Aus der Neurochirurgische Klinik und Poliklinik
der Universitätsmedizin der Johannes Gutenberg-Universität Mainz

The effectiveness of operative therapy on the distress of brain tumor patients

Die Effektivität der operativen Therapie auf den Distress von Hirntumorpatienten

Inauguraldissertation
zur Erlangung des Doktorgrades der
Medizin
der Universitätsmedizin
der Johannes Gutenberg-Universität Mainz

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aus Jakarta, Indonesien

Mainz, 2023

Tag der Promotion: 15. Juli 2023

Abstract

Amongst the population of cancer patients, brain tumor patients are one of the most severely affected by their illnesses. They suffer tremendous quality of life reductions due to functional impairment, neurocognitive dysfunction, and psychosocial distress. Psychosocial distress, despite having a large impact on quality of life, is often an afterthought and overlooked. Some patients do not receive supportive care until the palliative stage, if at all. Recognizing the need for psychosocial care and quantifying its different aspects is therefore important to integrate into standard neurooncological clinical practice. This can be done through questionnaires or interviews conducted by healthcare professionals or filled out by the patients themselves. This study aimed to explore how operative resection of brain tumors impacts patient distress, specifically their physical and psychosocial burdens, using the Distress Thermometer (DT) and Signaling Questions (SQ) as measuring instruments. Along with this, we also sought to determine how other factors such as socioeconomic status, treatment effectiveness or patient difficulties may impact distress. Using both measuring instruments before and after operations, we were able to collect data from 41 patients for analysis. Our results showed a post-operative increase in physical distress and a decrease in emotional distress. This was consistent across the entire population, even among severely distressed patients (DT≥6). DT and SQ correlated to each other significantly and SQ proved to be a good predictor for distress. Other factors that can significantly impact distress are sex, marital status, and occupational status. Difficulties with the interview did not seem to impact the data that we gathered and neither did treatment effectiveness. However, we must note that the parameters used to quantify both the aforementioned aspects are disputable. All in all, operative therapy does increase overall stress. Nevertheless, a nuanced view is worth looking into, as different aspects of stress behave differently. SQ and DT are suitable instruments to measure distress, however SQ may be better suited as a screening instrument, whereas DT is a proven instrument to quantify the different aspects of distress.

Zusammenfassung

Hirntumorpatienten leiden enorm unter einer Einschränkung der Lebensqualität. Diese wird durch eine Vielzahl von Faktoren verursacht, wie z. B. einem reduzierten körperlichen Allgemeinzustand, funktionellen Beeinträchtigungen, einer neurokognitiven Dysfunktion und psychosozialen Belastungen.

Psychosoziale Belastung umfasst nicht nur die psychische Belastung eines Patienten aufgrund der Erkrankung, aber auch Einschränkung im sozialen und beruflichen Leben, da Hirntumorpatienten oft nicht mehr arbeiten können und Schwierigkeiten in ihrem Sozialleben aufweisen. Psychosoziale Belastungen werden trotz ihres enormen Einflusses auf die Lebensqualität sowie einer großen Anzahl bestehender Messinstrumente oft übersehen und entsprechend nicht behandelt. Gesellschaftliche Stigmatisierung und organisatorische Engpässe im klinischen Alltag sind oft die Gründe dafür. Die Erkennung von psychosozialer Belastung stellt einen wichtigen Bestandteil in der Therapie dar. Befragungen haben sich als eine der zuverlässigsten Methoden etabliert, um Belastung zu erkennen und zu quantifizieren.

In dieser Studie sollte untersucht werden, wie sich die operative Therapie von Hirntumoren auf die Belastung des Patienten auswirkt. Zudem sollte untersucht werden, wie die Therapie, der sozioökonomische Status und mögliche Schwierigkeiten bei der Befragung selbst die Daten dieser Studie beeinflussen können.

Um die Patientenbelastung zu erfassen, wurden zwei unterschiedliche Messinstrumente ausgewählt, nämlich das Distress Thermometer (DT) und Signaling Questions (SQ/Signalfragen). Das DT beinhaltet eine visuelle Analogskala (VAS) von 0 (keine Belastung) bis 10 (maximale Belastung) und zusätzlich eine Problemliste von 40 Belastungsarten innerhalb von 4 verschiedenen Kategorien (praktischen, spirituellen, emotionalen und körperlichen Belastungen). Die Signalfragen bestehen aus 3 Fragen zu körperlichen, psychischen und kognitiven Belastungen. Zusätzlich haben wir einen eigenen Fragebogen erstellt, welcher neben den Signalfragen auch zusätzliche Informationen über den sozioökonomischen Status des Patienten, dem Krankheitsverlauf sowie Schwierigkeiten bei der Befragung erhebt. Die Patienten wurden gebeten, das DT und unseren eigenen Fragebogen zu beantworten. Um den

Einfluss der Operation besser zu beurteilen, wurden prä- und postoperativ Befragungen bei jedem Patienten durchgeführt. Die erste Befragung wurde meistens ein Tag vor und die zweite drei Tage nach der Operation während des stationären Aufenthalts durchgeführt. Die Patienten wurden aus der neurochirurgischen Klinik der Universitätsmedizin Mainz rekrutiert, die elektiv zur operativen Versorgung bei bekanntem Hirntumor aufgenommen wurden. Zusätzliche Information über Therapieerfolg, Tumorhistologie sowie postoperative kognitive Einschränkungen wurden nach dem stationären Aufenthalt aus den Patientenakten gewonnen.

Insgesamt wurden 51 Patienten in die Studie eingeschlossen. 41 Patienten davon haben an beiden Befragungen teilgenommen. 10 Patienten aus der Studie ausgetreten, 9 davon postoperativ. Alle Patienten haben eine operative Tumorresektion bekommen.

Unsere Ergebnisse zeigten, dass die Belastung der Patienten direkt nach der Operation insgesamt ansteigt. Es ist jedoch wichtig, die Nuancen dieser Änderung zu beachten. Emotionale Belastungen gehen nach Operationen deutlich zurück, während die Belastung durch körperliche Beeinträchtigungen zunimmt. Diese Veränderungen waren konsistent, selbst wenn nur schwer belastete Patienten berücksichtigt wurden. Die emotionale Belastung, die wir präoperativ beobachteten, könnte möglicherweise aus Angst vor dem bevorstehenden Eingriff kommen. Dies würde auch die deutliche Abnahme dieser Belastung direkt nach der Operation erklären. Genauso kann der Belastungsanstieg der körperlichen Beeinträchtigungen auf postoperative Schwäche, Schmerzen, Schwindel und andere typische postoperative Beschwerden zurückgeführt werden. Die praktischen Probleme, gemessen mit dem Distress Thermometer, können ebenfalls auf die gleichen Probleme zurückgeführt werden, da Patienten möglicherweise eine negative Zukunftsaussicht unmittelbar nach ihrer Operation haben. Es wurden Signalfragen als Screening-Instrument entwickelt, um zu erfassen, wann weitere Untersuchungen des Patienten erforderlich sind. Die körperliche Frage innerhalb der Signalfragen zeigte eine Reduktion der Belastung nach der Operation. Obwohl das DT eine umfangreiche DT-Problemliste aufweist, ist das DT ein zuverlässigeres Maß für die Erfassung der Belastung als die hier verwendeten Signalfragen. Zudem ist das DT ein vollwertiger Fragebogen zur Messung von Belastung, weshalb das DT bei der Quantifizierung von Belastung aussagekräftiger erscheint.

Um die Validität unserer Studie zu untermauern, entschieden wir uns, die Belastung der Patienten mit zwei Instrumenten, dem DT und den Signalfragen, zu messen. Während das DT und die Signalfragen hinsichtlich der Veränderungen des Leidensdrucks zwischen präoperativ und postoperativ diskrepante Ergebnisse ergaben, zeigten beide Instrumente im Bereich der schweren Belastung übereinstimmende Ergebnisse. Schwer belastete Patienten erzielten sowohl beim DT als auch bei den Signalfragen hohe Werte. Das DT und die Signalfragen korrelierten positiv miteinander und waren gute Prädiktoren füreinander. Dies verleiht der Validierung der Signalfragen als neues, praktisches Screening-Instrument für den klinischen Alltag zusätzliches Gewicht.

Desweiteren haben wir einen Anstieg des Betreuungswunsches nach der Operation beobachtet. Dies würde darauf hindeuten, dass die Patienten nach der Operation stärker belastet sind, was ebenfalls durch die von uns erhobenen Daten bestätigt wurde. Dieser Anstieg des Weiterversorgungswunsches konnte auf die postoperativen körperlichen Beeinträchtigungen zurückgeführt werden. Schwer belastete Patienten neigten auch dazu, nach unterstützender Pflege zu bitten. Insgesamt gestaltete es sich jedoch schwierig, die Wirksamkeit der Behandlung objektiv zu bewerten.

Während unserer Datenerhebung haben wir mehrere Faktoren aufgezeichnet, von denen wir vermuteten, dass sie sich auf die Belastung auswirken könnten. Darunter waren Alter, Geschlecht, WHO-Grad und sozioökonomische Faktoren wie Einkommen, Bildung, Familienstand, usw. Am Ende lässt sich feststellen, dass das Geschlecht einen signifikanten Einfluss auf die Belastung hat. Wir haben beobachtet, dass Patientinnen insgesamt deutlich stärker belastet sind. Die sozioökonomische Demografie hatte, außer bei Beziehungs- und Beschäftigungsstatus, keine signifikante Auswirkung auf die Belastung. Geschiedene und pensionierte Patienten gaben an, weniger Belastung zu haben als die anderen. Wir haben auch beobachtet, dass Patienten mit geringerem Einkommen und geringerer Bildung weniger Belastung angegeben haben. Die Ursache dafür könnte an fehlender oder nicht ausreichender Information über die Krankheit oder einem geringeren Verständnis dafür liegen. Aufgrund des umfangsreichen sozialen Sicherungsnetzes in Deutschland, führt ein Einkommensausfall im Krankheitsfall in der Regel nicht zu finanziellen Sorgen. Patienten mit einem Unterstützungsnetzwerk, beispielsweise durch einen Partner oder ihre Kinder, leiden ebenfalls unter weniger

Belastung. Wir vermuten, dass aufgrund des soliden Unterstützungssystems, die Patienten die schwierigen Zeiten besser überstehen bzw. besser damit umgehen.

Zudem haben wir bei der Auswertung festgestellt, dass wir die Schwierigkeiten, die die Patienten wegen des Interviews hatten, nicht sinnvoll erfassen konnten. Wir haben initial die Zeit, die für das Interview benötigt wird, als Maß benutzt. Da der sozioökonomische Status der Patienten nur präoperativ als zusätzliche Frage erhoben wurde, haben die präoperativen Interviews mehr Zeit in Anspruch genommen. Deshalb haben wir anstatt Zeit als Maßeinheit unsere subjektive Einschätzung zur Evaluation der Patientenschwierigkeiten genutzt. Trotz postoperativer Schwierigkeiten, was zu einem schwierigeren sowie längeren Interview führte, gelang es unseren Patienten, alle unsere Fragen ausreichend zu beantworten. Dadurch wurde die Qualität oder Gültigkeit unserer Daten nicht beeinträchtigt.

Zusammengefasst ergab unsere Studie, dass die operative Therapie von Hirntumoren die postoperative körperliche Belastung des Patienten erhöht, jedoch die emotionale Belastung verringert. Andere Faktoren, die die Belastung beeinflussten, waren vor allem Geschlecht, Familienstand, Beschäftigungsstatus und sozioökonomischer Status. Schwierigkeiten, die die Patienten bei der Befragung hatten, beeinträchtigten die Qualität der erhobenen Daten nicht. Weitere Studien zu diesem Thema und der Verwendung der Signalfragen sind erforderlich, insbesondere in der Zeit nach der postoperativen Genesung, um diese noch zu validieren. Dafür wird aktuell eine weitere Studie mit einer ähnlichen Methode in einem ambulanten Setting durchgeführt. Obwohl das DT und die Signalfragen unterschiedliche Ergebnisse lieferten, sind beide Fragebögen trotzdem gute Messinstrumente für die Erfassung der Patientenbelastung. Die Signalfragen waren effizienter in der Erkennung als in der Quantifizierung von psychosozialen Belastungen. Im Gegensatz dazu ist DT aussägekräftiger bei der Quantifizierung von psychosozialen Belastungen.

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List of Abbreviations

DT	Distress Thermometer
SQ	Signalling Question
EORTC QLQ C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
MoCA	Montreal Cognitive Assessment
HADS	Hospital Anxiety and Depression Scale
HRQOL	Health-related Quality of life
SES	Socioeconomic status
GBM	Glioblastoma
NCCN	National Comprehensive Cancer Network
PRO	Patient Reported Outcome
VAS	Visual analogue scale
SD	Standard deviation
WHO	World Health Organization
GTR	Gross total resection
STR	Subtotal resection
IBM SPSS	International Business Machines - Statistical Product and Service Solutions

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Background

Despite technological and medical advancements in previous decades, brain tumors, especially high-grade gliomas remain a death sentence with a severe course and a poor prognosis [1]. The median survival for glioblastoma (GBM) remains at 14.6 months to this day, staunchly unchanged despite treatment with the current multimodal standard therapy of surgical tumor removal and radio-chemotherapy [2]. Brain tumors severely burden their hosts especially due to their detrimental effect on neurocognitive function. The diagnosis itself typically goes hand-in-hand with cognitive decline, functional impairment, and the decline of psychosocial well-being. This results in a reduction of health-related quality of life (HRQOL) [3]. Patients with brain tumors suffer from high levels of physical, neurological, cognitive and psychological morbidity [4]. Furthermore, they also suffer from general cancer-related symptoms such as fatigue, anxiety or depression [1]. Patients with brain tumors report a higher rate of depression than the general cancer population [5]. The effect of this burden extends not only to the patients but to their proxies as well. These include higher rates of depression and anxiety [6], even up to a year post-diagnosis/post-treatment at the time of the final follow-up [3]. Neurocognitive dysfunction also impacts the daily functions and HRQOL of both patient and proxy [7]. Depression has also been linked to decreased HRQOL and even survival [8].

