

Anxiety in the preoperative phase of awake brain tumor surgery

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ABSTRACT

Objective: Awake surgery emerges as a standard of care for brain tumors located in or near eloquent areas. Levels of preoperative anxiety in patients are important, because anxiety can influence cognitive performance and participation, hence altering the outcome of the procedure. In this study we analyzed the prevalence and potential clinical predictors of anxiety in the pre-operative phase of an awake brain tumor surgery.

Patients and methods: Seventy consecutive candidates for an awake brain tumor surgery were included. All patients received a neuropsychological pre-operative work-up. The Hospital Anxiety and Depression Scale (HADS) was administered to investigate symptoms of anxiety. Demographic and medical data were extracted from patients' charts. Linear regression analyses, multiple regression analyses, *t*-tests for parametric and Mann-Whitney *U* tests for non-parametric data were used to analyze the relation between demographic and medical variables and pre-operative anxiety.

Results: Mean score on the anxiety scale of the HADS was 6.1 (SD = 4.2, range 1–19) and 25% of the patients scored on or above the cut-off for anxiety symptoms (score > 7). Women reported higher levels of anxiety than men ($p < 0.01$). Furthermore, younger patients were more anxious than older patients ($p < 0.05$). No other variables were significantly related to pre-operative anxiety.

Conclusions: Merely, one in every four patients reported significant anxiety symptoms in the pre-operative phase. Besides gender and age, none of the other demographic or medical factors were significantly associated with the level of anxiety.

1. Introduction

Intraoperative stimulation brain mapping helps maximize the extent of resection and reduce the surgical risk present and is performed increasingly in patients with brain tumors located in an eloquent area [1,2]. An important part of the pre-operative phase of awake craniotomies is the neuropsychological work-up, which evaluates the baseline performance of the patient especially at tests that will be performed during the surgery and patients' suitability for the procedure. Anxiety is an important factor herein for several reasons. First, the level of anxiety may influence the decision whether a patient is suitable for awake brain tumor surgery [4]. For example, a high suspicion or vulnerability for panic attack may be an exclusion criterion or request a specific preoperative work-up. Secondly, anxiety may influence cognitive performances [5], in the pre-operative phase but also during surgery. When a patient is anxious this will negatively influence the reliability of the cognitive monitoring. Attention and concentration will be drawn toward the anxiety with more mistakes and less focus on the cognitive tasks as result. Because the results of the cognitive tests are less valid

the resection may be more conservative.

Previous studies have focused on quality of life and psychological distress in patients with a brain tumor [6,7]. Few studies have analyzed the pre-operative anxiety in this patient group. Most patients undergoing awake surgeries are usually quite positive when asked about their experiences e.g. [8,9,10]. Nevertheless, anxiety is also reported in these patients [3,11,12], as well as in other neurosurgical patients [13]. A study of Palese et al. showed that pre-operative stress, anxiety and depression were similar on the day before surgery for a brain neoplasm in patients operated under general or under local anesthesia [14]. Unfortunately, the group size in this study was very small; only nine patients with local anesthesia (awake surgery) were included.

Our study specifically focuses on the prevalence of pre-operative anxiety while being candidate for awake brain tumor surgery. We focus on anxiety and not on other psychological complaints like symptoms of depression because of the course of those complaints in cancer patients. Usually, in the first period of being ill, high anxiety levels are described that decrease over time, whereas lower levels of depression in this period increase over time [15,16]. Because we focus on the pre-

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operative phase with the awake procedure ahead, anxiety is most relevant.

If we know what factors play a role in the increment of anxiety, the pre-operative preparation could be more adjusted for individual patients. Therefore, demographic and medical factors were studied in relation to the level of anxiety. Demographic variables were gender, age, educational level and having a support system or not. We expected women to be more anxious than men [13], and younger patients to be more anxious than older patients [17,18]. Social support of a partner and/or children could decrease levels of anxiety [19]. Medical factors were location of the tumor, having a suspected high or low-grade tumor and time between diagnosis and operation. Increasing this time might allow patients to cope with the situation and this could possibly decrease the anxious feelings. On the other hand, waiting time can be stressful and anxious [20]. We also expected patients with a frontal tumor to be more anxious because of the involvement of the prefrontal cortex in anxiety regulation [21,22], and suspected that being diagnosed with a potential high-grade tumor might also increase the anxiety levels.

