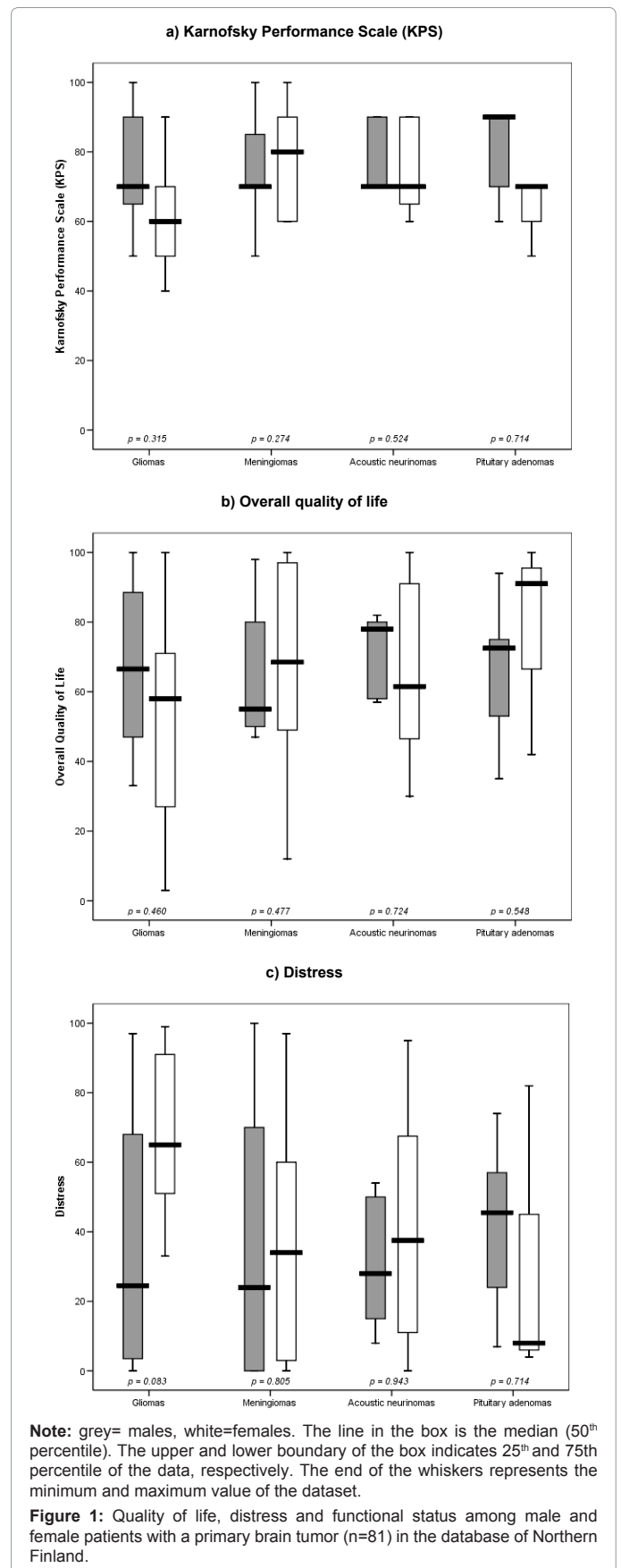
Karnofsky Performance Scale (KPS): The KPS is an ordinal scale of functional status that categorizes the patients from 0 (dead) to 100 (healthy) at 10 unit intervals. KPS is rated by the physician. The assessment of KPS scores was based on information from hospital files and postal inquiry. The KPS emphasizes the presence of symptoms, ability to work, physical activity and self care [11,12]. The KPS was assessed from patient files and the postal inquiries. In postal inquiries were asked ability to work and reason for changing the work or reason for inability to work, an ability to take care of home, need for assistance or need for aid. Neurological signs and symptoms were reviewed from hospital files and compared to the replies of the patients in postal inquiries. Comparisons and assessment of the KPS were made by one of the authors (AN).

Health Measurement Questionnaire (HMQ): The quality of life measure used in the study is called the HMQ [13]. It is a self-completed questionnaire, which includes five categorical assessments of disability in terms of general mobility, self-care, usual activities and social and personal relationships. The questionnaire also contains 16 items of feelings relating to distress in different health states. These items and the distress and overall QOL are measured with a visual analogue scale (VAS). Each item was valued on a 100 mm line, where 0 at the left end means no distress at all and 100 at the right end extreme distress [13]. The HMQ has been found to be a useful measure of generic health status in psychiatry settings [17,18]. The HMQ has been found to be a reliable tool for assessing quality of life among medical patients [13].

Statistical analysis: The QOL and KPS outcomes were analyzed using the mean values. Because of the skewed distribution of the QOL and KPS, non-parametric tests were used to assess the statistical significance of the measures (Mann-Whitney test). In case of categorical variables the relationships between different variable classes were tested with the X^2 test. All statistical analyses were performed by using SPSS for Windows version 15.