Surgical resection remains the most reliable treatment option for tumorous cancers. Adjuvant chemo- or radiotherapy ensures that all remaining cancerous cells are eliminated, which in turn prevents a recurrence. This is not the case with a large number of brain tumors, especially high-grade Gliomas and GBM. They are essentially incurable since despite complete resection and adjuvant therapy, cancerous cells remain which results in a recurrence [9]. Campos et al. suggest that initial therapy of the primary tumor or the immune response to it applies selective pressure, which results in a recurrence that is therapy resistant [10]. This makes surgery often a palliative approach to gain survival time while preserving maximum quality of life [11]. However, surgery itself brings its own myriad of problems and possibilities of complications which may reduce HRQOL [1, 12]. In one study, post-surgical patients report increased emotional distress, physical impairment, and anxiety [3]. This can naturally be attributed to post-anesthesia weakness, uncertainty over the future, or reaction to the histological results. Nevertheless,

Renovanz et al. recorded that 36% of postsurgical patients were severely distressed and of those, a large majority were in need of professional psychiatric treatment [13].

Distress, as conceptualized by the National Comprehensive Cancer Network (NCCN), has been utilized to diagnose significant emotional, social and physical burdens without stigmatization [5]. Distress has also been shown to serve as an indicator for clinicians to recognize unmet supportive care needs, especially in the psychological domain [14]. The concept of psychosocial needs is used to represent the mental and social needs of a patient and their families. These needs arise in response to their diagnosis, the limitations to their social roles, their physical or mental abilities, and the impact of the disease and treatment on their family and social circle [15]. Due to the nature of the illness, it is important to consider the impact of the illness on patients outside the clinical field. Patients with significant physical and neurocognitive impairment can no longer work or conduct social relations at the level they were previously accustomed to. They also face significant difficulties in pursuing activities that they previously enjoyed doing. Patients with less social support reported more practical and familial distress [5]. Unfortunately, this lack of support is not uncommon, especially among the elderly [16].

Another aspect to consider is whether or not socioeconomic demographics had an effect on distress or psychosocial needs. Baum et al. postulated that chronic stress is a product of social and environmental conditions such as discrimination, crowding, or noise pollution. Socioeconomic status (SES) is named as a public health factor and a predictor of health and illness outcomes [17]. SES seems to be inversely correlated to chronic stress. People with higher SES experience less chronic stress, which then results in better health outcomes [18]. Previous research has also shown that survival rates are higher amongst patients with higher SES [19, 20]. If socioeconomic differences were alleviated, a study by Siegel et al. estimated that 34% of cancer fatalities in America could be avoided [21].

Clinical depression is prevalent among tumor patients and it often goes unrecognized and untreated [22] due to its difficulty to diagnose [23]. This difficulty may stem from various factors such as neurocognitive impairment or underestimation of symptom severity by the patients themselves due to fear of stigmatization. Therefore, the challenge is to find a screening method that yields the most accurate picture of a patient's

psychosocial distress. However, this has proven difficult when utilizing only one tool for such a complex problem. It is therefore advantageous to utilize more than one questionnaire to avoid inherent bias and to get a more detailed overview of the patient's needs [24].

Even though the importance of assessing psychosocial needs is evident, that isn't to say that it's easily evaluated. Screenings instruments that have been validated do exist and are utilized by clinicians to react to pathological scores and subsequently initiate treatment [25].
However, stigmatization [26] along with difficulties in participating in screening programs [27] are major impediments in assessing psychosocial support care needs [28]. The involvement of health-care professionals in identifying supportive care needs and tailoring their patients' care is paramount [29].

Screening for these psychosocial needs through the use of patient-reported outcomes (PRO) has become standard during the treatment of glioma patients [24].
However, this is far from a perfect solution. An analysis by Rooney et al. of the difference between patient and proxy screening shows that while patients and their proxies tend to agree on objective signs such as mobility and physical function, patients tend to be less reliable in reporting objective behavioural symptoms of depression [30]. This difference is potentially clinically relevant. Patients have also been documented to shield their loved ones from their anxieties to lessen their suffering [31]. Another disadvantage of PRO is that it can be affected by neurocognitive impairments [32]. Therefore it is also important, on the part of the clinician, to make their own judgements or to interview proxies in addition to the patients themselves [24].

Another challenge with screening is its difficulty to implement in day to day practice. Despite the clinical, ethical, and financial value of screening and treating psychosocial needs [33], supportive care is a tool that is often used at the end of curative care [34]. It is also often not well integrated with standard oncological practice [35]. Carrieri et al. surmised that the barriers hindering the implementation of supportive care are lack of resources and organizational infrastructures, healthcare professional burnout, and cultural stigma towards death [36]. Added to this is also the fact that there are no blanket questionnaires to screen and address all aspects of patient burdens during all stages of

the disease. This leads to clinicians picking and choosing between questionnaires to implement in their practice and no standards being set across the board.

Goal

As mentioned above, patients with brain tumors suffer from a variety of symptoms that results in depression, anxiety, and a need for supportive care. These needs often go unrecognized and untreated, and often extends to the patients' families and caregivers. Thus, a screening program would be reasonable to implement, which already is at different points of the treatment.

As such, this study aims to determine, using screening instruments available as well as one of our own design, how operative therapy of brain tumor patients influences their psychosocial wellbeing and supportive care needs.

Question

Primary:
Does surgery significantly reduce or increase the distress in patients' lives including problems in the physical, emotional, and socioeconomic field, as measured by DT and the 3 signaling questions?

Secondary:

- Is there a difference in the effectiveness of operative treatment?
- Does the socioeconomic background of the patient influence the level of distress of the patient?
- Does the difficulty in conducting the interview effect the data that is collected in this study?

Method

In the quest of quantifying something as abstract and multifaceted as stress, there has been several different standardized tests developed to measure quality of life, neurocognitive deficits, and psychosocial supportive care needs.

In this study, we chose to rely on Patient Reported Outcomes (PRO), which is an established means to determine the patients' health-related quality of life (HRQOL) [37]. Despite the risk of false answers due to diminishing cognitive function, Rooney et al. established that patients and their proxies generally agree on most physical symptoms. Poorer cognitive function also does not seem to result in significant differences in their answers [30].

Data collection of the PROs will be conducted through active questioning across two interviews. The patients will be interviewed shortly before and after their operation during the same clinical stay. A questionnaire designed by ourselves and the German version of Distress Thermometer (DT), adapted in 2007 by Mehnert et al. [38] were applied.

Our questionnaire was developed internally based on several other established questionnaires, which have been shown to have a strong correlation to the patients' conditions and reported burdens [25]. They are the DT, EORTC QLQ-C30, and MoCA CRF and Feasibility Feedback Form. It also includes "Signaling Questions" (SQ) developed during the GLIOPT study in Universitätsmedizin Mainz [39]. The SQ was conceptualized with ease of use in mind. Due to the previously mentioned constraints in implementing screening questionnaires, as well as cognitive decline in later stages of the disease, patients are often excluded from studies [3, 40], which leads to false conclusions [41]. SQ consists of a set of 3 questions with an additional question upon a positive answer. They are:

1. Psychological: Has your mood worsened? (if yes: Are you unsure about your future?)
2. Physical: Are you burdened by the changes to your body? (if yes: Do you often have to take breaks due to fatigue?)
3. Cognitive: Has your ability to think worsened? (if yes: Is it difficult for you to concentrate?)

Positive answers to these questions signal the need to further probe into patients' psychosocial distress and supportive care needs. The concise nature of the questions enables them to be used practically during consultations by health-care professionals. The interview will also collect data on the patients' socioeconomic background, diagnosis, treatment, and the difficulties the patients experienced in completing the interview.

As a point of comparison to this untested questionnaire and the signaling questions, we will also simultaneously use the Distress Thermometer questionnaire to confirm the validity of our findings. DT was developed by the NCCN [42] and is a self-reporting instrument utilizing a visual analogue scale (VAS) from 0 (no distress) to 10 (maximal distress). It is followed by a problem list of 40 items assessing distress in practical/financial, emotional, spiritual, and physical fields. We chose DT as a point of comparison due to its ease of use, short duration, and the comprehensiveness of its 'problem list'. Previous research by Goebel et al. has shown that a DT score of ≥6 indicates a clinically relevant level of distress for brain tumor patients. [28]. A counterpoint to using DT would be its described ineffectiveness by Rooney et al. in comparison to other screening instruments to screen depression [23]. However, this may be due to the fact that DT identifies anxiety to a greater extent than it identifies depression [43]. It is also important to note that Rooney only utilized the single item distress scale and not the multi-faceted problems list.

The population that we included in the study was made up of patients of the neurosurgical clinic of the university hospital of Mainz. These patients have been diagnosed with brain tumors, both primary tumors, and metastases. The patients must be at least 18 years old and capable of holding a conversation, either independently or with the help of a family member. Patients with insufficient proficiency in either German or English were excluded from the recruitment process. They were also free to withdraw from the study at any point during the interview, after the surgery, or after the conclusion of their inpatient stay. Information about the degree of success of the operation and tumor histology, as well as neurocognitive symptoms before or after the operation, were collected from their medical records. Neurocognitive impairment before surgery can influence prognosis to some extent [44].

The data will be analyzed using the German version of IBM SPSS 23. A combination of descriptive statistics and graphing of means will be used to draw comparisons. To test for significance, we will conduct independent samples or paired samples t-test along with non-parametric significance tests where appropriate. Correlation analysis will be measured using the Kendall-tau correlation test. The relationship between DT and SQ will be explored using ordinal regression analysis. The exploration of the influence of other factors such as sex and age on both parameters will also be conducted using the same methods.

A similar study using the same questionnaire and the EORTC QLQ-C30 is being conducted in an outpatient setting on patients several months after their procedure as part of the same project.

Results

Patient Characteristics (Table 1)

51 Patients were recruited into this study. 41 Patients completed both the pre-operative and post-operative interviews. 10 patients withdrew from the study, 9 post-operatively and 1 during the pre-operative interview.

All patients underwent surgical resection of their tumors and were interviewed pre-operatively and on average 3.5 days postoperatively. The mean age was 61.15 years old (SD 12.6) and females represented a slight majority (56%) of the patient cohort. The patients had a wide range of tumor severity ranging from WHO Grade 1 (29.3%), WHO Grade 4 (22%), and brain metastases (26.8%). The patients were predominantly married (65.9%) with children (80.5%), living communally (73.2%), homeowners (63.4%), retired (53.7%), and had statutory health insurance (80.5%)

Table 1. Demographic data of patient population

Demographic characteristics of patients (n=41)		
	n	(%)
Age - mean (SD)	61.15 (12.6)	
Sex		
Male	18	(43.9)
Female	23	(56.1)
WHO Grade		
1	12	(29.3)
2	5	(12.2)
3	4	(9.8)
4	9	(22.0)
Metastases	11	(26.8)
Resection		
GTR	35	(85.4)
STR	5	(12.2)
Marital status		
Single	7	(17.1)
Married	27	(65.9)
Divorced	4	(9.8)
Widowed	3	(7.3)
Children		
Yes	33	(80.5)
No	8	(19.5)
Living status		
Alone	11	(26.8)
Communal	30	(73.2)
Ownership status		
Rent	14	(34.2)

Owner	26	(63.4)
Care Home	0	(0)
With Relatives	1	(2.4)
Education		
Hauptschule	15	(36.6)
Realschule	14	(34.1)
University	12	(29.3)
Job Status		
Working	13	(31.7)
Retired	22	(53.7)
Disabled	0	(0)
Housewife/husband	6	(14.6)
Annual income		
<10.000	6	(14.6)
<30.000	17	(41.5)
<50.000	9	(22.0)
<70.000	2	(4.9)
>70.000	5	(12.2)
Insurance		
Statutory	33	(80.5)
Private	8	(19.5)
Religion		
Yes	31	(75.6%)
No	10	(24.4%)

Perioperative stress

To measure the change in perioperative stress, we measured distress using both the 'Distress Thermometer' (DT) and 3 'Signaling Questions' (SQ). This allows us to compare both datapoints to each other and confirm their validity in accurately measuring patient stress.

Distress increased slightly on average after the operation (**Table 2**) from a mean score of 5.4 pre-operation to 5.63 post-operation out of a maximum of 10 points. The same increase was observed for the sum of the DT items with a mean of 8.17 pre-operation to 8.93 post-operation out of a maximum of 36 items. Both changes were determined to be statistically insignificant (**Figure 1**). Deeper analysis of the type of distress the patients were experiencing was possible through the different categories of the DT problem items. The items were grouped into 5 categories: practical problems, family problems, emotional problems, spiritual problems, and physical problems. Comparing these categories across both timepoints gives us a more nuanced view into the transformation of stress after an operation (**Table 3**). Spiritual problems remain low and unchanged across both time points with a mean of 0.07 out of a maximum of 1 point. Practical

problems and familial problems rose slightly post-operation from 0.61 to 0.76 out of a maximum of 5 points and 0.12 to 0.20 out of a maximum of 3 points respectively. The aforementioned changes were not statistically significant (**Figure 1**) and represented the minority in the total distress score of the patients. A significant increase was observed in physical problems, a rise from a mean score of 4.76 to 6.12 out of a maximum of 21 points. We also recorded a significant decrease in emotional problems from a mean score of 2.61 to 1.78 out of a maximum score of 6 points.