2. Patients and methods

2.1. Ethical statement

The study proposal was presented to the Medical Research Ethics Committee UMC Utrecht, who concluded that The Medical Research Involving Human Subjects Act (WMO) did not apply to this study and therefore an official approval of this study by the Medical Research Ethics Committee UMC Utrecht was not required.

2.2. Patients and inclusion criteria

Patients diagnosed with a suspected primary brain tumor in an eloquent area and candidate for their first ever awake brain tumor surgery (awake-awake-awake procedure, as described previously [12]) in the period between October 2013 and November 2015 in the University Medical Center Utrecht were included in this study. Patients who were candidate for a re-resection were excluded, because previous experiences with awake surgery could influence anxiety levels. Patients suffering from severe impaired language comprehension or no proficiency in the Dutch language were also excluded, because this could affect the validity of the anxiety questionnaire. A metastasis as suspected diagnosis was also an exclusion criterion. Patients with a suspected metastasis are already familiar with the status of being a patient. For them, a metastasis in the brain is usually a progression of the disease. In contrast, the sudden character of the diagnosis of a primary brain tumor may increase anxiety levels more. Finally, in some patients the awake brain tumor surgery was performed rather emergently because of severe and very progressive clinical symptoms or quick growth of the tumor. Those patients had a limited and focussed neuropsychological work-up without the standard protocol including the questionnaires on psychological aspects. Therefore, they were also excluded. At time of inclusion in this study no patients were being treated for an anxiety disorder.

2.3. Demographic and medical variables

Demographic and medical factors were retrieved from the patient's charts, as the considered factors are standard items of the medical chart at our center. Based on the median, age < 55 was categorized as young and age ≥ 55 was defined as old. The educational level was recorded based on the Dutch educational system using seven categories (1: < 6 years of education, 2: 6 years of education, 3: 7–8 years of education, 4: 9 years of education, 5: 10–11 years of education, 6: 12–18 years of education, 7: > 18 years of education) [23]. Since a few decades, children in the Netherlands must attend school from 5 years of age till

16, but for older patients it was possible to leave school after 6 years of education. Categories 1–4 were defined as low education, categories 5–7 were defined as high education. Furthermore, we asked patients about their support system ('in a relationship: yes or no' and 'children: yes or no').

Tumor location was defined as left or right hemisphere, and as involvement of frontal lobe or not (based on the radiology report). Based on the preoperative Magnetic Resonance Imaging (MRI) scans and preoperative multidisciplinary evaluations, the tumor was defined as a suspected low or high-grade tumor. Patients were always formally informed about this suspected diagnosis, but were also made aware of potential differential diagnostics as well. Finally, time between radiological diagnosis and surgery was measured in weeks. Three weeks or less between diagnosis and surgery was defined as short time, more than three weeks was defined as long time (according to guidelines for neurosurgery from the department of Neurology and Neurosurgery of the University Medical Center Utrecht).

2.4. Anxiety

To measure the level of anxiety in the pre-operative phase the Anxiety Scale of the Dutch version of the Hospital Anxiety and Depression Scale (HADS) was used [24,25]. The HADS was developed to identify cases of anxiety disorders and depression among patients in non psychiatric hospital clinics [24]. This questionnaire has a 7-item anxiety scale and a 7-item depression scale. Answers are rated on a 4-point Likert scale that ranges from 0 to 3. The maximum score on each subscale is 21 points. The HADS was administrated during the pre-operative work-up (clinical care as usual) within two weeks before surgery. All patients were informed about undergoing awake brain surgery at that moment. A cut-off score > 7 for the anxiety scale is used as the most optimal sensitivity and specificity as a case finder for anxiety disorders [26].

2.5. Statistical analyses

All factors were analyzed as both linear and nonlinear (dichotomized) variables. First, as explorative analyses, simple linear regression analyses were used to study the relation between anxiety and the abovementioned factors (nominal variables were transformed in to dummy variables). We used simple regression analyses because of the size of our study group and the fact that we made use of many predictors. In the next step, significant factors were analyzed in multiple regression analyses. Then, as additional post-hoc analyses, parametric (independent sample *t*-test) or nonparametric (Mann-Whitney *U* test) tests were used to further study group differences.

3. Results

3.1. Patients

In a period of two years 125 patients underwent an awake brain tumor surgery. Seven patients were excluded from this study because the suspected diagnosis was a metastasis and eleven were excluded because they had been operated before for the same lesion. Thirty-seven patients were excluded because of severe impaired language comprehension, no proficiency in the Dutch language or emergency procedure. Seventy patients fulfilled our criteria and were included in this study. Descriptive statistics of the demographic and medical variables can be found in Table 1.

