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A cross-sectional audit of distress in patients undergoing adjuvant therapy or follow-up in central nervous system malignancies

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Abstract

Background. Unaddressed high distress leads to noncompliance with treatment, negatively affects quality of life, and may also have a negative impact on the prognosis of cancer patients. Patients with brain tumors have higher levels of distress than the general population and hence we hypothesize that even routine visits during adjuvant treatment or follow-up are likely to be stressful. This analysis was performed to identify the incidence of distress and factors affecting it.

Methods. This was an audit of 84 consecutive patients seen in an adult neuro-medical oncology outpatient department who were either receiving adjuvant chemotherapy or were on follow-up. Distress screening with the National Comprehensive Cancer Network (NCCN) distress thermometer was performed. Patients in whom distress was scored as 4 or above were considered as having high distress. Descriptive statistics and logistic regression analysis were performed to identify factors affecting distress.

Results. The median age of the cohort was 40 years (interquartile range, 28.3 to 50 years). Actionable distress defined as a distress score of 4 or more was seen in 52 patients (61.9%, 95% CI 51.2% to 71.5%). Presence of physical deficit (odds ratio [OR] = 3.412, P = .020) and treatment under the private category (OR = 5.273, P = .003) had higher odds of having high distress.

Conclusion. A high proportion of brain tumor patients either on adjuvant chemotherapy or on follow-up have high distress levels that need to be addressed even during follow-up.

Keywords

brain tumors central nervous system counseling distress physician

The examination of vital signs is an important component of clinical evaluation. Distress assessment is considered as the sixth vital sign and needs to be evaluated in patients treated with malignancy.¹The word "distress" has multiple meanings; however, all definitions commonly consider this as an aversive negative state in which coping and adaptation processes fail.² National Comprehensive Cancer Network (NCCN) guidelines suggest that distress needs to be measured at all important junctures of treatment and follow-up at which distress is likely to be high, like at diagnosis and relapse.³ In a study conducted by Rooney et al in glioma patients on active treatment, the incidence of distress at the start of chemo-radiotherapy/radiotherapy, at 3 months, and 6 months posttreatment was $36.4 \pm 7.6\%$, $35.9 \pm 9.3\%$, and $33.7 \pm 10.2\%$, respectively, when assessed with the NCCN distress thermometer (DT).⁴ In another study reported by Keir and colleagues, 52% of brain cancer patients met the criteria for high distress when

screened with NCCN DT at any point during their treatment trajectory. $^{\rm 5}$

Unaddressed high distress levels negatively affect quality of life and may also have a negative impact on the prognosis of these patients.^{6,7} The cause of high distress is multifactorial.^{1,8} Physical, emotional, social, family, or spiritual problems can give rise to them.^{4,5,9–12} Emotional problems or psychological stress may be heightened at cancer diagnosis or relapse, and other problems can occur at any juncture during the course of treatment. Patients with brain tumors frequently have physical or cognitive loss and higher levels of distress than other cancer patients;8-11 therefore, we hypothesized that even routine visits during adjuvant treatments or follow-up are likely to be stressful. We planned this study to test this hypothesis. The null hypothesis for this practice audit was that during adjuvant treatment or routine follow-up, less than 20% of patients would have high distress levels. We considered an arbitrary cutoff of 20%, as the incidence of high levels of distress at diagnosis was variably reported in the literature between 28.9% and $52\%^{4,5,12-15}$ and the upper limit of 95%CI of a value below 20% would not cross 30%. This would suggest that the incidence in our patient cohort is truly low. The information on distress in patients on follow-up or on adjuvant temozolomide is sparse in the literature and is helpful for planning measures to address distress in this population. Tackling distress requires distress counseling by a psychologist. Unfortunately, the availability of a psychologist is limited in our institute. Hence an innovative approach toward distress resolution was planned in this study. Patients with high distress were initially counseled by the treating physician and then were referred to a psychologist only if the distress had not resolved.

Methods

Study Conduct

The audit was conducted in the outpatient department of neuro adult medical oncology in a tertiary care cancer center in Mumbai, India, between September 15, 2017 and November 30, 2017. The medical oncology outpatient clinic has 2 medical oncologists, 1 to 2 trainees in medical oncology, and an outpatient nurse at its disposal. This clinic annually sees 400 to 450 new patients coming from all over India. All patients attending the outpatient department who underwent the following criteria were offered distress screening: adult patients (age \geq 18 years), with Eastern Cooperative Oncology Group Performance Status (ECOG PS) \leq 3, and willing to participate in distress screening. As distress is considered a vital sign, its evaluation was considered a part of standard protocol and hence no institutional ethics clearance was obtained for it; however, the study was conducted in accordance with the Declaration of Helsinki.