Table 2. Descriptive statistics of DT

	N	Minimum	Maximum	Mean	Std. Deviation
Distress pre-OP	41	0	9	5,40	2,518
Distress post-OP	41	1	10	5,63	2,525
Sum DT pre-OP	41	1	17	8,17	4,505
Sum DT post-OP	41	1	23	8,93	4,987
Valid N (listwise)	41				

Table 3. Descriptive statistics of DT categories and SUM DT

OP Status		N	Minimum	Maximum	Mean	Std. Deviation
Pre-OP	Practical problems	23	0	3	,87	,920
	Family problems	23	0	1	,22	,422
	Emotional problems	23	0	6	3,26	1,815
	Spiritual problems	23	0	1	,13	,344
	Physical problems	23	1	11	5,52	2,874
	Valid N (listwise)	23				
Post-OP	Practical problems	23	0	3	1,13	,815
	Family problems	23	0	2	,17	,576
	Emotional problems	23	0	6	2,13	1,890
	Spiritual problems	23	0	1	,13	,344
	Physical problems	23	1	16	7,30	3,819
	Valid N (listwise)	23				

Null Hypothesis	Test	Sig.	Decision
The median of differences between Distress pre-OP and Distress post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,678	Retain the null hypothesis.
The median of differences between Sum DT pre-OP and Sum DT post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,192	Retain the null hypothesis.
The median of differences between Practical problems pre-OP and Practical problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,186	Retain the null hypothesis.
The median of differences between Family problems pre-OP and Family problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,180	Retain the null hypothesis.
The median of differences between Emotional problems pre-OP and Emotional problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,003	Reject the null hypothesis.
The median of differences between Spiritual problems pre-OP and Spiritual problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	1	Retain the null hypothesis.
The median of differences between Physical problems pre-OP and Physical problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,009	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 1. Significance test of DT and its categories

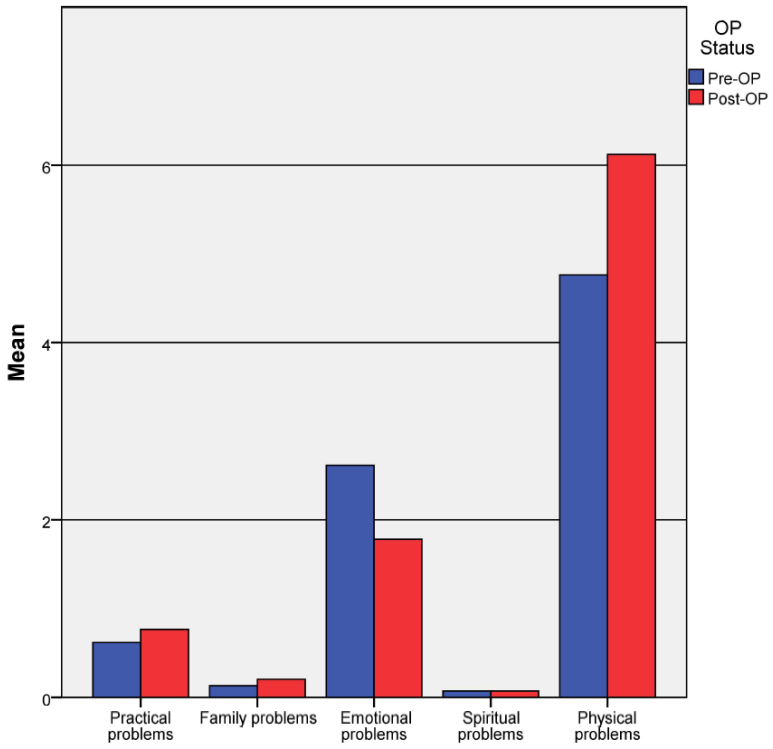

Figure 2. Mean distress of DT categories

Patients are considered distressed when their DT score equals or exceeds 6 (DT≥6). We analyzed this part of the patient population to see whether their stresses differ from the non-distressed patients. The same increase of DT and the sum of the items were also observed (**Table 4**). Mean DT for distressed patients was 7.24 pre-operation and 7.5 post-operation. The mean sum of the items was 10 pre-operation and 10.87 post-operation. Both these changes were, once again, not statistically significant (**Figure 4**). Analysis of the categories of distress showed similar trends in the mean scores compared to the whole population (**Table 5**). Spiritual problems once again remained unchanged at 0.13. Practical problems rose slightly from a mean score of 0.87 to 1.13 and familial problems decreased from 0.22 to 0.17. Both changes were insignificant. Emotional problems decreased significantly from a mean score of 3.26 to 2.13 while physical problems rose significantly from 5.52 to 7.3.

Table 4. Descriptive statistics of DT and SUM DT for distressed patients

OP Status		N	Minimum	Maximum	Mean	Std. Deviation
Pre-OP	Distress	23	6	9	7,24	1,043
	Sum DT	23	3	17	10,00	4,472
	Valid N (listwise)	23				
Post-OP	Distress	23	6	10	7,50	1,177
	Sum DT	23	1	23	10,87	5,521
	Valid N (listwise)	23				

Table 5. Descriptive statistics of DT categories for distressed patients

OP Status		N	Minimum	Maximum	Mean	Std. Deviation
Pre-OP	Practical problems	23	0	3	,87	,920
	Family problems	23	0	1	,22	,422
	Emotional problems	23	0	6	3,26	1,815
	Spiritual problems	23	0	1	,13	,344
	Physical problems	23	1	11	5,52	2,874
	Valid N (listwise)	23				
Post-OP	Practical problems	23	0	3	1,13	,815
	Family problems	23	0	2	,17	,576
	Emotional problems	23	0	6	2,13	1,890
	Spiritual problems	23	0	1	,13	,344
	Physical problems	23	1	16	7,30	3,819
	Valid N (listwise)	23				

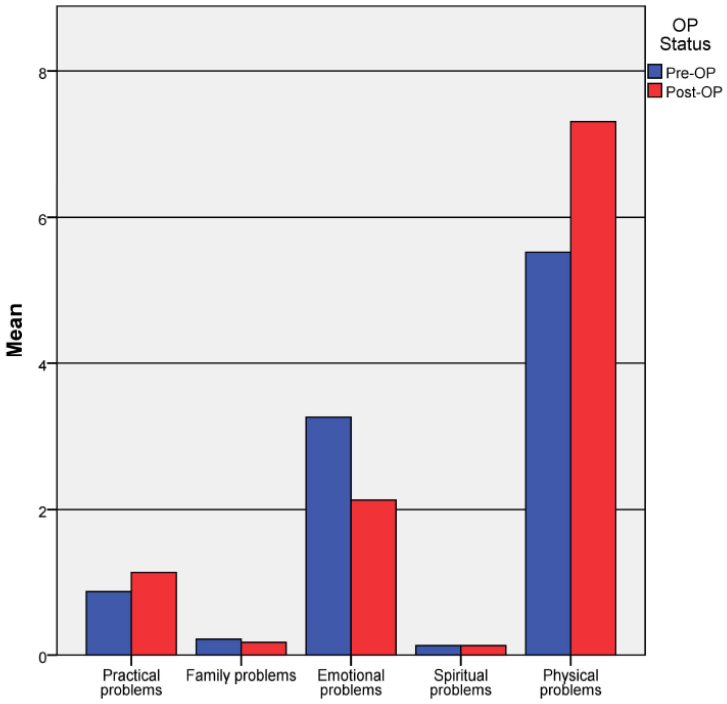

Figure 3. Mean distress of DT categories for distressed patients

Null Hypothesis	Test	Sig.	Decision
The median of differences between Distress pre-OP and Distress post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,659	Retain the null hypothesis.
The median of differences between Sum DT pre-OP and Sum DT post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,188	Retain the null hypothesis.
The median of differences between Practical problems pre-OP and Practical problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,115	Retain the null hypothesis.
The median of differences between Emotional problems pre-OP and Emotional problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,007	Reject the null hypothesis.
The median of differences between Physical problems pre-OP and Physical problems post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,023	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 4. Significance test of DT and its categories for distressed patients

Contrary to distress, we observed a post-operative drop in the number of positive responses to SQ, i.e. patients are less stressed post-operation according to SQ (**Table 6**). We saw the mean number of yes answers drop from 1.46 to 0.9 out of a maximum of 3. Breaking it down to each question addressing psychological problems, physical problems, and cognitive problems, we saw a drop across the board (**Table 7**). Psychological problems had a mean of 0.54 yes answers pre-operation which decreased to 0.24 after the procedure. Physical problems had a mean of 0.56 yes answers which decreased to 0.46 post-operation. Cognitive problems had a mean of 0.37 yes answers which went down to 0.22 after the operation. The statistical significance test showed that the drops in total answers and psychological problems were significant (**Figure 5**).

Table 6. Descriptive statistics of SQ

	N	Minimum	Maximum	Mean	Std. Deviation
Signalling Questions pre-OP	41	0	3	1,46	1,027
Signalling Questions post-OP	41	0	3	,90	1,068
Valid N (listwise)	41				

Table 7. Descriptive statistics of SQ questions

	N	Minimum	Maximum	Mean	Std. Deviation
Signalling Psych pre-OP	41	0	1	,54	,505
Signalling Psych post-OP	41	0	1	,24	,435
Signalling Physical pre-OP	41	0	1	,56	,502
Signalling Physical post-OP	41	0	1	,46	,505
Signalling Cognition pre-OP	41	0	1	,37	,488
Signalling Cognition post-OP	41	0	1	,22	,419
Valid N (listwise)	41				

Null Hypothesis	Test	Sig.	Decision
The median of differences between Signalling Questions pre-OP and Signalling Questions post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,004	Reject the null hypothesis.
The distributions of different values across Signalling Psych pre-OP and Signalling Psych post-OP are equally likely.	Related-Samples McNemar Test	0,004	Reject the null hypothesis.
The distributions of different values across Signalling Physical pre-OP and Signalling Physical post-OP are equally likely.	Related-Samples McNemar Test	0,388	Retain the null hypothesis.
The distributions of different values across Signalling Cognition pre-OP and Signalling Cognition post-OP are equally likely.	Related-Samples McNemar Test	0,180	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 5. Significance test of SQ

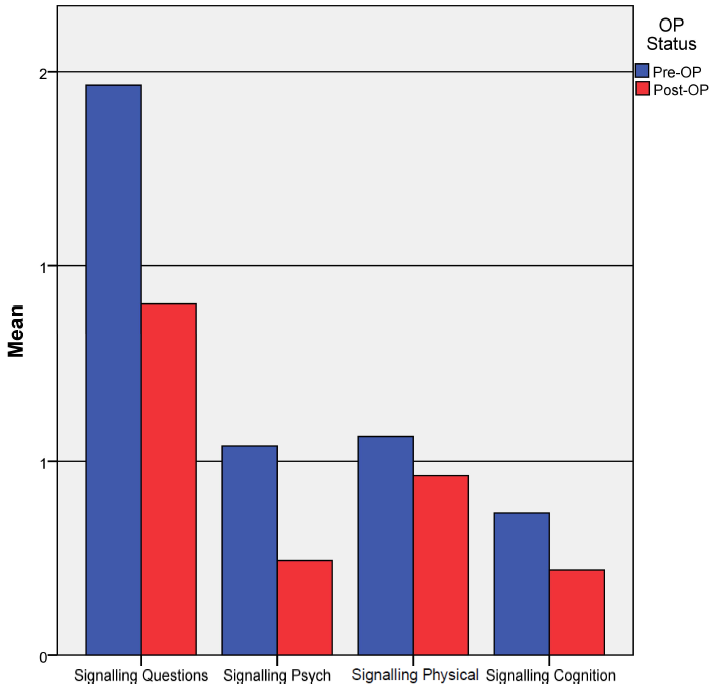

Figure 6. Mean number of yes answers to SQ and its individual questions

When isolated to distressed patients (DT≥6), we observed that the previous trend for SQ in the whole population remained. We saw a significant drop (**Figure 8**) in the mean number of yes answers from 1.74 to 1.3 (**Table 8**). When broken down to the individual questions, similar to the whole population, we observed drops across the board (**Table 9**). There was a statistically significant drop in the mean number of yes answers to psychological problems from 0.61 to 0.39. The drops in the mean number of yes answers in physical and cognitive problems from 0.7 to 0.65 and from 0.43 to 0.3 respectively were statistically insignificant.

Table 8. Descriptive statistics of SQ for distressed patients

OP Status		N	Minimum	Maximum	Mean	Std. Deviation
Pre-OP	Signalling Questions	23	0	3	1,74	1,010
	Valid N (listwise)	23				
Post-OP	Signalling Questions	23	0	3	1,30	1,105
	Valid N (listwise)	23				

Table 9. Descriptive statistics of SQ questions for distressed patients

OP Status		N	Minimum	Maximum	Mean	Std. Deviation
Pre-OP	Signalling Psych	23	0	1	,61	,499
	Signalling Physical	23	0	1	,70	,470
	Signalling Cognition	23	0	1	,43	,507
	Valid N (listwise)	23				
Post-OP	Signalling Psych	23	0	1	,39	,499
	Signalling Physical	23	0	1	,65	,487
	Signalling Cognition	23	0	1	,30	,470
	Valid N (listwise)	23				

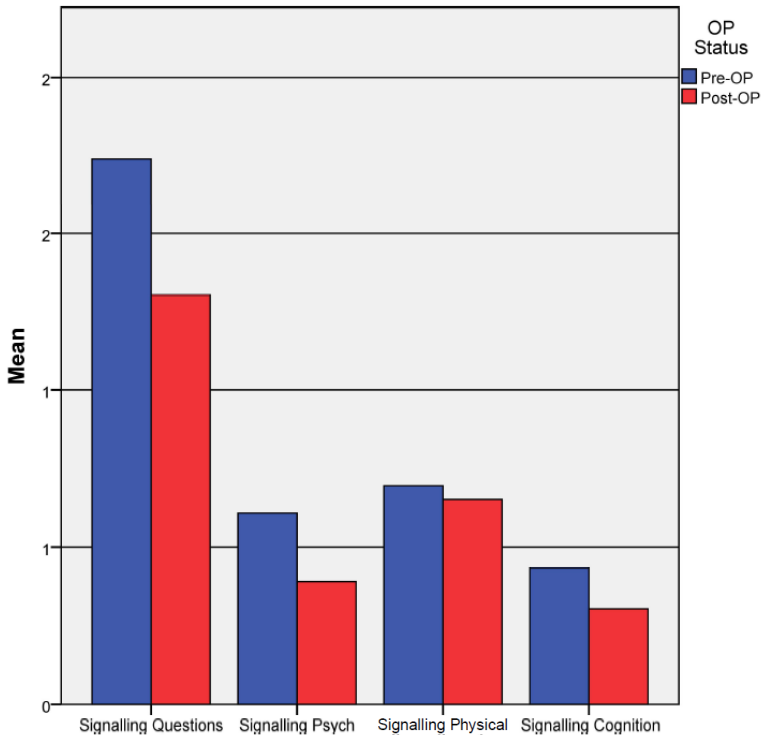

Figure 7. Mean number of yes answers to SQ and its individual questions for distressed patients