3.2. Anxiety

The mean score on the anxiety scale of the HADS was 6.1 (SD = 4.2, range 1–19). Fig. 1 shows the distribution of the anxiety scores. Twenty-five percent of all patients scored above 7, the threshold for

Table 1
Descriptive statistics of demographic and medical factors (N = 70).

Demographic and medical factors	
Sex	male (61.4%), female (38.6%)
Age	range 18–81, mean = 53, median 55 young = < 55 (50%) old = ≥ 55 (50%)
Education level ^a	median 5, IQR 4–6 low education = 1–4 (25.7%) high education = 5–7 (74.3%)
Relation Children	yes (85.7%), no (14.3%) yes (77.1%), no (22.9%)
Location of tumor	left (70%), right (30%) frontal (40%), other location (60%, namely temporal (25.7%), parietal (25.7%), insular (2.9%) and central (5.7%))
Suspected high or low grade tumor	low (48.6%), high (51.4%)
Time between diagnosis and surgery	range 2–884 weeks, median 4 weeks short 0–3 weeks (51.4%), long > 3 weeks (48.6%)

^a Recorded using seven categories; 1: < 6 years of education, 2: 6 years of education, 3: 7–8 years of education, 4: 9 years of education, 5: 10–11 years of education, 6: 12–18 years of education, 7: > 18 years of education.

significant anxiety using the HADS scale.

A simple linear regression was calculated to predict anxiety based on gender. A significant regression equation was found ($F = 12.274$, $p < 0.001$), with an R^2 of 0.153. All other regression analyses did not show any significant results (see Table 2).

Because scores on the HADS were not distributed normally Mann-Whitney tests were performed. Analyses indicated that women were more anxious than men ($U = 814.5$, $p = 0.005$), scores on the anxiety scale of the HADS were respectively 8.2 ($SD = 4.8$) versus 4.8 ($SD = 3.1$). When age was analyzed as a dichotomized variable (young versus old) a Mann-Whitney U test also showed a significant difference ($U = 436$, $p = 0.037$), whereby younger patients had a higher anxiety level ($M = 7.03$, $SD = 4.19$) than older patients ($M = 5.20$,

Table 2
Results simple regression analyses and Mann-Withney U tests.

	Regression analysis				Mann-Withney U test	
	B	Beta	t	p	U	p
Gender	3.311	0.391	3.503	0.001	814	0.005
Age	−0.045	−0.176	−1.471	0.146	436	0.037
Educational level	0.058	0.015	0.126	0.900	532.5	0.384
Relation	−0.367	−0.031	−0.257	0.798	283	0.774
Children	−0.391	−0.040	−0.329	0.743	381	0.473
Location tumor left	−0.163	−0.018	−0.150	0.881	529	0.847
right						
Location tumor frontal versus not frontal	0.607	0.072	0.597	0.553	594	0.942
Suspected grade tumor	−1.036	−0.126	−1.044	0.300	491	0.153
Time between diagnosis and surgery	0.001	0.050	0.409	0.684	652	0.637

$SD = 3.96$). No other significant results were found (see Table 2).

4. Discussion

In this study we analyzed how often anxiety is reported in the pre-operative phase of awake brain tumor surgery. Furthermore, we questioned what factors were related to the level of anxiety. Altogether, the mean score on the anxiety scale of the HADS was 6.1. In comparison, a general healthy population ($N = 1901$) with a comparable mean age of 61.3 years had a mean score of 3.9 ($SD = 3.5$) on this anxiety scale [24]. Only 25% of the patients suffered a significant level of anxiety prior to their awake surgery ($HADS > 7$). A comparable percentage has been found in a study of Janda et al. [27] where 30% of patients at various stages of their treatment for a brain tumor (surgery, but also chemotherapy or radiation therapy) reported anxiety complaints. As such, the fact of waiting for an awake