Variables	Males (n=30) % (n)	Females (n=51) % (n)	Gender difference P-value
<i>Psychosocial factors</i>			
Marital status			1.000
Married/cohabiting	73% (22)	73% (37)	
Not married	27% (8)	28% (14)	
Employment status			1.000
Employed	37% (11)	35% (18)	
Not employed	63% (19)	65% (33)	
Age in years, mean (S.D.)	43.8 (13.6)	47.5 (11.2)	0.192
Gliomas	31.6 (8.7)	47.9 (11.8)	0.005
Meningiomas	53.2 (12.9)	47.7 (11.0)	0.175
Acoustic neurinomas	49.4 (5.7)	48.0 (11.7)	0.809
Pituitary adenomas	38.0 (12.4)	42.0 (15.9)	0.687

Table 1: The socio-demographic characteristics of the patients with a primary brain tumor at five years after the surgery.



	Tumor category				p - value	Statistical difference between tumor categories, adj. p-value					
	GLI	ME	AC	PA		GLI/ ME	GLI/ AC	GLI/ PA	ME/ AC	ME/ PA	AC/ PA
KPS	60 (50-70)	80 (60-90)	70 (65-90)	70 (60-70)	0.032	0.038					
QOL	58 (27-71)	69 (49-97)	62 (47-91)	91 (67-96)							
Distress	65 (51-91)	34 (3-60)	38 (11-68)	8 (6-45)							
Feeling sad or depressed	46 (15-71)	0 (0-22)	0 (0-24)	7 (4-21)	0.014	0.012	(0.059)				
Tiredness	67 (51-89)	0 (0-23)	0 (0-2)	75 (46-88)	0.000	0.001	0.004		(0.064)	(0.054)	
Incontinence	33 (0-69)	0 (0-0)	0 (0-0)	0 (0-10)	0.010	0.006					
Feeling dependent on the other people	47 (10-92)	0 (0-31)	0 (0-28)	32 (16-58)	0.028	0.028					
Difficulty of concentration	24 (22-28)	0 (0-13)	0 (0-26)	18 (11-24)	0.049	0.068					
Memory disturbance	66 (56-76)	13 (0-39)	3 (0-20)	81 (41-89)	0.016	(0.066)	0.024				

GLI = Gliomas, Men = Meningiomas, PA = Pituitary adenomas, AC = Acoustic neurinomas

KPS = Karnofsky Performance Scale, QOL = Quality of Life

Values are median (IQR, interquartile range) if not otherwise stated

* Non-parametric Kruskal-Wallis one-way ANOVA test with pairwise differences corrected for multiple comparisons, two-sided tests

Table 2: Median (IQR) values of quality of life related variables in different tumor categories of brain tumors for females. Table 2 shows the mean values of the quality of life variables by different tumor categories for females. Only those results which showed statistically significant differences among patients in different histological subgroups are shown. In Table 2 the data is shown only for females, because among male brain tumor patients there were no statistical differences in quality of life variables.

Results

Female patients with gliomas were significantly older ($p = 0.004$, Mann-Whitney test) than male ones (48 ± 12 years vs. 32 ± 9 years, respectively); otherwise there were no significant differences in socio-demographic variables between the genders (Table 1).

When socio-demographic characteristics of the patients were compared separately by gender, female patients had no significant differences in socio-demographic characteristics between the tumor groups. Male patients with gliomas were younger (32 ± 9) than male patients with meningiomas (53 ± 13 , $p = 0.001$) and acoustic neurinomas (49 ± 6 , $p = 0.039$). There was also a tendency of older age in males with pituitary adenomas (38 ± 13) compared to those with meningiomas ($p = 0.052$; Mann-Whitney test).

The KPS and overall measures of QOL and distress in the HMQ were chosen to be the primary outcome measures of QOL. When all tumors were examined together, there were no significant differences between the genders. Tumors were then divided into histological subgroups and then the QOL of the genders was studied (Figure 1). Female patients with gliomas and with pituitary adenomas seemed to have lower KPS scores than did males. Female patients with gliomas also seemed to have poorer QOL and more distress. However, the differences between the genders were not statistically significant.

Then, the primary outcome measures were examined between tumor groups separately for males and females. Results showed that in females there was a statistically significant difference in the KPS ($p = 0.032$, Mann-Whitney test) between the tumor groups. In males there were no significant differences between the tumor groups in any of the primary outcome measures.

In specific items of the HMQ, when patients were studied as a single group, significant gender differences were seen in feeling sad or depressed ($p = 0.044$), in feeling anxious or worried ($p = 0.029$) and in feeling dependent on others ($p = 0.051$) (Mann-Whitney test). When the histology of the tumors was taken into account, further analysis showed that these gender differences were in patients with gliomas, but not in those with other types of tumors.

