



Anxiety, memories and coping in patients undergoing intracranial tumor surgery



Tom J. van Ark^{a,1}, Markus Klimek^{a,*}, Peter de Smalen^a, Arnaud J.P.E. Vincent^b, Robert Jan Stolker^a

^a Dept. of Anesthesiology, Erasmus University Medical Center, Rotterdam, The Netherlands

^b Dept. of Neurosurgery, Erasmus University Medical Center, Rotterdam, The Netherlands

ARTICLE INFO

Keywords:

Anesthesia
Anxiety
Awake craniotomy
Brain tumor
Coping
Memory
Neurosurgery
Patient satisfaction

ABSTRACT

Objectives: The diagnosis and the surgical removal of a brain tumor can have serious impact on the quality of life of a patient. The question rises, whether having more or just less memories of the procedure is better for coping with such an event. Furthermore, for preoperative information of future patients it is important to know how patients process their emotions and memories. The primary objective of this study was to investigate the link between preoperative anxiety, the perioperative experience and the quantity and quality of postoperative memories in patients who underwent intracranial tumor surgery.

Patients and methods: This study was a retrospective observational study; all patients who underwent intracranial tumor surgery at the Erasmus Medical Centre Rotterdam between January 1st 2014 and December 31st 2015 were identified. In May 2016, all patients who were not registered as deceased were sent a questionnaire about their anxieties, perceptions and memories of the perioperative period.

Results: In total 476 patients were included. 272 patients responded, which resulted in a response rate of 57.14%. In the general anesthesia (GA) group there was a significant negative correlation between anxiety in the perioperative period and the quantity and quality of memories. In the awake craniotomy group, there was a significant negative correlation between anxiety after the operation and the quantity of memories.

Conclusion: Patients in the GA group who experienced anxiety in the perioperative period had less quantity and quality of memories and less patient satisfaction. Patients in the AC group who experienced anxiety after the operation had only a lower quantity of the memory; there was no correlation with patient satisfaction.

1. Introduction

The diagnosis of a brain tumor and the surgical removal of this tumor can have serious impact on the quality of life of the patient. As patient centered care and value-based health care have become increasingly important, information about the quality of postoperative recovery and management of patient expectations are especially relevant [1,2]. Patients may undergo this procedure awake or under general anesthesia (GA), which has impact on the quantity, but possibly also on the quality of the memories about the perioperative period. It may be questioned, whether more or less memories about the procedure are an advantage for coping with such a major life event?

Only a few earlier studies investigated patient experience of patients who underwent an awake craniotomy (AC) [3–5]. These studies showed that according to the patients' memories this anesthesia technique is well tolerated by the patients, but nevertheless still can have

considerable impact. This impact did not only reflect on the direct perioperative period, but also on the period of recovery and rehabilitation after the procedure.

Therefore, we strived to learn more about how patients process and cope with their emotions and memories of the perioperative period in order to better inform future patients and manage their expectations about the operation.

Recently, we published data of a different, previous, small patient population on the quality and quantity of memories in patients who all underwent an awake craniotomy [6]. These data showed, that patients did not remember a lot of the procedure despite being awake during the whole period of resection, but also that the majority of these memories were very positive.

Inspired by these findings, this study is the first one to compare the correlation between anxiety and the quantity and quality of memories of the perioperative period, in patients who underwent brain tumor

* Corresponding author at: Dept. of Anesthesiology, Office Na-1719, Erasmus University Medical Center, P.O. box 2040, 3000 CA Rotterdam, The Netherlands.

E-mail address: m.klimek@erasmusmc.nl (M. Klimek).

¹ Both authors contributed equally to the manuscript.

resection awake or under general anesthesia. The primary objective of this study was to investigate the link between preoperative anxiety, the perioperative experience and the quantity and quality of postoperative memories. Our hypothesis was, that preoperative anxiety will result in more negative memories and less patient satisfaction.