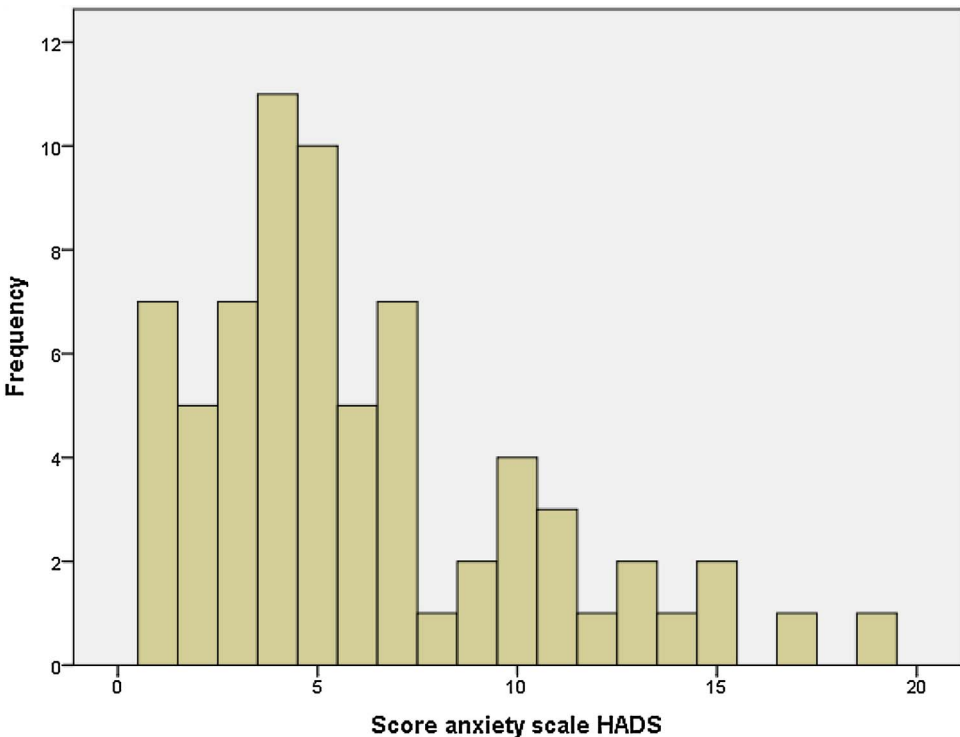


Fig. 1. Histogram of anxiety scores of the HADS of patients included in this study ($n = 70$).

craniotomy procedure does not appear to increase the general anxiety of suffering from a brain tumor. In the study of Yilmaz and colleagues [19] where levels of anxiety were measured just before different surgical procedures under general anesthesia, even higher anxiety levels are reported (55.4% in female, 46% in male). In the study of Palese and colleagues [14] 39% of the patients reported anxiety complaints one day before surgery for a brain neoplasm (HADS > 7). Possibly, the higher percentage in these studies in comparison to our results may be due to the short time before surgery (1 day versus within two weeks).

In our study, women reported higher anxiety levels in the pre-operative phase than men and younger patient were more anxious than older patients. This is also in line with previous literature [13,27–30]. Besides gender and age, no other factors included in this study were significantly related to the reported amount of anxiety in the pre-operative phase. This contrasts with several reports on pre-surgical anxiety. Yilmaz and colleagues [19] found for instance a correlation between the level of preoperative anxiety and gender, educational level and social support. Another recent study of Basak et al. [31] showed that socioeconomic status and education level were strong predictors of anxiety in surgical inpatients. That our study could not replicate the findings may be the result of the fact that we have included a more specific patient group (only patients that were candidate for an awake brain tumor surgery). It however also suggests that having a brain tumor and being a candidate for an awake surgery induces anxiety in a more general way instead of in relation to specific factors. Aspects such as having a suspected high or low grade tumor seem less important in this specific moment just before surgery for patients and do not influence the anxiety level.

Strengths of this study are the relatively large study population and the large variety within our sample with respect to the demographic and medical variables. Although we targeted a very specific group of patients (i.e., candidates for an awake primary brain tumor surgery), this variation made it possible to study the relation between anxiety and previously described factors.

Limitation of this study is the self-report of anxiety by use of a questionnaire. The HADS is a self-reporting instrument and requires self-insight. Patients were not psychiatric evaluated. Likewise, social support was defined as being in a relation and having children or not. We did not actively ask patients about their experienced social support. Furthermore, factors such as personality traits, coping styles and pre-operative cognitive functioning may play a role in the pre-operative anxiety but were not analyzed in the study. These aspects should be studied in future research.

In conclusion, significant anxiety only occurs in one fourth of patients scheduled to undergo an awake craniotomy for primary brain tumors, a prevalence that is similar to that of other surgical candidates. Despite the fact that an awake surgery impresses like a fearful life-event, real feelings of anxiety are reported in just minority of the patients. Besides gender and age, we did not identify any potential predictor of pre-operative anxiety in patients that are candidate for awake brain tumor surgery. Therefore, it remains important to ask patients about their specific anxieties so that those can be managed in each individual in the most optimal way.

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Conflicts of interest

None.

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