Null Hypothesis	Test	Sig.	Decision
The median of differences between Signalling Questions pre-OP and Signalling Questions post-OP equals 0.	Related-Samples Wilcoxon Signed Rank Test	0,009	Reject the null hypothesis.
The distributions of different values across Signalling Psych pre-OP and Signalling Psych post-OP are equally likely.	Related-Samples McNemar Test	0,039	Reject the null hypothesis.
The distributions of different values across Signalling Physical pre-OP and Signalling Physical post-OP are equally likely.	Related-Samples McNemar Test	0,289	Retain the null hypothesis.
The distributions of different values across Signalling Cognition pre-OP and Signalling Cognition post-OP are equally likely.	Related-Samples McNemar Test	0,227	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 8. Significance test of SQ for distressed patients

Relationship between Distress as measured by DT and SQ

In comparing both datapoints, we can conclude that patients with higher distress generally have more positive responses to SQ as well. Distressed patients with DT scores equal to or higher than 6 have significantly more positive answers to SQ with a mean number of yes answers of 0.75 for non-distressed patients and 1.52 for distressed patients (**Table 10**). The individual questions also displayed the same trends for non-distressed and distressed patients with a mean increase of yes answers from 0.25 to 0.5 for psychological problems, from 0.31 to 0.67 for physical problems, and from 0.19 to 0.37 for cognitive problems respectively. The differences are all statistically significant except for cognitive problems (**Figure 10**). Using Kendall's tau correlation test, we demonstrated that DT and SQ are significantly correlated with one another with a coefficient of 0.332 (**Table 11**). Further analysis using ordinal regression with DT and Sum DT as independent variables and SQ as the dependent variable showed a significant model with significant goodness of fit, R square value of 0.738 (Nagelkerke), and significant test of parallel lines (**Figure 11**). Another model with only DT as the independent variable showed similar results with an R square value of 0.434 (Nagelkerke) (**Figure 12**).

Table 10. Descriptive statistics of SQ for distressed and non-distressed patients

Dist >= 6 (FILTER)		N	Minimum	Maximum	Mean	Std. Deviation
Not Selected	Signalling Questions	36	0	3	,75	,937
	Signalling Psych	36	0	1	,25	,439
	Signalling Physical	36	0	1	,31	,467
	Signalling Cognition	36	0	1	,19	,401
	Valid N (listwise)	36				
Selected	Signalling Questions	46	0	3	1,52	1,070
	Signalling Psych	46	0	1	,50	,506
	Signalling Physical	46	0	1	,67	,474
	Signalling Cognition	46	0	1	,37	,488
	Valid N (listwise)	46				

Table 11. Correlation table between DT and SQ

			Distress	Signalling Questions
Kendall's tau_b	Distress	Correlation Coefficient	1,000	,332**
		Sig. (2-tailed)	.	,000
		N	82	82
	Signalling Questions	Correlation Coefficient	,332**	1,000
		Sig. (2-tailed)	,000	.
		N	82	82

**. Correlation is significant at the 0.01 level (2-tailed).

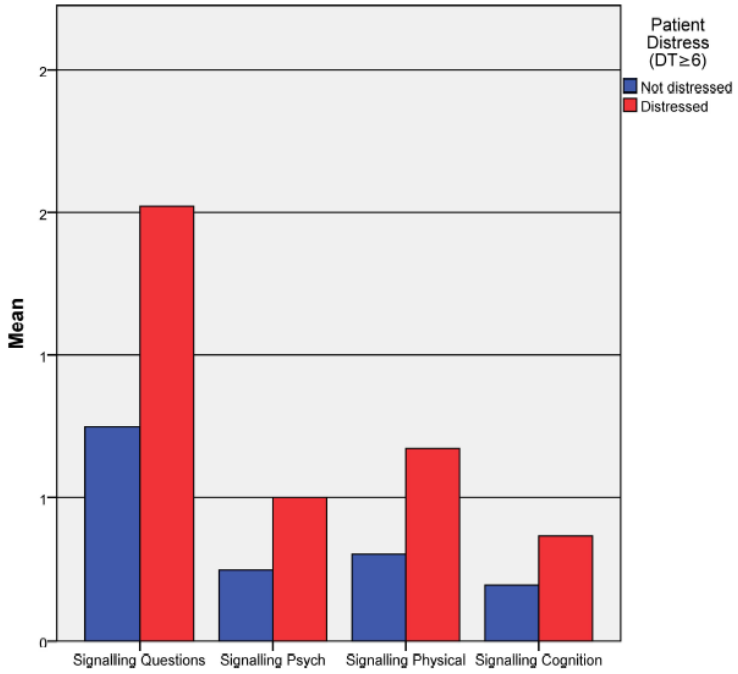

Figure 9. Mean number of yes answers to SQ and its individual questions for distressed patients and non-distressed patients

Hypothesis Test Summary

Null Hypothesis	Test	Sig.	Decision
The distribution of Signalling Questions is the same across categories of distressed patients.	Independent-Samples Mann-Whitney U Test	0,001	Reject the null hypothesis.
The distribution of Signalling Psych is the same across categories of distressed patients.	Independent-Samples Mann-Whitney U Test	0,022	Reject the null hypothesis.
The distribution of Signalling Physical is the same across categories of distressed patients.	Independent-Samples Mann-Whitney U Test	0,001	Reject the null hypothesis.
The distribution of Signalling Cognition is the same across categories of distressed patients.	Independent-Samples Mann-Whitney U Test	0,086	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 10. Significance test of SQ for distressed and non-distressed patients

Case Processing Summary

		N	Marginal Percentage
Signalling Questions	0	30	36,6%
	1	18	22,0%
	2	23	28,0%
	3	11	13,4%
Distress	0	2	2,4%
	1	6	7,3%
	2	5	6,1%
	3	5	6,1%
	4	7	8,5%
	5	1	1,2%
	5	10	12,2%
	6	14	17,1%
	7	8	9,8%
	8	1	1,2%
	8	16	19,5%
	9	1	1,2%
	9	5	6,1%
	10	1	1,2%
Sum DT	1	2	2,4%
	2	3	3,7%
	3	5	6,1%
	4	7	8,5%
	5	7	8,5%
	6	12	14,6%
	7	5	6,1%
	8	8	9,8%
	9	1	1,2%
	10	2	2,4%
	11	10	12,2%
	12	3	3,7%
	13	2	2,4%
	14	4	4,9%
	15	3	3,7%
	16	2	2,4%
	17	3	3,7%
	18	2	2,4%
	23	1	1,2%
Valid		82	100,0%
Missing		0	
Total		82	

Model Fitting Information

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	192,166			
Final	97,251	94,915	31	,000

Link function: Logit.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	299,458	143	,000
Deviance	75,174	143	1,000

Link function: Logit.

Pseudo R-Square

Cox and Snell	,686
Nagelkerke	,738
McFadden	,436

Link function: Logit.

Test of Parallel Lines[a]

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Null Hypothesis	97,251			
General	,000[b]	97,251	62	,003

The null hypothesis states that the location parameters (slope coefficients) are the same across response categories.

a. Link function: Logit.

b. The log-likelihood value is practically zero. There may be a complete separation in the data. The maximum likelihood estimates do not exist.

Figure 11. Ordinal Regression of DT and Sum DT to SQ

Case Processing Summary

		N	Marginal Percentage
Signalling Questions	0	30	36,6%
	1	18	22,0%
	2	23	28,0%
	3	11	13,4%
Distress	0	2	2,4%
	1	6	7,3%
	2	5	6,1%
	3	5	6,1%
	4	7	8,5%
	5	1	1,2%
	5	10	12,2%
	6	14	17,1%
	7	8	9,8%
	8	1	1,2%
	8	16	19,5%
	9	1	1,2%
	9	5	6,1%
	10	1	1,2%
Valid		82	100,0%
Missing		0	
Total		82	

Model Fitting Information

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	101,865			
Final	59,568	42,297	13	,000

Link function: Logit.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	27,483	26	,384
Deviance	20,924	26	,746

Link function: Logit.

Pseudo R-Square

Cox and Snell	,403
Nagelkerke	,434
McFadden	,194

Link function: Logit.

Test of Parallel Lines[a]

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Null Hypothesis	59,568			
General	,000[b]	59,568	26	,000

The null hypothesis states that the location parameters (slope coefficients) are the same across response categories.

a. Link function: Logit.

b. The log-likelihood value is practically zero. There may be a complete separation in the data. The maximum likelihood estimates do not exist.

Figure 12. Ordinal Regression of DT to SQ

Role of age, sex and WHO grade on stress

Aside from socioeconomic background, we wanted to see whether other factors might affect patient stress such as age, sex, or tumor severity. For brain tumors, WHO Grade is the commonly accepted measure of severity with grade 1 including tumors such as meningiomas, and grade 4 including tumors such as glioblastomas. We compared the DT and SQ scores of patients with these factors to determine whether they exhibit unique characteristics. In regards to age, we found no significant correlation or effect on DT or SQ through regression analysis. Age does not seem to have an impact on stress. For tumor severity or WHO Grade, we saw no statistically significant changes to DT or SQ across the groups (**Figure 15**). However, we observed that WHO Grade 4 patients had higher distress (**Figure 13**), something we did not observe with SQ (**Figure 14**). Regression analysis for both DT and SQ against WHO Grade showed no significant impact.

Comparatively, we observed different results when it comes to sex. We saw significantly higher distress levels in female patients compared to male patients (**Figure 17**). The mean distress score for female patients was 6.11 compared to 4.76 for male patients (**Table 12**). This constituted a statistically significant difference between the DT of male and female patients (**Figure 16**). This was not reflected in the SQ which had mean scores of 1.22 for female patients and 1.14 for male patients. Further regression analysis showed that sex has a significant albeit small impact on distress with an R square value of 0.072 (**Figure 18**).

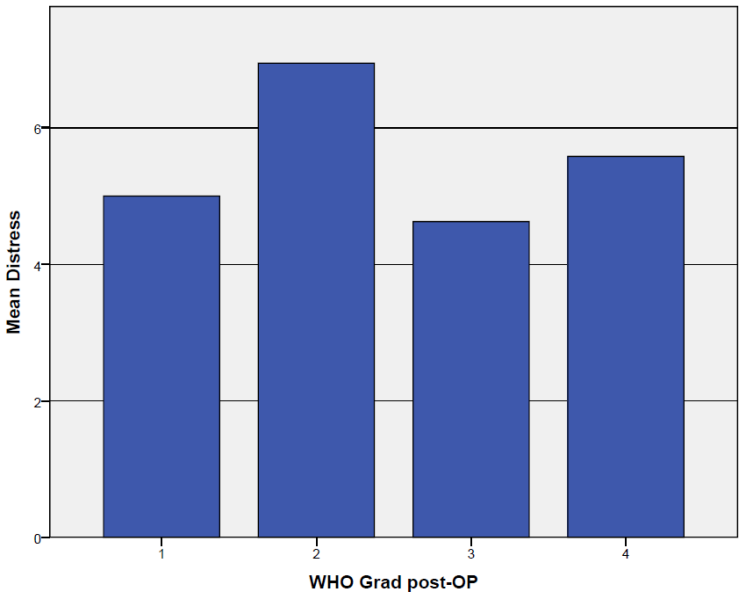

Figure 13. Mean DT across different WHO Grades

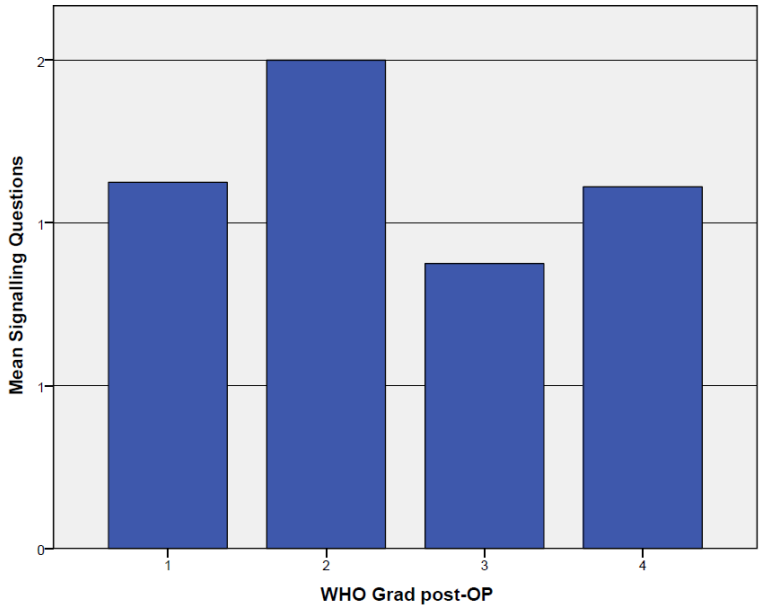

Figure 14. Mean number of yes answers to SQ across different WHO Grades

Null Hypothesis	Test	Sig.	Decision
The distribution of Distress is the same across categories of WHO Grad post-OP.	Independent-Samples Kruskal-Wallis Test	0,211	Retain the null hypothesis.
The distribution of Signalling Questions is the same across categories of WHO Grad post-OP.	Independent-Samples Kruskal-Wallis Test	0,751	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 15. Significance test of WHO Grade on DT and SQ

	Sex	N	Mean	Std. Deviation	Std. Error Mean
Distress	Female	46	6,11	2,646	,390
	Male	36	4,76	2,126	,354
Signalling Questions	Female	46	1,22	1,114	,164
	Male	36	1,14	1,046	,174

Table 12. Descriptive statistics of DT and SQ for different sexes

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Distress	Equal variances assumed	1,547	,217	2,485	80	,015	1,345	,541	,268	2,422
	Equal variances not assumed			2,552	79,930	,013	1,345	,527	,296	2,394
Signalling Questions	Equal variances assumed	,668	,416	,325	80	,746	,079	,241	-,402	,559
	Equal variances not assumed			,328	77,317	,744	,079	,240	-,398	,555

Figure 16. Significance test of gender on DT and SQ

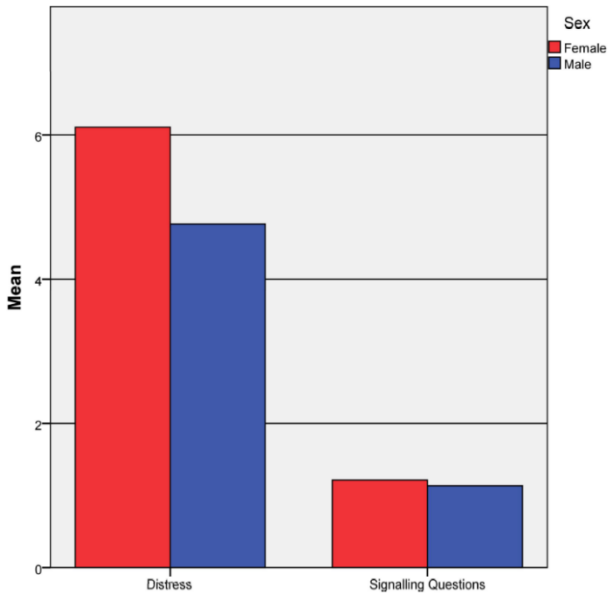

Figure 17. Mean DT and SQ for different sexes

Regression

Variables Entered/Removed[a]

Model	Variables Entered	Variables Removed	Method
1	Sex[b]	.	Enter

a. Dependent Variable: Distress

b. All requested variables entered.

