

Stress and long-term survivors of brain cancer

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Abstract

Introduction Adult brain tumor patients are joining the ranks of cancer survivors in increasing numbers in the United States. As a result, health care providers are faced with new challenges to address the need for psychosocial support in this population.

Methods Using the Perceived Stress Scale and the National Comprehensive Cancer Network's Distress Thermometer, levels of stress and cancer-related items of concern were assessed in adult long-term survivors of brain cancer.

Results Sixty-one percent of the sample population experienced elevated levels of stress. Scores were not significantly associated with age, gender, treatment status, or tumor grade. Long-term survivors were just as likely to report being stressed ($\chi^2=0.032$, NS), while reporting fewer numbers of items of concern (5.02, SD=3.509), compared to brain tumor patients diagnosed <18 months ($M=6.82$, SD=3.737, $t=2.467$, $p<0.05$).

Discussion/conclusion Despite their long-term survival status, long-term survivors of brain cancer continue to experience elevated levels of stress. Predictors of stress in this population are related to familial, emotional, and practical concerns. While the scientific community continues to examine the specific impact of stress on both the physical and mental outcomes of cancer patients, understanding the sources of stress within cancer populations is key in designing targeted interventions to help patients manage the stress associated with this disease.

Implications for brain tumor survivors This study provides a better understanding of the unique needs of long-term survivors of brain cancer. An awareness of the sources and levels of stress experienced by this population could lead to the development of effective supportive care interventions to improve the quality of life of the survivor.

Keywords Stress · Brain cancer · Long-term cancer survivors

Introduction

Cancer survivors represent a rapidly growing segment of the population. The Institute of Medicine reports that more than ten million cancer survivors live in the United States today. [1, 2] Similar to data for other cancer populations, population-based Surveillance Epidemiology and End Results data indicate that the survival for adult patients with brain cancer has improved over the last three decades despite historically poor prognosis for patients diagnosed with a primary brain tumor. [3] As such, adult brain tumor patients are joining the ranks of cancer survivors.

From 1995 to 2001, the median range of survival for patients with WHO Grades I/II tumors was between 2 and 10 years depending on the type of tumor. [4] The median survival for patients with WHO Grades III/IV tumors was about 1 year. [5] Despite these dismal statistics, data suggest that cases are either being diagnosed at an earlier stage or that improvements in treatment have, at least partially, been responsible for increase in survival rates. [6] Today, the outcomes for brain cancer patients has improved, with the estimated 5- and 10-year relative survival rates for malignant tumors being 28 and 24%, respectively. [3] However, there is a large variation in survival between types of brain tumors. For example, the 5-year survival rates exceed

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85% for astrocytomas but are less than 5% for glioblastomas. [7] Given this variation, an encompassing definition of long-term survivorship was needed to begin to characterize the brain tumor population. As such, long-term survivorship among brain tumor patients has been characterized as 18 months or more after diagnosis. [8]

Research on long-term cancer survivors focuses primarily on the health and life of a person after the acute diagnosis and treatment phase. Factors such as time since diagnosis and treatment have been cited in the literature to mitigate the stress effects of cancer. [9] For many types of cancer, such as breast and colorectal, some sources of stress decline as the possibility of recurrence becomes less likely with time. [9] However, brain tumor patients are different; many patients who would be considered “long-term” survivors continue to receive treatment even 18 months post diagnosis. In addition, the fear of recurrence for brain tumor patients seems to increase with time instead of decreasing. [10]

A number of studies have identified significant acute psychological health-related problems associated with an adult brain tumor diagnosis and its subsequent treatment. Mood problems, including increased risk of depression, perceived stress, distress, sadness, anxiety, anger, and low self-esteem, which adversely affect activity and life satisfaction, have been cited in the literature. [11–13] While the long-term psychological effects of brain tumors have been studied in childhood survivors, few studies have looked at the long-term effects in adult survivors of brain cancer. [14–16] Like other cancer survivors, long-term survivors of brain cancer can experience a number of health related issues even after treatment. In addition, brain tumor patients frequently experience cognitive impairment that is associated with the tumor itself and/or its subsequent treatment, including surgery, radiotherapy (RT), chemotherapy, corticosteroids, and antiepileptics. [17] For those patients with relatively long survival times, the cognitive impairment and personality change can create a scenario of dementia and dependence.