Study Methodology

Adult patients with central nervous system tumors who were either receiving adjuvant chemotherapy or were on follow-up and had their outpatient visits during the above-mentioned period were selected for this study. Patients were informed of the importance of distress identification and were then administered the NCCN DT in the waiting hall. The NCCN DT is a guick distress screening tool.⁵ Use of the NCCN DT is validated in Indian clinical settings.¹⁶ Patients who had actionable distress as identified by a score of 4 or more were then counseled by the physician. The distress counseling was centered around the list of problems provided by the patients. Practical solutions, hope, and social worker help was provided as necessary. The distress reading was taken again after the physician counseling and those below the score of 4 were given standard management for the disease while patients who still had persistent high distress levels were referred to the psychologist for standardized distress counseling.¹⁷

Sample Size

No formal sample size calculation was performed. Eightfour patients were recruited during this time period. This sample size had a power of 80%, with a type 1 error of 5% to rule out with a 95% Cl interval whether the distress incidence was above 20%. If 17 or more of 84 patients had high distress levels, then we would recommend routine distress screening.

Outcome Measures

Distress is scored on a visual analog scale from 0 to10 on the DT. In addition, it has a problem list, accounting for practical, emotional, family, spiritual, and physical problems. High distress was defined as a distress score of 4 or more on the NCCN DT.⁵ The incidence of distress was defined as the percentage of patients having high initial distress among the 84 screened patients. Distress resolution was defined as having a low distress score (distress score of 0 to 3) postphysician counseling among the patients with high initial distress.¹⁸ Demographic factors (age, gender, file status, place of stay), treatment status, and presence of physical deficit (defined as power below 5/5 in any limb) were collected and noted at the time of interview.

Statistical Analysis

SPSS version 16 and R Studio version 3.1.2 were used for analysis. Descriptive statistics were performed. Continuous variables were expressed in medians with respective interquartile ranges (IQR). The incidence of initial distress was expressed in a percentage with respective 95% CI. Factors affecting high initial distress were sought, and binary logistic regression analysis was performed. High initial distress (a distress score of 4 or more) was considered as the dependent variable. The factors age (continuous variable), gender (male/female), category (general/private), physical deficit (present/absent), treatment status (on treatment or follow-up), and place of stay (Mumbai or other areas) were tested to identify the independent variable associated with high initial distress. Age was selected as younger age is associated with high distress.¹⁹⁻²¹ Gender was selected as gender-related bias in females leads to a high incidence of distress.²² File category reflected the financial status of the patients, with the general category usually associated with low annual income, which in turn, is associated with high distress. Presence of physical deficit, ongoing treatment, and long travel distance are associated with high distress. The percentage of patients having distress resolution postphysician counseling with its 95% CI is provided.

Results

Baseline Characteristics

Distress was assessed in 84 consecutive patients during this period. The median age of the cohort was 40 years (IQR, 28.3 to 50 years) and predominantly consisted of male patients (57, 67.9%). The ECOG PS was 0 to 2 in 77 patients (89.6%), 3 to 4 in six (7.1%) patients, and the data for PS were missing in 1 patient (1.2%). The majority of the patients hailed from outside the city in which the hospital is located (47, 56.0%). The financial status of 37 patients (44.0%) permitted them to have a file in the private category while the rest of the files were opened in the general category (56.0%). The 4 most common tumors in this cohort of patients were glioma in 64 (76.1%), intracranial germ cell tumors in 5 (6.0%). The baseline characteristics have been detailed in Table 1.

Distress Status

The median distress score was 4 (IQR, 1 to 5). Actionable distress, defined as a distress score of 4 or more, was seen in 52 patients (61.9%, 95% Cl 51.2% to 71.5%). The factors affecting distress are shown in Table 2. Among the tested factors, 2 factors were associated with a statistically significant risk of high distress. These were the presence of physical deficit (odds ratio [OR] = 3.412, P = .020) and treatment under the private (file category) category (OR = 5.273, P = .003). The details of problems associated with distress are shown in Table 3. The highest number of problems identified were emotional in 44 (52.4%) of patients. Among emotional problems, "worry" was the problem identified in 36 patients (42.9%).

Distress Postphysician Counseling

The median time for the whole appointment with counseling was 30 minutes (range, 25-45 minutes). The distress score postphysician counseling was lower (below 4) in all but one patient (51 out of 52, 98.1%). This patient refused to attend counseling by a psychologist.