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Durbin-Watson
1	,268[a]	,072	,060	2,432	2,051

a. Predictors: (Constant), Sex

b. Dependent Variable: Distress

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	36,523	1	36,523	6,175	,015[b]
	Residual	473,200	80	5,915		
	Total	509,723	81			

a. Dependent Variable: Distress

b. Predictors: (Constant), Sex

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	6,109	,359		17,035	,000
	Sex	-1,345	,541	-,268	-2,485	,015

a. Dependent Variable: Distress

Residuals Statistics[a]

	Minimum	Maximum	Mean	Std. Deviation	N
Predicted Value	4,76	6,11	5,52	,671	82
Residual	-6,109	3,891	,000	2,417	82
Std. Predicted Value	-1,123	,879	,000	1,000	82
Std. Residual	-2,512	1,600	,000	,994	82

a. Dependent Variable: Distress

Figure 18. Regression analysis of DT on sex

Impact of treatment effectiveness on stress

In order to measure treatment effectiveness directly after the operation, we decided to ask our patients whether or not they required further supportive care. By determining this and comparing the results between the 2 timepoints, we can get a sense of whether the operation itself addressed the supportive care needs of the patients, or if there are underlying issues that needs to be addressed. We observed that 29.3% of patients wished for further supportive care after their operation compared to 22% before (**Table 13**). This increase is not statistically significant. Of those who wanted care before the procedure, 77.8% also wish for further care afterwards (**Table 14**).

Table 13. Descriptive statistics of further care wish

Further care wish

OP Status			Frequency	Percent	Valid Percent	Cumulative Percent
Pre-OP	Valid	no	32	78,0	78,0	78,0
		yes	9	22,0	22,0	100,0
		Total	41	100,0	100,0	
Post-OP	Valid	no	29	70,7	70,7	70,7
		yes	12	29,3	29,3	100,0
		Total	41	100,0	100,0	

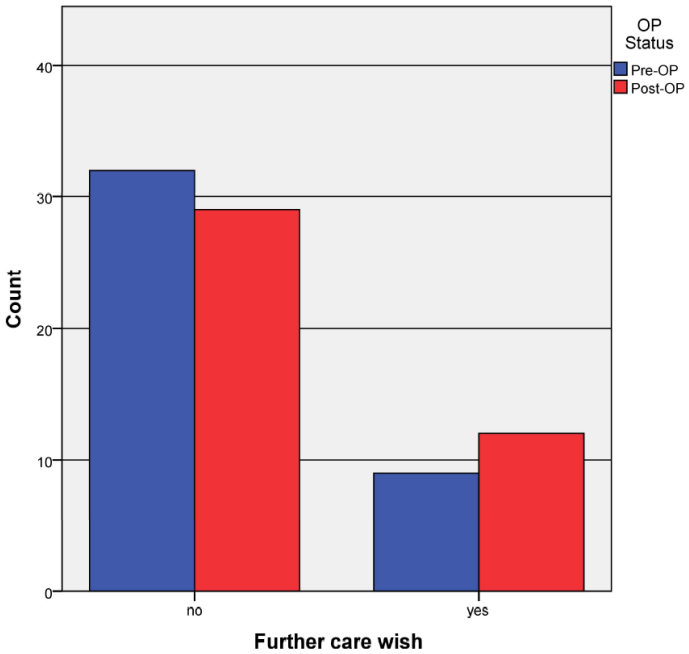

Figure 19. Number of patients requiring further supportive care before and after their operation

Further care wish pre-OP * Further care wish post-OP Crosstabulation

			Further care wish post-OP		
			no	yes	Total
Further care wish pre-OP	no	Count	27	5	32
		% within Further care wish pre-OP	84,4%	15,6%	100,0%
		% within Further care wish post-OP	93,1%	41,7%	78,0%
	yes	Count	2	7	9
		% within Further care wish pre-OP	22,2%	77,8%	100,0%
		% within Further care wish post-OP	6,9%	58,3%	22,0%
Total		Count	29	12	41
		% within Further care wish pre-OP	70,7%	29,3%	100,0%
		% within Further care wish post-OP	100,0%	100,0%	100,0%

Chi-Square Tests

	Value	Exact Sig. (2-sided)
McNemar Test		,453[a]
N of Valid Cases	41	

a. Binomial distribution used.

Table 14. Crosstabulation of further care wish

We decided to look further into this increase of supportive care wish by looking only at the distressed patient population (DT≥6). Amongst distressed patients, there was a slight increase of further care wish after the operation from 30.4% to 34.8% (**Table 15**). However, this difference constituted of only 1 patient newly wanting further care. When we compare the distressed patients with the others, however, we get a clearer picture. 15 distressed patients wished for further care, whereas only 6 non-distressed patients gave the same answer (**Table 16**). This increase is not statistically significant (**Figure 22**).

Table 15. Descriptive statistics of further care wish for distressed patients

Further care wish

OP Status			Frequency	Percent	Valid Percent	Cumulative Percent
Pre-OP	Valid	no	16	69,6	69,6	69,6
		yes	7	30,4	30,4	100,0
		Total	23	100,0	100,0	
Post-OP	Valid	no	15	65,2	65,2	65,2
		yes	8	34,8	34,8	100,0
		Total	23	100,0	100,0	

Table 16. Descriptive statistics of further care wish between distressed and non-distressed patients

Further care wish

Patient Distress (DT≥6)			Frequency	Percent	Valid Percent	Cumulative Percent
Not distressed	Valid	no	30	83,3	83,3	83,3
		yes	6	16,7	16,7	100,0
		Total	36	100,0	100,0	
Distressed	Valid	no	31	67,4	67,4	67,4
		yes	15	32,6	32,6	100,0
		Total	46	100,0	100,0	

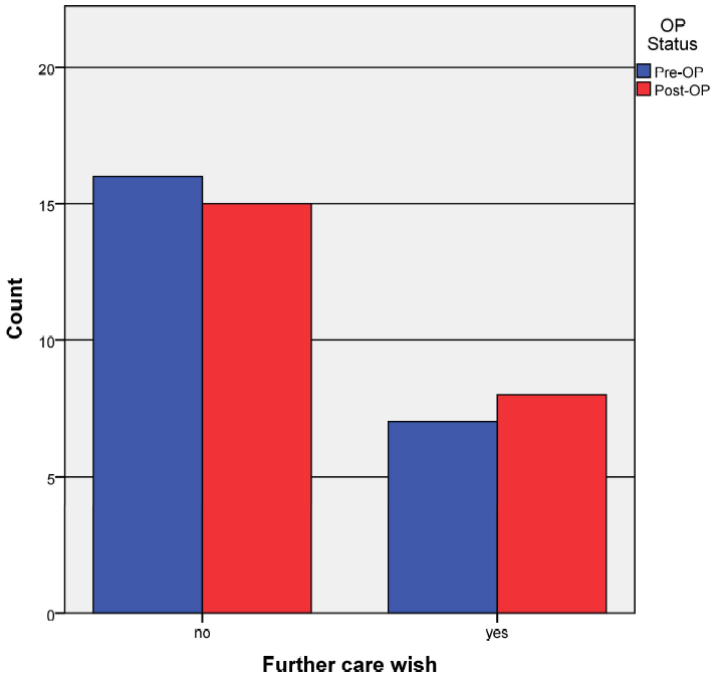

Figure 20. Number of distressed patients requiring further

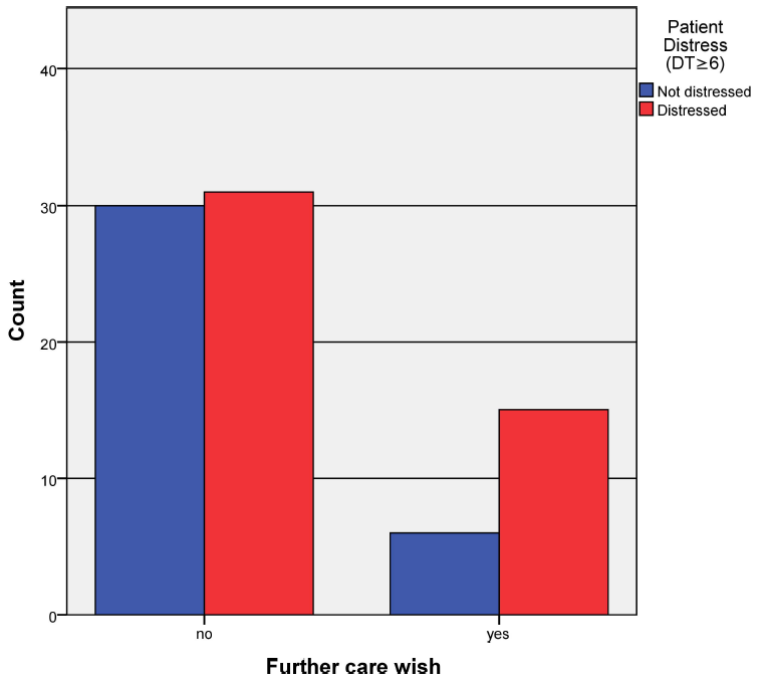

Figure 21. Number of patients requiring further supportive care before and after

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The medians of Further care wish are the same across categories of distressed patients	Pearson Chi-Square Test	0,101	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 22. Significance test of further care wish between distressed and non-distressed patients

We were also interested in finding out whether further care wish is related to higher stress as measured by DT and SQ. We compared the DT and SQ values of patients with both answers to the further care question and observed that patients with further care wish are statistically significantly (**Figure 24**) more stressed than the patients without further care wish (**Figure 23**). This increase in stress is measured by both DT 5.19(no) to 6.48(yes) as well as SQ 0.98(no) to 1.76(yes) (**Table 17**). Further care wish is significantly correlated with DT and SQ with r-values of 0.188 and 0.297 respectively (**Table 18**). Comparing distressed and non-distressed patients, we saw a similar trend (**Figure 25**). Mean DT increased from 7.31(no) to 7.5(yes) and mean SQ increased from

1.23(no) to 2.13(yes) (**Table 19**). Contrary to the general population, the increase of DT in the distressed population was not significant, whereas the increase in SQ remained so (**Figure 26**).

Table 17. Descriptive statistics of DT and SQ for patients requiring further supportive care

Descriptive Statistics

Further care wish		N	Minimum	Maximum	Mean	Std. Deviation
no	Distress	61	0	10	5,19	2,598
	Signalling Questions	61	0	3	,98	1,057
	Valid N (listwise)	61				
yes	Distress	21	2	9	6,48	1,984
	Signalling Questions	21	0	3	1,76	,944
	Valid N (listwise)	21				

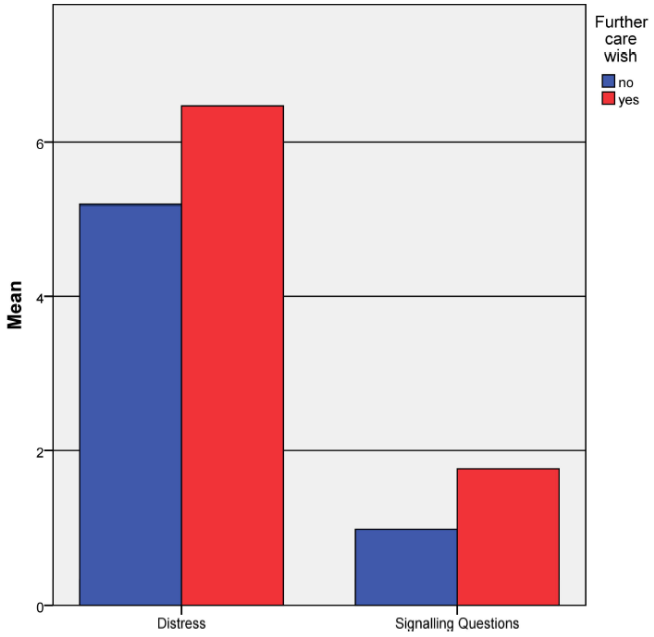

Figure 23. Mean DT and SQ for patients requiring further supportive care

Hypothesis Test Summary

Null Hypothesis	Test	Sig.	Decision
The distribution of Distress is the same across categories of Further care wish.	Independent-Samples Mann-Whitney U Test	0,049	Reject the null hypothesis.
The distribution of Signalling Questions is the same across categories of Further care wish.	Independent-Samples Mann-Whitney U Test	0,004	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 24. Significance test of DT and SQ for patients with further supportive care needs