Recent research on psychosocial concerns and interventions in the general cancer population calls for increased attention to issues specific to long-term survivors. A review of the literature by A.L. Stanton of psychosocial interventions describes the depth of the literature concerning interventions targeted at patients recently diagnosed or undergoing treatment for cancer and the paucity of attention to long-term survivors. The acute nature of distress and other psychological disturbances early in the cycle of cancer treatment demands attention. To date, interventions have had varying success. When focusing on distress, employing more experienced therapists to deliver interventions, and interventions of at least 12 weeks in length, yield the most significant positive results. [18] Stanton suggests that psychosocial interventions designed to address concerns specific to long-term survivors could be similarly effective.

To date, no study has assessed the levels of perceived stress in long-term survivors of brain cancer or has determined if their perception differs from other brain tumor patients. Elevated levels of stress has been shown to be a prevalent issue for brain tumor patients as well as for those diagnosed with other types of cancer. [11, 19–22] However, the severe functional, cognitive, and neuropsychological sequelae of the disease make patients with brain tumors particularly susceptible to stress and its negative effects. [11] Prolonged exposure to stress can lead to anxiety and depression. [11] Psychological stress may also have adverse physical manifestations including muscular aches and pains, heart palpitations, lowered immune function, sexual dysfunction, and problems with sleeping. Epidemiological, clinical, and experimental animal studies have shown that stress may influence the onset and progression of cancer. [23–25] In addition, studies have shown that stress might influence the development and metastasis of cancer via neuroendocrine suppression of the immune system, including decreased cytotoxic T-cell and natural killer cell activities. [23, 25, 26] In vitro and in vivo studies provide further information that stress enhances tumor angiogenesis and growth via increased expression and secretion of vascular endothelial growth factor. [27–29] Managing the stress long-term survivors of brain cancer experience is important due to its impact on a patient’s overall psychological and physiological health. Understanding the sources of stress in the long-term survivor population is important to address the supportive care needs and reduce the amount of stress these survivors experience.

Using the Perceived Stress Scale (PSS) and the National Comprehensive Cancer Network’s (NCCN) Distress Thermometer, we sought to: (1) evaluate the level of stress in an outpatient population of long-term survivors of brain tumors, (2) document the cancer related items of concerns of this population, (3) compare stress scores of patients based on time since diagnosis (<18 vs >18 months), and (4) explore the relationship between stress levels, total number of concerns, and patient demographics for each group.

Materials and methods

Subjects

The subject pool consisted of a convenience sample of 75 patients diagnosed with a primary brain tumor who were being followed by The Preston Robert Tisch Brain Tumor Center at Duke during the month of December 2006. The inclusion criteria for study participants were as follows: diagnosis of a primary brain tumor at ≥ 18 years of age, Karnofsky score ≥ 70 , and ability to speak, write, and understand English.

Procedure

Institutional Review Board approval was obtained before commencement of study. Data collection was conducted in conjunction with the patients' regularly scheduled neuro-oncology visit. Study participants were consented by a research assistant in a private room and were provided with instructions on how to complete the questionnaire. All study questionnaires were completed before the patients' interaction with the attending physician.

Assessment

Demographics Demographic information and medical data were collected using the patient's most recent medical note. The data included date of birth, gender, race, treatment regimen, tumor grade, date of diagnosis, treatment status (on vs off), and disease status (stable vs not stable).

Perceived Stress Scale The PSS is the most widely used psychological instrument for measuring the perception of stress. It is a measure of the degree to which situations in life are appraised as stressful. This 10-item scale was designed to determine how unpredictable, uncontrollable, and overloaded individuals find their life. The scale also includes a number of direct queries about current levels of stress. Scores from the PSS can range from 0 to 40 points. The mean threshold for stress in the general population is 12.1 and 13.7 for men and women, respectively. The PSS is a relatively brief measure and is completed in approximately 10 min. [30] The PSS-10 has been established as both a reliable and valid instrument ($r=0.85$).