When the data was examined again separately for males and females, the result was that in males there were no significant differences between the tumor groups. Among female patients differences between the tumor groups were significant in feeling sad or depressed ($p =$

0.014), tiredness ($p = 0.000$), incontinence ($p = 0.01$), feeling dependent on others ($p = 0.028$), difficulty of concentration ($p = 0.049$), and memory disturbance ($p = 0.016$) (Mann-Whitney test).

Discussion

The purpose of our study was to elucidate gender differences and long-term consequences of the brain tumor in terms of QOL. By using the present database we had the possibility of studying gender differences in quality of life at 5-8 years after surgery. One of the main issues in the outcome studies has been the question of using general or disease-specific measures. It has been said that generic measures are necessary to compare outcomes across different populations and interventions, particularly for cost-effectiveness studies. Disease-specific measures assess the special states and concerns of diagnostic groups. Patrick and Deyo [19] further stated that specific measures may be more sensitive for the detection and quantification of the small changes that are important to clinicians or patients.

In the present study, general measures of QOL, namely the KPS and items of overall QOL and distress in the HMQ, showed no differences between the genders. More specific items measuring QOL in the HMQ showed that female patients felt sadness and depression, anxiety and worry, and dependence on others more than did males. These differences reflected suffering especially in female patients with gliomas. Among male patients there were no differences between the tumor groups in the KPS or in any of the items of the HMQ.

We found that female brain tumor survivors with glioma were older compared to males in this diagnostic subgroup. Former studies have found that older adult brain tumor patients have reported lower functional well-being and poorer neurocognitive functioning than younger adults. For example, support from friends was a significant predictor of QOL for younger adults, whereas the capacity to continue enjoying life was a significant predictor for older adults [20]. On the contrary, among meningioma survivors younger patients have poorer QOL in levels of cognitive performance and satisfaction of life. As a major problem, younger patients described an inability to accept having this severe disease as a young person [21].

Recently Tsay et al. [22] found that both distress and depression were significantly related with decreased quality of life among patients with a benign brain tumor at one month after surgery but they didn't report gender differences and the follow-up period was only a month.

The results of studies on the relationship between QOL scores and gender have been mixed [8]. However the present study is in line with the former studies of worse quality life among female patients with a primary brain tumor [7,9,23]. These studies didn't explain the etiology of this gender difference. It has been suggested that predisposition of gender as a risk factor for worse QOL is not disease-specific phenomenon [23]. Quality of life studies among patients with coronary heart diseases, inflammatory bowel diseases and other malignancies than brain tumors have reported decreased QOL among females [24-26].

According to the present results it seems that females and males score differently some aspects of their QOL such as depression and dependence on others.

The main hypothesis for worse QOL among female patients is that female patients have more psychiatric symptoms, usually depression, which correlates with worse QOL [7]. We suggest that females with primary brain tumors need specific interventions to enhance their quality of life during the many years that they survive with normal life after tumor treatment. Formerly, among cardiac female patients group support and sense of belonging were suggested to be factors to improve quality of life in this patient group [24,25].

Psychosocial intervention methods for brain tumor patients should include treatment with antidepressants and psychotherapy [11]. The main psychological methods have to consist of psychotherapy with supportive elements and psycho-educational techniques. By supportive therapy the patient's productive coping strategies are strengthened. In a dynamic approach of individual psychotherapy the patient is helped to bring meaning to the illness [28]. However, studies focusing on effective psychotherapy for depression among brain tumor patients are rare [29]. Thus, further work is needed to determine the most efficient treatment modalities for depression in brain tumor patients and whether the effect of adequate therapy will increase the QOL among patients.

The major limitation of the present study is that the long-term follow-up data was collected in 1991. While results of surgery and adjuvant treatment of brain tumor patients have improved, the QOL issues confronting long-term survivors of especially gliomas are still the same because these patients cannot be definitively cured. The number of patients in the present extensive database is comparable to those of other QOL studies involving brain tumor patients. One of its strengths is that the data has been collected from a geographical cohort of consecutively operated patients. The follow-up concentrated on the quality of life of patients 5-8 years after surgery, giving a rather homogenous group in terms of survival. Also, from a methodological point of view, since several statistical tests were performed, some possibility of chance findings (type I error) exists, but due to the small number of cases in some of the subgroup analyses a certain degree of type II error may also have occurred. In addition, measurement bias in KPS is possible even though we have tried to minimize this kind of error. KPS scores have been gathered from hospital files and postal inquiries at the same time and by the same author.

The present study confirms differences in QOL between genders in patients with primary brain tumors. The background of worse QOL among female brain tumor patients is suggested to be depression. There is no RCT (Randomized Controlled Trials) evidence for treatment of depression among this patient group. Also, in future there will be more population studies of brain tumor survivors [8]. Treatment of psychosocial aspects of QOL among brain tumor patients deserves

special attention in further research.

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