Table 18. Correlation of DT and SQ with further care wish

Correlations

			Further care wish	Distress	Signalling Questions
Kendall's tau_b	Further care wish	Correlation Coefficient	1,000	,188*	,297**
		Sig. (2-tailed)	.	,049	,004
		N	82	82	82
	Distress	Correlation Coefficient	,188*	1,000	,332**
		Sig. (2-tailed)	,049	.	,000
		N	82	82	82
	Signalling Questions	Correlation Coefficient	,297**	,332**	1,000
		Sig. (2-tailed)	,004	,000	.
		N	82	82	82

Table 19. Descriptive statistics of DT and SQ for distressed patients requiring further supportive care

Descriptive Statistics

Further care wish		N	Minimum	Maximum	Mean	Std. Deviation
no	Distress	31	6	10	7,31	1,101
	Signalling Questions	31	0	3	1,23	1,087
	Valid N (listwise)	31				
yes	Distress	15	6	9	7,50	1,150
	Signalling Questions	15	1	3	2,13	,743
	Valid N (listwise)	15				

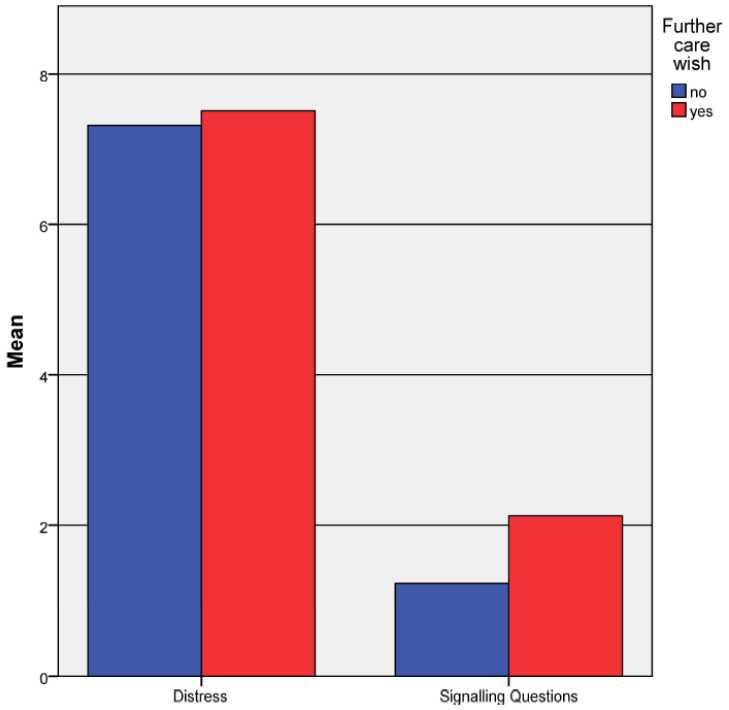

Figure 25. Mean DT and SQ of distressed patients requiring further supportive care

Hypothesis Test Summary

Null Hypothesis	Test	Sig.	Decision
The distribution of Distress is the same across categories of Further care wish.	Independent-Samples Mann-Whitney U Test	0,495	Retain the null hypothesis.
The distribution of Signalling Questions is the same across categories of Further care wish.	Independent-Samples Mann-Whitney U Test	0,008	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 26. Significance test of DT and SQ for distressed patients with further supportive care needs

To measure treatment effectiveness, we also recorded whether the operation was successful in removing the tumor in its entirety. However, we eventually realized that with only 5 patients that we recorded of having a subtotal resection (STR), any conclusions drawn from this would be an invalid comparison. Another aspect to this is that a STR is often evaluated as a gross total resection (GTR) intraoperative, only for the post-operative scan or a recurrence further down the line to prove otherwise. Therefore, our data of extent of resection has a high probability of being erroneous.

Socioeconomic factors affecting stress

Socioeconomic status (SES) recorded during the interview were compared with DT and SQ (**Table 20**). A tendency for higher stress was reported for widowed patients (DT 6.83/SQ 2) compared to singles (DT 5.89/SQ 1.14) and married patients (DT 5.68/SQ 1.19). Patients with higher education (DT 6.27/SQ 1.38) also reported higher stress compared to those with lower qualifications (DT 4.96/SQ 1.07). These increases were, however, not statistically significant. On the other hand, tendencies for lower stress were observed in patients with children (DT 5.26/SQ 1.14) compared to childless patients (DT 6.59/SQ 1.38), patients with lower income (DT 4.67/SQ 1.33) compared to higher-income patients (DT 6.45/SQ 1.5), and patients with private insurance (DT 5.06/SQ 1.38) compared to statutory insurance (DT 5.63/SQ 1.14). Patients who did not work and stayed at home, i.e. Housewives/husbands, (DT 5.08/SQ 0.75) were also observed to have lower stress compared to working patients (DT 6.63/SQ 1.46). These changes were, similar to the previous increases to stress, also statistically insignificant. Significant changes (**Figure 27**) were observed in lower stresses in retired patients (DT 4.98/SQ 1.14) compared to working patients (DT 6.63/SQ 1.46), as well as divorced patients (DT 2.81/SQ 0.63) compared to married patients (DT 5.68/SQ 1.19). Interestingly, neither residential nor ownership status has a marked effect on stress.

Table 20. Mean DT and SQ compared with socioeconomic factors

Effect of socioeconomic factors on Distress and Signalling Questions			
	n	Mean DT (SD)	Mean SQ (SD)
Marital status			
Single	14	5.89 (2.65)	1.14 (1.03)
Married	54	5.68 (2.32)	1.19 (1.1)
Divorced	8	2.81 (2.75)	0.63 (0.74)
Widowed	6	6.83 (1.33)	2 (1.1)
Children			
Yes	66	5.26 (2.6)	1.14 (1.09)
No	16	6.59 (1.8)	1.38 (1.03)
Living status			
Alone	22	5.8 (2.44)	1.18 (1.05)
Communal	60	5.42 (2.55)	1.18 (1.1)
Ownership status			
Rent	28	5.38 (2.28)	1.07 (1.09)
Owner	52	5.50 (2.65)	1.21 (1.07)
Care Home	0	0	0
With Relatives	2	8 (0)	2 (1.41)
Education			
Hauptschule	30	5.43 (2.16)	1.13 (1.14)
Realschule	28	4.96 (2.83)	1.07 (1.02)
University	24	6.27 (2.43)	1.38 (1.1)
Job Status			
Working	26	6.63 (2.42)	1.46 (1.10)
Retired	44	4.98 (2.35)	1.14 (1.05)
Disabled	0	0	0
Housewife/husband	12	5.08 (2.68)	0.75 (1.06)
Annual income			
<10.000	12	4.67 (2.57)	1.33 (1.23)
<30.000	34	5.44 (2.69)	1.38 (1.07)
<50.000	18	5.92 (1.87)	0.78 (0.94)
<70.000	4	7.63 (2.29)	1.25 (0.96)
>70.000	10	6.45 (1.89)	1.5 (1.08)
Insurance			
Statutory	66	5.63 (2.53)	1.14 (1.08)
Private	16	5.06 (2.46)	1.38 (1.09)

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Distress is the same across categories of Relationship status.	Independent-Samples Kruskal-Wallis Test	0,027	Reject the null hypothesis.
2	The distribution of Signalling Questions is the same across categories of Relationship status.	Independent-Samples Kruskal-Wallis Test	0,154	Retain the null hypothesis.
1	The distribution of Distress is the same across categories of Job status.	Independent-Samples Kruskal-Wallis Test	0,013	Reject the null hypothesis.
2	The distribution of Signalling Questions is the same across categories of Job status.	Independent-Samples Kruskal-Wallis Test	0,147	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is ,05.

Figure 27. Significance tests of DT and SQ across relationship and job status

Patient difficulties with survey and cognitive issues

To measure difficulties the patients may have with the interview, we noted several parameters, such as time to complete the interview, whether an impairment/impediment was present (aphasia, language barrier, noise disturbances, physical symptoms, etc.), and the presence of a proxy/relative. We also noted whether the patients who had new difficulties after the operation exhibited cognitive impairment. Through our observations and the recorded information in their files, we also noted whether these cognitive symptoms existed prior to their admission and if they persisted after discharge.

The time required to complete the interview was categorized into different intervals (less than 10 minutes, 10-20 minutes, 20-30 minutes, and more than 30 minutes) and recorded both pre- and post-operatively. However, the post-operative interviews required significantly less time because the socioeconomic background of the patients did not need to be questioned a second time. Therefore, whereas 75.6% of patients needed 20-30 minutes to complete the interview pre-operatively, only 41.5% required the same amount of time post-operation (**Table 21**). Whether or not the interview was conducted in the presence of a proxy/relative also turned out to be an unreliable parameter. Due to visiting hours and differing interview times, their help during the interview was mostly coincidental. The number of patients needing help from a proxy/relative during the interview was 6 both pre- and post-operation.

Table 21. Amount of time required to do the interviews

Time

OP Status			Frequency	Percent	Valid Percent	Cumulative Percent
Pre-OP	Valid	<10 Minutes	3	7,3	7,3	7,3
		10-20 Minutes	31	75,6	75,6	82,9
		20-30 Minutes	7	17,1	17,1	100,0
		Total	41	100,0	100,0	
Post-OP	Valid	<10 Minutes	21	51,2	51,2	51,2
		10-20 Minutes	17	41,5	41,5	92,7
		20-30 Minutes	3	7,3	7,3	100,0
		Total	41	100,0	100,0	

We also noted whether the patients had difficulties completing the interview due to physical or cognitive impairments, as well as outside influence such as noise. This proved to be more reliable, as we observed a statistically significant (**Table 22**) increase in the number of patients with post-operative difficulties (**Figure 28**). Pre-operative difficulties were recorded in 12.2% of patients, whereas 34.1% of patients experienced post-operative difficulties (**Table 23**). Patients who had difficulties with the interview tended to require more time (**Figure 29**). Time and difficulty are, however, not significantly correlated (r: 0.53/Sig: 0.617) (**Table 24**). 13 of the 14 patients who had post-operative difficulties did not previously have them before the operation (**Table 22**). This particular niche of the patient population tended to have more severe cases with 30.8% of cases being WHO Grade 4 compared to 17.9% of the rest of the population (**Table 25**).

Difficulty Survey pre * Difficulty Survey post Crosstabulation

Count

		Difficulty Survey post		
		none	yes	Total
Difficulty Survey pre	none	23	13	36
	yes	4	1	5
Total		27	14	41

Chi-Square Tests

	Value	Exact Sig. (2-sided)
McNemar Test		,049[a]
N of Valid Cases	41	

a. Binomial distribution used.

Table 22. Crosstabulation and significance test of difficulty with interview

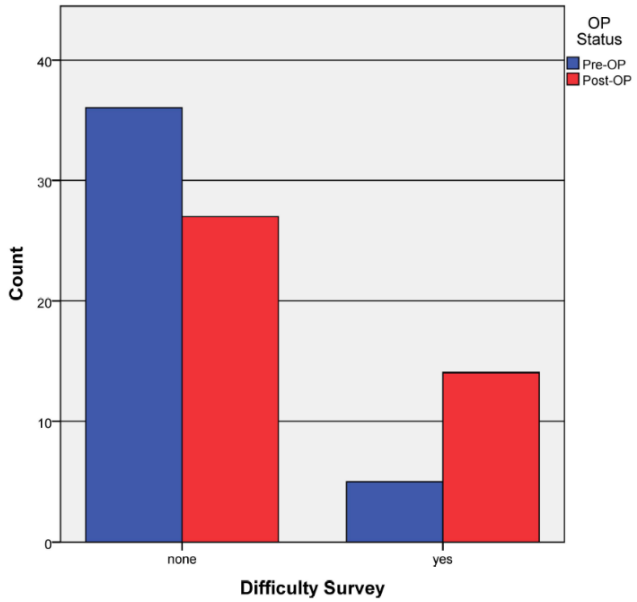

Figure 28. Number of patients experiencing difficulties with the interview

Difficulty Survey

OP Status			Frequency	Percent	Valid Percent	Cumulative Percent
Pre-OP	Valid	none	36	87,8	87,8	87,8
		yes	5	12,2	12,2	100,0
		Total	41	100,0	100,0	
Post-OP	Valid	none	27	65,9	65,9	65,9
		yes	14	34,1	34,1	100,0
		Total	41	100,0	100,0	

Table 23. Number of patients having difficulties with the survey

Correlations

			Time	Difficulty Survey
Kendall's tau_b	Time	Correlation Coefficient	1,000	,053
		Sig. (2-tailed)	.	,617
		N	82	82
	Difficulty Survey	Correlation Coefficient	,053	1,000
		Sig. (2-tailed)	,617	.
		N	82	82

Table 24. Correlation table between time and difficulty with interview

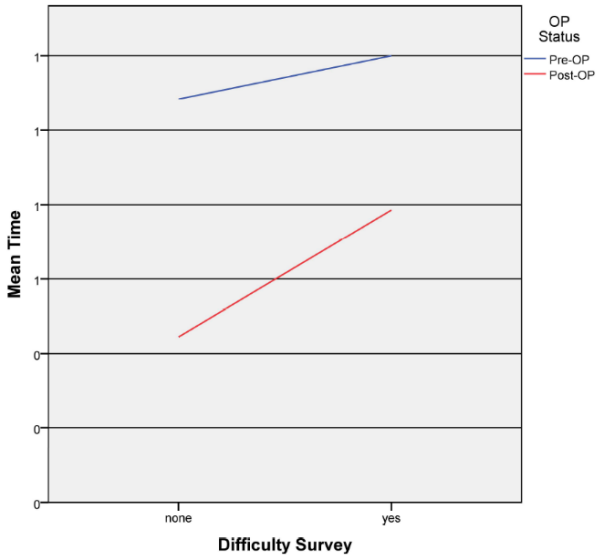

Figure 29. Mean time compared to difficulty with interview

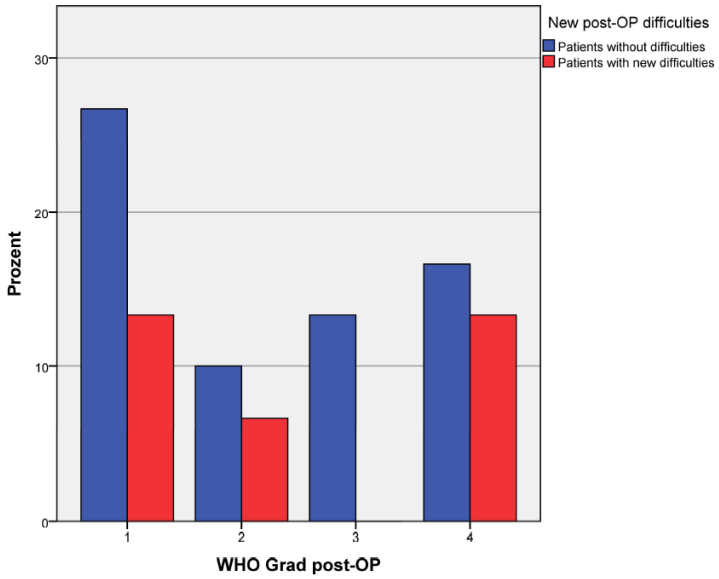

Figure 30. WHO Grade of patients with new difficulties and the rest of the population