Cancer related items of concern The NCCN's Distress Thermometer's cancer-related items of concern ask participants to designate which items from a 34-item list constitute sources of distress. The 34 items represent five categories of problems: physical, family, emotional, spiritual/religious, and practical. In addition, participants were asked about concerns pertaining specifically to brain tumor patients such as memory/cognition, seizures, and changes in vision, balance, and speech. The Distress Thermometer's 34-item list of concerns is a relatively brief measure and can be completed in approximately 5 min. [31–33]

Results

Demographics

The sample population consisted of a total of 75 brain tumor patients. Forty-two patients were long-term survivors (≥ 18 months since date of diagnosis), and 33 patients

(< 18 months since date of diagnosis) were used as a comparison group. In general, the majority of the sample population was Caucasian (97%) and male (63%). The median age of the sample was 49 with a range from 24 to 70 (Table 1, study demographics). Eighty-four percent of subjects were diagnosed with Grade III/IV tumors, eighty one percent had stable disease, and 79% were considered "on-therapy." Scores from the PSS were not significantly associated with age, gender, treatment regimen, or tumor grade. The sample population did not have sufficient numbers of patients that were either off therapy or had progressive disease to determine association with stress.

Stress

Results of a chi-square analysis indicated that long-term survivors were as likely to be categorized as "stressed" by

Table 1 Study demographics

Characteristics	Percent	Number
Age	Mean	50
	Median	49
	Range	24–70
Patient gender	Male	63 47
	Female	37 28
Race	Caucasian	97 73
	African-American	1 1
	Asian	1 1
Treatment	Surgery	95 71
	Radiation	83 62
	Chemotherapy	88 66
	Surgery and Radiation	80 60
	Surgery, Radiation and Chemotherapy	77 58
Therapy	On therapy	79 59
	Off therapy	21 16
Patient tumor grade	Grade I/II	16 12
	Grade III/IV	84 63
Status	Stable	81 61
	Not stable	19 14
	Date since diagnosis	1–3 months 5 4
Date since diagnosis	3–6 months	11 8
	6–12 months	16 12
	12–18 months	12 9
	18–24 months	8 6
	24–30 months	16 12
	30–36 months	32 24
	Mean	3.2 years
	Median	1.8 years
Range	10 days–22 years	
Survivors	<18 months	44 33
	≥ 18 months	56 42
Response rate	Yes	94 75
	No	6 5

Table 2 PSS by gender and date of since diagnosis

		Mean	Median	Range	“Stressed”
Men	<18 months	15.2	14.0	1 to 28	57%
	≥18 months	13.7	14.5	2 to 29	54%
	Total	14.4	14.0	1 to 29	
Women	<18 months	16.1	16.5	6 to 27	67%
	≥18 months	17.6	16.5	10 to 27	69%
	Total	17.0	16.5	6 to 27	

the PSS as patients diagnosed <18 months ($\chi^2=0.032$, NS). Moreover, there were no significant differences in PSS scores overall between the two groups ($t=0.363$, NS) with 61% of long-term survivors reporting elevated levels of stress as compared to 60% of patients diagnosed <18 months. Fifty-four percent ($N=14$) of men and 69% ($N=11$) of women categorized as long-term survivors identified themselves as “stressed” (Table 2, PSS by gender and date since diagnosis).

Cancer-related items of concern

Long-term survivors reported fewer total concerns on the Distress Thermometer ($M=5.02$, $SD=3.509$) compared to brain tumor patients diagnosed <18 months ($M=6.82$, $SD=3.737$, $t=2.467$, $p<0.05$). With regard to specific concerns, long-term survivors reported significantly fewer physical concerns ($t=2.587$, $p<0.05$), brain-tumor specific concerns ($t=2.262$, $p<0.05$), and a trend for fewer emotional concerns ($t=1.918$, $p=0.06$; Table 3, items of concern). For long-term survivors, significant predictors of stress included family ($\beta=0.319$, $p<0.05$), emotional ($\beta=0.327$, $p<0.05$), and a trend for practical concerns ($\beta=0.237$, $p=0.08$). Of note, there were no differences in reported concerns according to patients’ treatment (on vs off) or disease status (stable vs unstable). Compared to males, female long-term survivors reported significantly higher emotional concerns ($t=2.2026$, $p=0.05$).