Discussion

Actionable distress was seen in 61.9% of patients. This high incidence of actionable distress mandates routine distress

Table 1 Baseline Characteristics of Patients				
Variable	Value			
Age	Median age 40 years (IQR 28.3 to 50 years)			
Gender				
Male	57 (67.9%)			
Female	27 (32.1%)			
ECOG PS				
0 to 1	56 (64.6%)			
2	21 (25.0%)			
3 to 4	06 (7.1%)			
Missing	01 (1.2%)			
Category				
General	47 (56.0%)			
Private	37 (44.0%)			
Presence of physical deficit				
Present	39 (46.4%)			
Absent	45 (53.9%)			
Place of stay				
Local	37 (44.0%)			
Nonlocal	47 (56.0%)			
Treatment status				
On adjuvant treatment	45 (53.6%)			
On follow-up	39 (46.4%)			
Diagnosis				
Gliomaª	64 (76.1%)			
Intracranial germ cell tumor	05 (6.0%)			
Medulloblastoma	4 (4.8%)			
Meningioma	4 (4.8%)			
Pituitary adenoma	2 (2.4%)			
Hemangiopericytoma	01 (1.1%)			
Others	04 (4.8%)			
Chemotherapy				
Temozolomide	29 (34.5%)			
PCV	02 (2.4%)			
Bevacizumab	05 (6.0%)			
Other	06 (7.1%)			
Abbreviations: ECOG PS Eastern Cooperative Operatory Group				

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; IQR, interquartile range; PCV, procarbazine hydrochloride, lomustine (CCNU), and vincristine sulfate. ^aOf 64 patients, 56 patients had high-grade glioma. Of these 56, a total of 47 patients had glioblastoma.

screening even during adjuvant treatment and follow-up in adult central nervous system malignancies. The proportion of patients with brain tumors having high distress at diagnosis varies between 28.9% and 52%.^{13–15} The differential proportion is due to different instruments being used in distress screening like the NCCN DT, questionnaires, and the Functional Assessment of Cancer Therapy-Brain quality of life module. The proportion at first recurrence is 75.0%.²³

Table 2 Details of Factors Affecting Distress

Variable	Туре	Odds Ratio	95% Cl Odds Ratio	P value
Age	Continuous	0.993	0.957 to 1.031	.723
Gender	Categorical	1.108	0.374 to 3.285	.853
File category	Categorical	5.273	1.753 to 15.863	.003
Presence of physical deficit	Categorical	3.412	1.214 to 9.615	.020
Place of stay	Categorical	0.531	0.189 to 1.492	.230
Treatment status	Categorical	0.971	0.334 to 2.826	.957

Table 3 Details of Problems in Patients With High Levels of Distress

Problems	Numbers (%)	Problems	Numbers (%)
Practical problems	12 (14.3%)	Physical problems	24 (28.6%)
Child care	02 (2.4%)	Appearance	01 (1.2%)
Housing	-	Bathing/dressing	-
Insurance/Finance	08 (9.5%)	Breathing	-
Work/school	03 (3.6%)	Changes in urination	01 (1.2%)
		Constipation	01 (1.2%)
		Diarrhea	-
Family problems	10 (11.9%)	Eating	-
Dealing with children	05 (6.0%)	Fatigue	20 (23.8%)
Dealing with partner	07 (8.3%)	Feeling swollen	-
Dealing with close	-	Fevers	-
Friend/relative	-	Getting around	-
Emotional problems	44 (52.4%)	Indigestion	-
		Memory/concentration	8 (9.5%)
Depression	10 (11.9%)	Mouth sores	-
Fears	19 (22.6%)	Nausea	01 (1.2%)
Nervousness	05 (6.0%)	Nose dry/congested	-
Sadness	10 (11.9%)	Pain	-
Worry	36 (42.9%)	Sexual	-
Loss of interest in usual activities	-	Skin dry itchy	-
		Sleep	-
Spiritual/religious concerns	2 (2.4%)	Tingling in hands and feet	_

The magnitude of distress seen on follow-up in our study lies between that reported at diagnosis and at first recurrence. This highlights the fact that an uncertainty of the future, which is prevalent in these patients, can lead to high distress.²⁴ It is known that this uncertainty is higher in the early point of the treatment trajectory and is believed to decrease subsequently. Our data refute this belief, however, with 61.9% of our patients on follow-up/adjuvant treatment having high distress proportions. There was no relationship of the treatment status (ongoing or follow-up) on the distress levels, further confirming that patients on follow-up have high distress levels, and high distress levels on treatment may persist during the follow-up period.