WHO Grad post-OP

WHO Grade of patients with new difficulties			Frequency	Percent	Valid Percent	Cumulative Percent
Patients without difficulties	Valid	1	8	28,6	40,0	40,0
		2	3	10,7	15,0	55,0
		3	4	14,3	20,0	75,0
		4	5	17,9	25,0	100,0
		Total	20	71,4	100,0	
	Missing	System	8	28,6		
	Total		28	100,0		
Patients with new difficulties	Valid	1	4	30,8	40,0	40,0
		2	2	15,4	20,0	60,0
		4	4	30,8	40,0	100,0
		Total	10	76,9	100,0	
	Missing	System	3	23,1		
	Total		13	100,0		

Table 25. WHO Grade of patients with new difficulties with interview

Several of our patients experienced new difficulties after their operations. We were interested in finding out whether these patients had cognitive impairments that may impact the difficulties they were having with the questionnaire. To determine this, we relied on the patients' files prior to admission as well as after their discharge, for example during a follow up outpatient appointment. Complementing this, we also relied on our own judgement during the interview and noted our observations accordingly. We defined cognitive symptoms as problems with concentration, speech, memory, personality, and emotion.

There was a drop in the number of patients with cognitive issues after their operation from 7 (53.8%) to 4 (30.8%) (**Table 26**). This was, however, not statistically significant. All the patients with cognitive issues after the operation had them prior to their procedures as well (**Table 27**). There was no newly recorded cognitive issues after the operation.

Table 26. Frequency of cognitive issues pre- and post-operation

Cognitive Issues pre-OP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	6	46,2	46,2	46,2
	Yes	7	53,8	53,8	100,0
	Total	13	100,0	100,0	

Cognitive Issues post-OP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	9	69,2	69,2	69,2
	Yes	4	30,8	30,8	100,0
	Total	13	100,0	100,0	

Table 27. Crosstabulation table of cognitive issues

Cognitive Issues pre-OP * Cognitive Issues post-OP Crosstabulation

Count

		Cognitive Issues post-OP		
		No	Yes	Total
Cognitive Issues pre-OP	No	6	0	6
	Yes	3	4	7
Total		9	4	13

Chi-Square Tests

	Value	Exact Sig. (2-sided)
McNemar Test		,250[a]
N of Valid Cases	13	

a. Binomial distribution used.

Discussion

Perioperative Stress

As seen through our observations, stress consists of many different aspects. This rings especially true for a severe, impactful, and long-lasting disease like brain tumors and during a clinical stay which involves major operations. Our two instruments measuring stress displays that. It is of note, however, that both our instruments gave different results in the trends of perioperative stress. This will be discussed in the next section. During the initial couple of interviews, we found that the second question of SQ, which was asked when given a positive answer to the first, often led to confusion to most patients. We decided that for our data gathering purposes, it was unnecessary to ask and record the second question since they would indicate the same kind of burdens as the first question. Therefore, we only utilized the first questions of SQ for our interviews.

Mitchell et al. ascertained that DT is very effective in quantifying anxiety, more so than identifying depression [43]. This observation is corroborated by our data which saw significantly higher emotional distress prior to the operation, an understandable reaction to patients who are about to undergo major operations for an especially severe disease. Since the patients are extensively informed about their procedures and the accompanying risk attached to that, it is to be expected that they are anxious about it. Operations, especially brain operations, brings with it a myriad of risks such as postoperative delirium and cognitive dysfunction [45]. Not to mention other typical surgical complications such as bleeding, pain, general weakness, etc. General anesthetic is also associated with post-operative nausea and vomiting, as well as dizziness. These factors could have contributed to a significant postoperative rise in physical and practical problems that we observed in our cohort. Patients who are having difficulties with conducting basic functions such as walking or eating may have a negative outlook on the practicality of their normal lives such as doing the housework or going back to work. The absence of a difference in spiritual problems may reflect the steadfastness of belief through adversity. In fact, due to the severity of their hardships, patients might be more inclined to hold on to their lifelong beliefs. Patients who undergo surgery to remove a brain tumor, malignant or otherwise, use religion as a beneficial coping strategy [46]. Strang et al. found however, that spiritual needs does not necessarily need to be fulfilled by religion, but by a belief and confidence in oneself, in science and positive thinking [47]. These changes persist even amongst distressed

patients. Although they are significantly more stressed than the non-distressed patients, the nuances in their types of stress remain constant.

Meanwhile, we saw drops in the mean number of yes answers to SQ, indicating a decrease of stress in the same population of patients who indicated a rise of stress through DT. When broken down to the individual questions, we saw that those psychological problems decreased significantly after the operation. This change reflects the decrease in emotional problems in DT and can be attributed to pre-operative anxiety. Cognitive issues also decreased, albeit not significantly. This may be due to patients immediately recognizing that their previous cognitive symptoms have disappeared after the tumor mass was resected. However, this theory may be unreliable since post-operative swelling may not result in improved cognitive function directly after the operation [45]. The most interesting decrease was in physical problems. Our patients reported significantly fewer physical problems. However, when asked specifically through the DT questionnaire, they reported significantly more physical issues. An argument can be made that patients underestimate their physical impairments as a whole, but answer more accurately when asked about individual symptoms. Distressed patients displayed similar trends when compared to non-distressed patients. The only difference was that the decrease in physical problems was not statistically significant in distressed patients.

Relationship of Distress as measured by DT and SQ

Contrary to expectations, we saw differing results from both our stress-measuring instruments. Whereas DT saw a rise in stress, we saw a decrease in the mean number of yes answers to SQ. This would imply that DT and SQ measure different things. DT was specifically designed to diagnose significant emotional, social, and physical burdens [5], and was validated as a screening instrument for patients with intracranial tumors [28]. Goebel and Mehdorn determined through comparing DT with the Hospital Anxiety and Depression Scale (HADS), that DT is excellent at correctly identifying significantly distressed patients [28]. The signaling questions, on the other hand, was developed in order to signal to healthcare professionals that further inquiry into patients' psychosocial distress was required [39]. These questions are quick and to the point, and thus can be asked easily and efficiently during consultations as a screening instrument. These differences in how these questionnaires measure stress may explain the trends that we

observed. We can therefore argue that DT carries more weight than SQ when measuring distress.

Looking at our data, we can conclude that patients with higher distress as measured by DT also indicated higher stress, measured through SQ. This was evident through our observations of distressed patients compared to non-distressed patients. This was true for all the SQ questions. This would suggest a correlation exists between SQ and DT. We did test this and found that DT and SQ are significantly correlated to each other. Since DT was one of the questionnaires, whose main points were used to develop SQ, this was hardly a surprise [39]. DT has also been validated through comparison to other measurement instruments such as the Hospital Anxiety and Depression Scale – Depression subscale (HAD-D) and the Patient Health Questionnaire-9 (PHQ-9)[23, 28].

We decided to establish the relationship between DT and SQ through ordinal regression. Through this, we determined that SQ is a statistically significant predictor of DT and the sum of its items. This suggests that SQ is a valid instrument in measuring stress in brain tumor patients, as is the case with DT. As discussed above, however, we must recognize that SQ and DT measure stress in different ways and with different emphasis.

Role of age, sex, and tumor severity on stress

Stress is ultimately a subjective perception with a physical response, leading to a myriad of different effects on the immune system, cognitive functions as well as multiple organ systems [48]. People experience stress in different ways and different groups worry about different things. Differences across cultures on how stress is perceived even lead to differing results in stress-measuring instruments [49]. We sought to find out whether factors such as age, sex, and tumor severity might affect this. Interestingly, age seemed to have no perceptible impact on stress. Regardless of age group, our patients mostly had similar levels of stress across the ages. This may be due to the fact that most of our patients were older and retired, since these demographics are most likely to suffer from cancer [50]. These patients are also less likely to worry about work, finances, or their children, who are most likely grown up. We also saw no significant difference across tumor severity. Likely, the diagnosis of brain tumor itself is enough for patients to experience severe stress, therefore the severity of the illness itself presents no large impact. We did however notice that patients with WHO Grade 4 tumors had higher

distress after their operations. Through our questioning, we determined that a number of these patients have had consultations with their doctors about their histological results and prognosis, and thus this would be reflected in their stress scores.

Sex presented itself as a significant impacting variable. This was confirmed through a regression analysis which showed a small but significant impact on stress. Women had significantly higher stress compared to men. Young women, especially, also generally suffer from more psychological illness at admission than men [51]. The reason for this is difficult to ascertain. Women do generally suffer more stress than men according to the American psychological association [52]. Women also tend to have higher numbers of cancer compared to men, albeit with a higher survival rate [53]. This may be due to their higher life expectancy [54], which given that cancer is a later age disease [53], would explain the discrepancy in frequency. Women may also be more stressed than men since they tend to worry about other people than themselves more than men. Research by Christov-Moore et al. has shown that women tend to be more empathetic than men, even across cultures and age [55].

Impact of treatment effectiveness on stress

As mentioned in the results section, we did record operation success during the interview from the operation reports or post-operative histological results. Due to the lack of sufficient patients with a subtotal resection (STR), we are unable to draw any valid conclusions about whether the extent of resection impacts stress. Common sense would suggest that patients with an unsuccessful resection would be more stressed than patients with successful operations. The prospect of another procedure in the future coupled with disease progression is certainly grounds for distress. Another aspect to consider is that a STR isn't always immediately apparent. Oftentimes, STR is only determined after a post-operative scan upon reduction of swelling or at the point of a recurrence.

Therefore, we chose further care wish as a measure of operation success/effectivity. Through this, we are able to get an idea of whether our patients feel that their care needs or their stress were treated by the operation. We saw a rise in the number of patients who required further supportive care. Supportive care, as previously mentioned, encompasses both clinical and psychosocial needs [36], applicable from the curative all

the way to the terminal stage of cancer [56]. This new increase could be attributed to their physical needs, as patients are still in their post-operative recovery period during the interview. One could also argue that our patients realize that their concerns were still present and remained unchanged after their operations. They still worry about similar things, such as practical issues or their futures. We also established that patients who previously wanted further supportive care are more likely to want it after their procedures. This would support our theory. As a counterpoint, however, our data showed that emotional concerns as measured by DT and SQ decrease significantly after the operation.

An interesting note is that we saw that distressed patients are more likely to ask for further supportive care than non-distressed patients. Patients with further care wish also have significantly higher stress levels. This would suggest that further supportive care wish is positively correlated with DT and SQ, which we proved to be the case. Logically, people with higher stress seek supportive care from health professionals. The role of healthcare professionals in building trust with their patients and recognizing their distress is therefore paramount.

Socioeconomic factors affecting stress

We sought to determine whether socioeconomic factors impact stress in brain tumor patients. Studies have shown that lower socioeconomic factors are linked to chronic stress [17]. From this, we can infer the theory, that patients with lower economic standings or education are more likely to be more stressed by disease. This is supported by Ford et al. who found that depression was associated with patients with lower levels of education and lower tumor grades [6]. Contrary to this, however, we saw that patients with private insurance and higher education suffer from higher stress levels compared to their counterparts. This would suggest the opposite of our theory, that in fact patients higher on the socioeconomic hierarchy have more concerns and stress related to their illness. Speculation can perhaps be made that patients who are higher in this hierarchy are more capable of understanding their illness in a more comprehensive manner. Thus, they have a fuller picture of the severity and consequences of their illness. In fact, there is an argument that patient confusion comes from access to too much health information [57]. A failure of information filters on the internet leads to patients receiving misleading or out of context information that may lead to more stress. An argument can also be

made that patients with higher SES have more to lose when they fall ill or succumb to their illness. Despite the higher stress however, research has shown that patients with higher SES have a higher rate of survival [19, 20].

Adding to this, patients in lower-income households suffer from less stress than patients in higher-income households. Being ill usually means loss of economic means as the patients cannot work and require care services, all of which costs money down the line. This severely impacts the familial and job responsibility of a patient [58]. Thus the drop in average stress is confounding in this regard, since Hanly et al. found that even with publicly funded care, cancer patients experience objective financial stresses due to loss of income, draining savings, borrowing money, etc. [59]. This may be explained by the healthcare system that we have in Germany. Being a federally supported social health care insurance system based on solidarity, all members of German society are insured [60]. Regardless of income or insurance provider, all patients receive the standard available medical care as decided by the federal government and are not charged for the price of their medical treatment aside from a small flat-rate surcharge. Patients who cannot work are also entitled to their full income for a set period and then a reduced sick pay, followed by their pensions. Thus, the financial stability of patients in Germany is ensured at every stage of their illness. This is contrary to the system in other countries with no universal health care, less rigorous safety nets, and medical copayments which may lead to personal bankruptcy, even amongst insured patients [61].