Discussion

The objectives of the this study were to (1) evaluate the level of stress in an outpatient population of long-term survivors of brain cancer, (2) document the cancer related items of concerns of this population, (3) compare stress scores of patients based on time since diagnosis (<18 months vs ≥18 months), and (4) explore the relationship between stress levels, total number of concerns, and patient demographics for each group.

To this end, this study documents that long-term survivors of brain cancer are indeed stressed. Predicators

of stress for this population include family, emotional, and practical concerns. Long-term survivors in this sample were just as likely to report elevated levels of stress as other brain tumor patients. Overall, demographic information did not explain differences in reported stress levels.

Previous studies have documented that 18 to 43% of cancer survivors continue to experience stress at varying times; time since diagnosis, stages of diagnosis, and type of cancer have been found to play a role. [34] This study documents that 61% of long-term survivors of brain cancer continue to report elevated levels of stress. One reason why brain tumor patients may report higher levels of stress than other cancer populations is the functional, cognitive, and neuropsychiatric sequelae of this disease. In addition, brain tumors are often associated with profound physical and cognitive impairments, which can also impact a person’s personality.

Long-term survivors of brain cancer continue to report profound levels of stress similar to other brain tumor patients. This may result from the treatment trajectory of brain tumor patients within this sample. While 81% of sample had stable disease, 79% were currently on therapy. As such, the active treatment trajectory for many long-term survivors of brain cancer is similar to other brain tumor patients despite their stable disease.

The Institute of Medicine has specified four essential components of survivorship care that are important targets for greater research, one of them being interventions to alleviate psychological symptoms that persist or occur beyond active cancer treatment and to improve quality of life. Previous research has highlighted the need to address the stress that brain tumor patients experience. [11] This study clearly documents that the stress brain tumor patients experience extends into survivorship as well. Clearly, the need exists to address the psychosocial stress that long-term survivors experience if we are to improve their quality of life.

Table 3 Items of concern—mean scores

Domain	Time since diagnosis	Mean	Standard deviation
Family	<18 months	0.33	0.595
	≥18 months	0.43	0.590
Emotional	<18 months	1.55	1.121
	≥18 months	1.10	1.265
Practical	<18 months	0.52	0.667
	≥18 months	0.48	0.707
Physical	<18 months	4.39	2.761
	≥18 months	2.95	2.197
Spiritual	<18 months	0.03	0.174
	≥18 months	0.07	0.342
Total concerns	<18 months	6.82	3.737
	≥18 months	5.02	3.509

Conclusion

Receiving a diagnosis of cancer and its subsequent treatment has been cited as being psychologically taxing; however, little is known about the long-term psychological effects on cancer survivors. This study documents that long-term survivors of brain cancer (those surviving 18 months or more) are just as likely to report themselves as stressed as other patients with brain tumors. Although these long-term survivors report fewer numbers of concerns than other brain cancer patients, significant predictors for stress for these groups remain the same. Unlike other cancer populations, time since diagnosis and treatment did not mitigate the stress effects of cancer. Despite their long-term status elevated levels of stress continue across the disease trajectory for patients with brain tumors.

Research on long-term cancer survivors focuses primarily on the health and life of a person after the acute diagnosis and treatment phase. [9] For many types of cancer, such as breast and colorectal, some sources of stress decline as the possibility of recurrence becomes less likely with time. [9] However, brain tumor patients are different; many patients who would be considered “long-term” survivors continue to receive treatment even 18 months post diagnosis. In addition, the fear of recurrence for brain tumor patients seems to increase with time instead of decreasing. [10]

Clinical implications This study provides a better understanding of the unique needs of this population. Familial and emotional concerns, rather than physical concerns, tend to be more prevalent sources of stress for brain tumor patients. As such, understanding the sources of stress for patients with brain tumors will aid clinical teams in better developing targeted supportive care interventions to help address and reduce stress for this population.

Research implications Future research needs to explore whether supportive care interventions designed specifically to address the familial and emotional concerns of patients with brain tumors help to reduce the overall distress they experience. This might include but is not limited to quality of life, treatment compliance, management of the disease, and treatment symptoms.

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