2. Materials and methods

The institutional medical ethics committee of the Erasmus University Medical Centre approved this study (MEC-2016-125). Written informed consent was obtained from all patients who participated in this study.

2.1. Study design

For this study, all consecutive adult patients who underwent neurosurgery at the Erasmus Medical Centre Rotterdam between January 1st 2014 and December 31st 2015 were identified. Based on surgery coding, 739 patients with an intracranial tumor resection were found.

2.2. Participants

In May 2016, after excluding patients registered as deceased in our hospitals patient registry, 503 of these 739 patients received a questionnaire about their perception of the perioperative period. Patients who did not reply, were sent a reminder in August 2016. Non-responders were included in the final analysis to check for structural factors differing significantly between responders and non-responders.

2.3. Setting

In case of general anesthesia, the technique was chosen by the responsible anesthetist (Total Intra-Venous Anesthesia or balanced anesthesia). Our standardized technique of awake craniotomy has been described previously, and has not been changed for the patients included in this study [6]. In summary, we rely on a detailed, personal preoperative patient information and psychological preparation. Intraoperatively we use a combination of local anesthesia with propofol sedation during craniotomy and closure in spontaneous breathing patients with a nasal oxygen probe (non-invasive asleep-awake-asleep technique).

2.4. Study size

In this study, all adult patients who underwent (stereotactical) biopsies, intra-cranial tumor surgery and pituitary adenoma surgery were included. After removing double cases (of patients who had multiple operations in this period only the first procedure was included), a total number of 739 cases remained (see Fig. 1).

Patients undergoing a supratentorial tumor resection were mostly extubated on the OR, patients with infratentorial tumors were frequently transferred intubated to the Intensive Care Unit/Post Anesthesia Care Unit (ICU/PACU), where extubation was performed on a later moment. For uniformity reasons in our questionnaire extubation was put after the transport to the PACU/ICU. It is worth mentioning, that in our hospital the PACU is a high dependency unit with the option for mechanical ventilation, which is independent from the recovery room and dedicated to postoperative care for up to the first 24 h.

2.5. Variables

Our questionnaire focused on anxiety and memories. Questions addressing anxiety referred to different time-points of the perioperative process and to the patients and their relatives. The measured anxiety in the relatives of patients was reported by the patients. These questions could be answered on a 10-point scale (0 = no anxiety, 10 = maximum

anxiety). The questions addressing the quality and quantity of memories were divided in 13 sub-questions, referring to the consecutive events during the perioperative period, e.g. preoperative night on the ward, arrival on the OR etc. (see Table 1). The questionnaire is added (appendix).

All 13 sub-questions could be answered on a 5-point scale. For the sub-questions in question 1 the scale ranged from no memory at all (1) to a full and complete memory (5) and in question 2 the scale ranged from totally negative (1) to totally positive (5). To analyze the quantity and quality of memories the authors computed a sum score per patient of all given answers. If the patient underwent an awake craniotomy the answers to the questions about in- and extubation were not taken into account for the sum scores concerning the quantity and quality of the memories. So, the maximum sum scores of questions 1 and 2 were $11 \times 5 (= 55)$ (Table 1). Furthermore, if the patient received general anesthesia, the answers to the question about testing of the brain function were not taken into account for the sum scores of the quantity and quality of the memories. So the maximum sum scores of question 1 and 2 in the general anesthesia group was $12 \times 5 (= 60)$ (Table 1).

If the respondent did report to have no memories of the specific sub-question of the perioperative period when asked about the quantity, any quality score on that specific sub-question was considered invalid and not taken into account.

If the respondent did report to have any memory of the specific sub-question of the perioperative period, answered “no memories” when asked about the quality, the quality score was counted as “neutral” for that specific sub-question. Furthermore, if a respondent did not completely answer a question, then for the respective sub-question(s) the responder was counted as a non-responder.