Distress in brain tumor patients is known. In a study reported by Goebel et al among 159 newly diagnosed intracranial tumor patients, 117 had high distress (73.6%) that was significantly associated with depression and anxiety.¹³ These symptoms have an impact on the quality of life and everyday activities of patients and their partners. This is confirmed in the study reported by Kvale and colleagues, in which 28.9% of brain tumor patients identified a distress score of 4 or above, and it statistically correlated with poor social and emotional well-being quality-of-life scores.¹⁴ Very few studies have longitudinally captured the distress levels in brain tumor patients. Keir et al compared distress between long-term survivors of glioblastoma (>18 months) and patients diagnosed within 18 months.¹² Long-term survivors had fewer items of concern but had higher distress. Guidelines are available for management of distress, but they are often not suitable for brain tumor patients as they have very specific problems and needs.²⁵ This is highlighted in the recently published European Association for Neuro-Oncology guidelines for palliative care in adults with glioma. Common problems that are specific to brain tumor patients and contribute to increased distress are cognitive decline, mood, and behavioral disorders.¹⁷ The management of these symptoms is difficult and pharmacological management does little to help.¹⁷

Identifying factors predicting high distress is emphasized in the literature. Many publications highlight the importance of knowing such factors and focusing on patients with these factors.^{4,5,12–15,23} However, this approach is fallacious. Such strategies based on predictive markers carry the inherent risk of missing patients on follow-up who have developed new distress. In our population, the high distress scores at follow-up mandate they be measured in all patients irrespective of presence or absence of high-risk factors and treatment status. In our study, 2 groups of patients had high distress: those with physical deficit and those with files in the private category. Presence of physical deficit is a known factor for development of distress in brain tumor patients.¹⁵ Physical deficit is common in patients with brain tumors, hindering activities of daily living and affecting quality of life.^{8,10} Socioeconomic status has a complicated relationship with distress. Non-Englishspeaking patients and less-educated patients are at a high risk of developing distress.¹⁵ Patients in the private category are socioeconomically better off and are more likely to be highly educated. Surprisingly, they still had higher distress levels in our setting.

Screening for distress during adjuvant therapy and follow-up, in addition to screening at diagnosis, can be helpful. However, the feasibility of such an exercise in institutes with a high patient load is questionable. Dessai et al has highlighted the problems of routine distress screening in such institutes.²⁶ In a single-day pilot study, with an incentive for the oncologists, distress screening could be offered to only 85% of patients. Lack of manpower for screening was the single most important hindrance for distress screening.²⁶ Identification of distress is just the initial step toward distress management. Patients with high distress require counseling. Identification of a large proportion of patients with distress will require a higher number of psychologists for counseling. Unfortunately, not many cancer institutes are equipped with such personnel.²⁷ Hence, in the current study, patients with high distress were initially counseled by the physicians themselves and only those patients who had high distress postrepeat counseling were referred to a psychologist. The policy was satisfactory with resolution of distress in all but one patient. A similar strategy was adopted by our group in head and neck cancer patients and it led to a resolution of distress.¹⁸ This highlights the importance of communication with patients and caregivers during the oncological consultation. When concerns that may lead to distress are addressed by oncologists, the distress is also addressed. In addition, multiple patients have anticipatory anxiety, which is often relieved by communication of results of imaging. There is a subtle difference between communication and therapeutic counseling. Communication involves providing information with sensitivity while therapeutic counseling is a psychotherapeutic intervention with acceptance, positive regard, genuineness, and empathy focusing on facilitating the patient to understand and enabling him or her to cope with and resolve concerns. These results do not suggest, however, that physician counseling can substitute for psychologist counseling.

This study is not without its strengths and limitations. All consecutive patients seen in the outpatient department were included in the study. It is one of the rare studies reporting on distress in neuro-oncology practice, not only during adjuvant chemotherapy but also during follow-up (off-treatment patients). The study is limited by its design of being cross-sectional. A longitudinal study would have enabled us to understand the temporal profile of distress. The patient population was heterogeneous in terms of variable sites. Patients with benign brain tumors have a lower rate of distress than those with malignant brain tumors.¹³ The distress score cutoff was not adjusted for follow-up visits as there is a suggestion in the literature that a score of 3 or above during follow-up would suggest high distress.^{28,29}

In spite of these shortcomings, however, the study provides valuable insight into distress among patients on routine follow-up and adjuvant treatment, revealing that nearly 60% of patients on adjuvant chemotherapy or follow-up had high distress levels. Patients with physical limitations had high distress that could be resolved with counseling.

Conclusion

In this practice audit, a large proportion of brain tumor patients either on adjuvant chemotherapy or on follow-up had high levels of distress (61.9%). Counseling by physicians led to a resolution of distress in nearly all of them.

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