Further supporting our speculation regarding the minimal effect on stress from loss of income is the significant fall of stress we saw in retired patients. No longer working, with presumably a retirement savings account, loss of income is not a big factor that comes into play for them. We must however consider that patients suffering from cancer are more likely to be older and retired since cancer is a late-in-life illness [50]. That being said, a significant part of our patient population are still working, therefore our conclusions from the data are reasonably representative. A similar drop in stress was observed in our patients who were housewives/husbands. Since they are not the major breadwinner in the house, the loss of the ability to work may not be a large contributing factor to their stress levels.

Lastly, the role of a support system is something that can be discussed. Humans are social creatures who rely on other members of society or their families for many things. A support system is critical in dealing with the stresses of one's daily lives, let alone a life crisis such as cancer [62]. Widowed patients were observed to have higher stress than married patients. The death of their life partner, a traumatic experience all by itself, leaves them with a smaller support system to deal with their illness. Depending on their relationship with other family members or friends, these patients may truly be alone. Williams et al. demonstrated that high levels of unmet social support needs were prevalent in older adults with cancer, especially if they were alone [16]. Singer et al. also observed that patients who lacked their own social support structure desired support from doctors and nursing staff [51]. Patients with children also have lower stress compared to childless patients, further supporting the support system theory.

Patient difficulties with survey and cognitive issues

The easiest parameter to record as a measure of the difficulties patients had with the interview was time. However, as previously mentioned, our recorded times can hardly be compared between the two timepoints as the second interview was always shorter. Not only was the SES unchanged, patients also remembered the questions in the interview and could answer faster without requiring further clarification. Both these factors certainly contributed to the significantly faster post-operative interviews.

Determining patient difficulties was rather subjective than objective. Although some cognitive problems like aphasia or other barriers such as language proficiency can be determined to a large degree of accuracy, other disturbing factors such as noise or difficulty in understanding questions are subject to the interviewers judgement and biases. The interviewer effect must be accounted for since it is ultimately impossible to eliminate. Davis et al. found that interviewer effects are most likely to present itself when querying items concerning socioeconomic characteristics or engagements in sensitive behaviors [63].

We did indeed saw an increase in the number of patients having difficulties post-operation. This may be partly due to post-operative weakness, nausea, pain, or cognitive symptoms [45]. We can conclude that post-operative difficulties reflect the physical or cognitive stress patients are experiencing. Patients who were having difficulties also

tended to require more time completing the interview compared to their counterparts. Interestingly, most of the patients with new difficulties did not have them prior to their operations. It begs the question as to why this is the case. They did represent a part of the population with higher tumor severity. Due to this severity, one can argue that their resection was more extensive, thus causing more damage to surrounding tissues and more cognitive/physical symptoms after the operation [1]. These patients with new difficulties were found to have less cognitive issues. Therefore, their difficulties may arise from post-operative physical impairment, but not cognitive deficits as previously assumed.

Conclusion

Brain tumor patients suffer tremendously due to quality of life reduction. This is caused by a variety of factors such as a decline in physical well-being, functional impairment, neurocognitive dysfunction, and psychosocial distress. The latter has a large impact on quality of life, but is often overlooked or undertreated. Referring back to our research objectives, we sought to explore how operative resection of brain tumors impact distress and how treatment effectiveness, socioeconomic status, and difficulties with the interview may impact our data.

Our results showed that overall, patient distress rises directly after surgery. However, it is important to note the nuances in this change. Emotional burdens significantly decline after operations, whereas stress due to physical impairments rises. These changes were consistent, even when only accounting for severely distressed patients. The emotional burden that we saw could represent pre-operative anxiety, thus the decline after the operation. Similarly, the rise in physical burdens can be attributed to post-operative symptoms such as weakness, pain, dizziness, etc. The practical problems as measured by DT can also be attributed to the same problems, as patients may have a negative outlook on their future immediately after their operation. The physical question of SQ saw a drop in distress after their operations. However, due to the multifaceted nature of the DT problems list, one can argue it is a more reliable measurement of distress. SQ was made as a screening instrument to signal when further inquiry is needed, whereas DT is a full-fledged questionnaire designed to measure distress. Therefore in quantifying distress, DT carries more weight.

In an effort to solidify the validity of our study, we decided to measure distress using 2 instruments, DT and SQ. Whereas DT and SQ disagreed on the change in distress between operations, they both concurred in measuring severe distress. Severely distressed patients scored highly on both DT and SQ. DT and SQ were also positively correlated to each other and were good predictors of each other. This adds weight to validating SQ as a new, practical screening instrument for everyday clinical use. The validity of DT itself has been explored and confirmed in several studies.

We saw a rise in further care wish after the operation. This would indicate that patients are more distressed after their respective operations, which is true, as discussed above.

This rise in further care wish can be attributed to the physical impairments that patients have after their procedures. Distressed patients are also more likely to ask for supportive care, suggesting that illness severity and operation outcome does push some patients to ask for further care. All in all, however, it was difficult to determine treatment effectiveness objectively. The extent of resection during the operation made the most sense as a parameter. However, due to the lack of patients with subtotal resection, any conclusions would have been unrepresentative.

During our data gathering, we recorded several factors that we surmised might have an effect on distress. Amongst them were age, sex, WHO Grade and socioeconomic factors such as income, education, marital status, etc. In the end, we can conclude that sex has a significant impact on distress, with female patients being significantly more stressed across the entire patient cohort. Socioeconomic demographics did not have significant effects on distress other than relationship and employment status. Divorcees and retired patients reported having less stress than their counterparts. We did see that patients with lower income and lower education suffer from less stress. We speculated that this may be due to lack of information or understanding of it. Due to the extensive social safety net in Germany, loss of income during an illness does not generally lead to personal bankruptcy. Patients with a support system such as from a partner or their children also suffer from less stress, presumably due to their solid support system, who can help them go through difficult times.

As previously mentioned in our discussion, the time required to complete the interview was unsuitable as a measure of the difficulties our patients had with the interviews. Instead, we chose our subjective assessment of patient difficulties. We saw that the presence of post-operative difficulties reflects high distress, most probably due to physical impairment. We observed that these patients had fewer cognitive symptoms. They also tend to have had these difficulties prior to their operations and have higher tumor severity. That aside, although these difficulties did lead to a more difficult interview, which also tended to last longer, our patients managed to sufficiently answer all our questions. Thus not affecting the quality or validity of our data.

In conclusion, operative therapy does increase physical distress but decreases emotional distress. The success of the operation is reflected in the patients' distress, with

distressed patients requesting further supportive care. Other factors affecting distress was most notably sex, familial status, employment status and SES. Patient difficulties with the interview did not seem to affect the quality of the data obtained. Further study into this topic and the use of SQ is required, especially during the period after the post-operative recovery. A study examining patients during ambulatory therapy is being conducted using a similar method to ours. SQ and DT, despite delivering differing results are good measuring instruments for patient distress. SQ, as the name implies, is better suited in recognizing psychosocial distress, rather than quantifying it. Conversely, DT is a more suitable instrument in quantifying patient distress.

Limitations of the Study

There are several limitations in this study that leaves room for improvement in similar studies in the future. One of them is a lack of patient variety. Most of our patients suffered from WHO Grade 1 tumors such as meningiomas or WHO Grade 4 tumors such as glioblastomas. Some patients also suffered from brain metastases. This lack of variety gives us the 2 extreme ends of brain tumor illnesses but not much data on the middle of the pack.

The signaling questions that we used were also not utilized in its complete form. As previously mentioned, since both the question and sub-question were asking about similar things, we decided to only use the first main question to avoid confusion. The modified use of SQ may put our conclusions from the data into dispute since we arguably utilized SQ in a manner different from how it was conceptualized.

A number of parameters that we decided upon also did not meet our expectations. They are the time to complete the interview and the extent of resection. Whereas time to complete the interview was erroneously planned, the extent of resection did not yield a representative dataset for all the groups. The result is that both parameters could not be utilized to make a conclusion about patient difficulty and treatment effectiveness respectively.

Of the patients that withdrew their consents during the study, most of them were after their operations. Although not recorded in the data, most of them either did not have a successful operation or were experiencing substantial complications that led to them being unable or unwilling to conduct the interview. In future studies, perhaps it would be prudent to compare pre-operative data with data from a later timepoint, when patients are more capable and willing to participate and not still recovering from a large operation.

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Appendix

Distress Thermometer

Patientenfragebogen
Belastung (Distress)

Bitte kreuzen Sie mit einem **X** auf der nebenstehenden Skala eine Zahl von **0** bis **10** an.
Diese Zahl zeigt an, wie stark Sie Ihre Belastungen in der letzten Woche einschließlich des heutigen Tages empfinden.

Kreuzen Sie bitte an, ob für Sie in der letzten Woche einschließlich des heutigen Tages folgende Bereiche belastend gewesen sind.
Bitte vergewissern Sie sich, dass Sie alle Bereiche mit **JA** oder **NEIN** beantwortet haben:

JA	NEIN	Praktische Probleme
☐	☐	Kinderbetreuung
☐	☐	Wohnsituation
☐	☐	Versicherung/Finanzen
☐	☐	Mobilität/Beförderung
☐	☐	Arbeit/Ausbildung
		Familie
☐	☐	Umgang mit Kindern
☐	☐	Umgang mit Partner
☐	☐	Umgang mit Eltern
		Emotionale Probleme
☐	☐	Depressivität
☐	☐	Angst
☐	☐	Nervosität
☐	☐	Traurigkeit
☐	☐	Sorgen
☐	☐	Interesselosigkeit für alltägliche Aktivitäten
☐	☐	**Spirituelle/religiöse Angelegenheiten**

JA	NEIN	Körperliche Probleme
☐	☐	Aussehen
☐	☐	Körperpflege/Ankleiden
☐	☐	Atmung
☐	☐	Wasserlassen
☐	☐	Verstopfung
☐	☐	Durchfall
☐	☐	Appetit
☐	☐	Müdigkeit
☐	☐	Ödeme/Stauungen
☐	☐	Fieber
☐	☐	alltägliche Verrichtungen
☐	☐	Verdauung
☐	☐	Gedächtnis/Konzentration
☐	☐	Mundschleimhaut
☐	☐	Übelkeit
☐	☐	trockene/verstopfte Nase
☐	☐	Schmerz
☐	☐	Sexualität
☐	☐	trockene/juckende Haut
☐	☐	Schlaf
☐	☐	Kribbeln in Händen/Füßen

Andere Probleme:_____

Wünschen Sie Unterstützung bezüglich Ihrer Belastung? **Ja ☐** **Nein ☐**

(V.2.2009, © NCCN, TUZ-Rheinland-Pfalz)

Patient Questionnaire GLIOPT II

Fragebogen GLIOPT

Datum:_____ Alter:_____ ID:_____ Geschlecht: m ☐ w ☐

Zeitpunkt der Erhebung: präOP ☐ postOP ☐ Follow-up ☐

Diagnose:

Verdachtsdiagnose: _____

WHO-Grad:
I ☐ II ☐ III ☐ IV ☐

endgültige Diagnose (nach ICD-10/-O):_____

Zeitpunkt d. Diagnose (Datum):_____

Therapieart:
kurativ ☐ palliativ ☐

Resektionsausmaß (postOP)
GTR ☐ STR ☐ Biopsie ☐

Stadium d. Krankheit
Erstdiagnose ☐ Rezidiv ☐ Re-Rezidiv ☐ Komplikation d. Krankheit ☐

Sozioökonomische Anamnese:

Beziehungsstatus
ledig ☐ verheiratet/Partnerschaft ☐ geschieden ☐ verwitwet ☐

Kinder
ja ☐ nein ☐

Wohnungssituation

allein ☐ Gemeinschaft ☐

Miete ☐ Haus/Wohnung ☐ Pflegeheim ☐ bei Angehörigen ☐

höchster schulischer Abschluss

keiner ☐ Haupt-/Volksschule ☐ Realschule ☐ allgemeine/ Fachhochschulreife ☐

Beruf

berufstätig ☐ Rente/Pension ☐ erwerbsunfähig ☐ Hausmann/-frau ☐

Profession:_____

Brutto-Einkommen im Haushalt: (gemessen an Steuern)

<10.000€ ☐ <30.000€ ☐ <50.000€ ☐ <70.000€ ☐ >70.000€ ☐

Versicherungsstatus

privat ☐ gesetzlich ☐ keine ☐

Religion:_____

<u>Belastung:</u>

ECOG:_____

Distress Thermometer:_____

Kopfschmerzen

Migräne ☐ Cluster ☐ Spannung ☐ sonstige ☐

Mobilität

eigener PKW ☐ ÖPNV ☐ Fahrdienst ☐ zu Fuß ☐

in vollem Umfang möglich ☐

eingeschränkt (z.B. mit Gehhilfe) ☐

kaum ohne fremde Hilfe möglich ☐

Psyche: Hat sich Ihre Stimmung verschlechtert? (Wenn ja: Sind Sie sich unsicher in Bezug auf Ihre Zukunft?)

ja☐ _____ nein☐

Körper: Belasten Sie körperliche Veränderungen? (Wenn ja: Mussten Sie sich wegen Müdigkeit öfter ausruhen?)

ja☐ _____ nein☐

Kognition: Hat sich Ihr Denkvermögen verschlechtert? (Wenn ja: Ist es schwer für Sie, sich zu konzentrieren?)

ja☐ _____ nein☐

Weitere psychoonkologische Betreuung erwünscht?

ja☐ nein☐

<u>Schwierigkeiten beim Interview:</u>

Zeit

<10min ☐ 10-20min☐ 20-30min☐ >30min ☐

(genaue Zeit:_____)

Art der Schwierigkeit

- körperlich (Parese, Müdigkeit, Übelkeit, Schmerzen, Schwindel) ☐
- motorisch ☐
- kommunikativ (sensorisch, motorisch, Schwerhörigkeit) ☐
- Verständnis (Demenz, häufiges Nachfragen) ☐
- externe (Lärm, Unterbrechung) ☐
- sprachlich (Muttersprache nicht deutsch) ☐

Ort der Erhebung

Wartezimmer ☐ Besprechungszimmer☐ Krankenzimmer ☐

Begleitung

ja☐ nein☐