2.6. Data sources

The following data were collected from the electronic patient record system of the Erasmus MC: age, gender and ASA (American Society of Anesthesiologists)-class of the patient - a rough indicator of the general state of health [1 = healthy to 4 = seriously reduced vital functions], type and side of the tumor, pathological determination of the tumor and degree of resection of the tumor. The degree of resection of the tumor was extracted from postoperative MRI scans and was categorized as complete resection or a resection with remnant of tumor. If the first postoperative MRI scan was inconclusive due to edema or residual blood, findings from later scans were analyzed.

Our primary outcome was the correlation between the quantity and quality of memories of patients and the experienced anxiety. We also analyzed the following possible influencing factors on the quantity and quality of the memories: the amount of time elapsed between answering the questionnaire and date of surgery (time-q) and the technique of anesthesia (awake craniotomy or general anesthesia). Furthermore, we analyzed the correlation between the overall satisfaction score and the quantity and quality of the memories, the correlation between anxiety prior and anxiety after the surgical procedure with the quantity and quality of memories and the correlation between anxiety prior and after the operation procedure and the overall satisfaction score. In addition, we analyzed which parts of the procedure were seen as discomforting by patients.

Because we had a quite large group of patients (91/476) who underwent surgery for pituitary adenoma or craniopharyngeoma, we also analyzed whether there was a difference between those operated via a transphenoidal approach and those via a frontal craniotomy.

2.7. Statistical methods

All data were gathered by two of the authors (TvA, PdS) and any inconsistencies and controversies were discussed with a third author (MK), until consensus was reached. Processing of data and statistical analysis was done using IBM SPSS Statistics, version 23, (Armonk, NY:

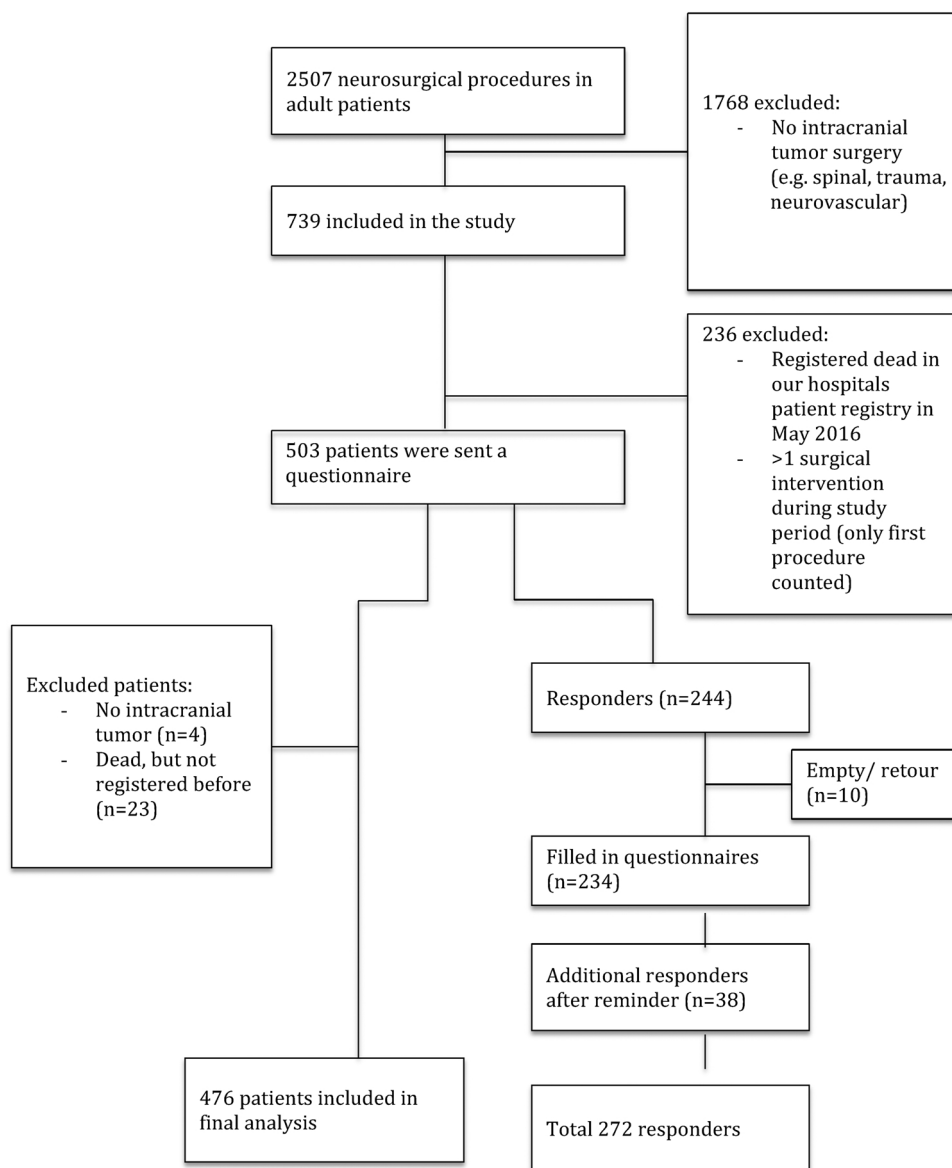


Fig. 1. Flowchart of patients included in the study.

Table 1

Sub-questions about the consecutive events in time of the perioperative period and the analyzed questions in each group.

Sub-questions of question 1 and 2	Analyzed in the awake craniotomy group	Analyzed in the general anesthesia group
Preoperative night on the ward	✓	✓
Arrival on the OR	✓	✓
Inserting the i.v.-lines	✓	✓
Intubation	×	✓
Fixing the head in the Mayfield clamp	✓	✓
Local anesthesia of surgical field	✓	✓
Craniotomy	✓	✓
Testing brain function	✓	×
Tumor resection	✓	✓
Closure of surgical field	✓	✓
Transport to the ICU/PACU	✓	✓
Extubation	×	✓
First night on the ICU/PACU	✓	✓

IBM Corp.) Differences in mean scores for quality and quantity of memories between the awake craniotomy and general anesthesia group were calculated using Mann-Whitney U tests. Differences in mean scores for anxiety prior to surgery and looking back to surgery were calculated using the paired T-test. Correlations were analyzed using Spearman’s correlation coefficient. The threshold for significance was set on a two-sided P value < 0.05.

3. Results

Fig. 1 shows a flowchart of the included and excluded patients.

In total, 476 patients were included. 272 patients responded, which resulted in a response rate of 57.14%. There were no differences found in baseline characteristics between responders and non-responders (Table 2).

3.1. Primary outcome

In the general anesthesia group there is, as expected, a relative large percentage of patients who do not know anything about the operation. However, in the awake craniotomy group there is also a relatively high

Table 2
Baseline characteristics of responders versus not responders.

	Responders (N = 272)	Non-responders (N = 204)
Male N (%)	131 (48.2)	99 (48.5)
Mean age (Years)	53.58	53.26
Body mass index (BMI, kg/m ²)	26.89	26.92
ASA class N (%)		
I	52 (19.1)	44 (21.6)
II	176 (64.7)	118 (57.8)
III	43 (15.8)	39 (19.1)
IV	1 (0.4)	2 (1.0)
V	0 (0.0)	1 (0.5)
Complete resection N (%)	80 (29.5)	59 (28.9)
Awake craniotomy (%)	27 (9.9)	8 (3.9)
Side of tumor (%)		
Left	108 (39.7)	69 (33.8)
Right	92 (33.8)	77 (37.7)
Bilateral/midline ^a	72 (26.5)	58 (28.4)
Outcome pathology N (%)		
Glioblastoma	33 (12.1)	31 (15.2)
Astrocytoma	47 (17.3)	35 (17.2)
Schwannoma	6 (2.2)	1 (0.5)
Metastasis	19 (7.0)	14 (6.9)
Adenoma/craniopharyngeoma	52 (19.1)	39 (19.1)
Meningioma GR I	61 (22.4)	35 (17.2)
Meningioma GR II	23 (8.5)	10 (4.9)
Other	31 (11.4)	39 (19.1)
Time-q ^b (year)	1.30	1.38

^a This means tumors in both hemispheres and midline tumors like pituitary adenomas that were transphenoidally resected.

^b Time-q: time between questionnaire and surgery date in years.

percentage of patients who do not recall anything from the intraoperative events.

Whilst almost no patients in the awake craniotomy group report ‘completely negative memories’ at any moment of the perioperative period (only 2 patients reported completely negative memories about their first night on the ICU/PACU), one patient in the general anesthesia group has ‘completely negative memories’ about the intra-operative period. In 3 other patients of the general anesthesia group some intraoperative memories were reported as “neutral”.

The mean scores for quantity of the memories of each sub-question of question 1 are shown in Table 3. The quantity of memory in the patients who underwent an awake craniotomy was significantly higher for fixing the head in the Mayfield clamp (P < 0.001), local anesthesia of surgical field (P = 0.001), tumor resection (P < 0.001), closure of surgical field (P = 0.001), transport to the ICU/ PACU (P < 0.001) and first night on the ICU/ PACU (P = 0.008). Despite these significant

Table 3
Mean scores for quantity of the memories in patients who underwent an awake craniotomy vs. patients who received general anesthesia. A Mann-Whitney U test was performed to test for differences between groups.

Sub questions in question 1 and 2	N	Mean score for quantity of memory in awake craniotomy (95% CI)	N	Mean score for quantity of memory in general anesthesia (95% CI)	P value
Preoperative night on the ward	27	3.11 (2.65–3.57)	242	2.90 (2.73–3.07)	0.586
Arrival on the OR	27	2.63 (2.01–3.25)	243	2.63 (2.44–2.83)	0.903
Inserting the i.v. lines	27	1.15 (0.55–1.75)	243	1.37 (1.17–1.58)	0.532
Intubation	–	–	244	0.23 (0.14–0.33)	–
Fixing the head in the Mayfield clamp	27	0.74 (0.27–1.21)	244	0.18 (0.09–0.27)	< 0.001
Local anesthesia of surgical field	27	0.67 (0.18–1.16)	244	0.19 (0.10–0.28)	0.001
Craniotomy	27	0.15 (0.00–0.36)	240	0.02 (0.00–0.04)	0.053
Testing brain function	27	2.44 (1.94–2.95)	–	–	–
Tumor resection	27	1.93 (1.36–2.50)	244	0.03 (0.00–0.06)	< 0.001
Closure of surgical field	27	0.07 (0.00–0.18)	239	0.00 (0.00–0.01)	0.001
Transport to the ICU/ PACU	27	1.37 (0.80–1.94)	243	0.27 (0.16–0.37)	< 0.001
Extubation	–	–	242	0.18 (0.10–0.26)	–
First night on the ICU/ PACU	27	2.48 (1.99–2.98)	241	1.72 (1.54–1.90)	0.008

differences, the mean scores of the patients who underwent an awake craniotomy still show a very low total quantity of memory in the period after the iv-lines were placed until the first night on the ICU/PACU.

The mean score for quality of the memories of each sub-question of question 1 and of each sub-question of question 2 are shown in Table 4. The only significant difference between both groups was that patients after an awake craniotomy experience the transport to PACU/ICU with more positive memories than those after a general anesthesia (P = 0.032).

We found no significant differences in quantity and quality of the memories in the general anesthesia group between patients who had a pituitary adenoma, which was transphenoidally resected, and patients who underwent a standard craniotomy.

Four patients in the GA group reported at least some intraoperative memories of their craniotomy. Those patients were not positive about their memories. In all four patients, we reviewed the files carefully, but could not find any other indicators (e.g. hemodynamic changes, post-operative complaints) of unwanted intraoperative awareness.

The mean scores for anxiety of patients and their relatives in the perioperative period for both the GA and AC group are shown in Table 5a. Patients undergoing an awake craniotomy experienced less pre-operative anxiety than patients who received general anesthesia (P = 0.020).

In both groups we performed a paired t-test to investigate the change of the mean scores of anxiety during the perioperative period. We found a significant decrease in mean anxiety score after the operation procedure in the GA group (6.16 vs 4.70; P < 0.001). There was only an insignificant decrease of the quite low mean anxiety score in the AC group (4.59 vs 4.26; P = 0.612). However, there was a significant decrease in anxiety experienced by the relatives, after the operation procedure for both GA (7.48 vs 6.30; P < 0.001) and AC (7.92 vs 6.16; P = 0.006).

There was a significant difference between men (N = 131) and women (N = 139) in mean scores for anxiety prior to surgery, (5.62 vs 6.36; P = 0.032). There was no significant difference between men (N = 127) and women (N = 137) in mean scores for anxiety post-operatively (4.33 vs 4.96; P = 0.087).

The degree of malignancy of a tumor might add an extra impact to the patients’ coping with the diagnosis and the surgical removal. Therefore, we performed a sub-group-analysis, pairing the malignant tumors glioblastoma, astrocytoma and metastasis (97 patients in total) on the one side and the benign tumors meningioma, adenoma and schwannoma (132 patients) on the other side. The only significant differences between the groups we found were a higher quality (16.9 vs. 13.62, P = 0.002) and quantity (11.78 vs. 9.42, P = 0.005) of memories for malignant tumors. However, when splitting the malignant group between those operated as an awake craniotomy and those

Table 4

Mean scores for quality of the memories in patients who underwent an awake craniotomy vs. patients who received general anesthesia. A Mann-Whitney *U* test was performed to test for differences between groups.

Sub questions in question 1 and 2	N	Mean score for quality of memory when awake craniotomy (95% CI)	N	Mean score for quality of memory when general anesthesia (95% CI)	P value
Preoperative night on the ward	25	4.48 (3.19–3.77)	217	4.12 (3.99–4.26)	0.144
Arrival on the OR	21	4.29 (3.88–4.70)	197	4.27 (4.14–4.40)	0.937
Inserting the i.v. lines	11	3.55 (2.85–4.24)	119	3.59 (3.40–3.77)	0.833
Intubation	–	–	29	3.34 (3.09–3.60)	–
Fixing the head in the Mayfield clamp	7	3.43 (2.70–4.16)	21	3.43 (3.01–3.85)	0.832
Local anesthesia of surgical field	7	2.86 (2.22–3.50)	20	3.55 (3.04–4.06)	0.097
Craniotomy	2	2.50 (0.00–5.00)	4	2.50 (0.91–4.09)	0.784
Testing brain function	22	4.14 (3.72–4.55)	–	–	–
Tumor resection	18	3.94 (3.48–4.41)	4	3.00 (0.40–5.60)	0.213
Closure of surgical field	1	–	1	–	–
Transport to the ICU/ PACU	15	4.27 (3.82–4.71)	30	3.57 (3.17–3.97)	0.032
Extubation	–	–	25	3.32 (2.83–3.81)	–
First night on the ICU/ PACU	24	3.54 (3.97–4.11)	172	3.76 (3.60–3.92)	0.541

Table 5a

Differences between awake craniotomy and general anesthesia in sum score of quantity and quality of memory, overall satisfaction and anxiety. A Mann-Whitney *U* test was performed to test for differences between groups.

	N	Awake craniotomy	N	General anesthesia	P value
Mean sum score of quantity of memory (95% CI)	27	16.74 (13.54–19.94)	245	9.63 (8.93–10.34)	< 0.001
Mean sum score of quality of memory (95% CI)	25	24.16 (20.79–27.53)	233	14.01 (13.19–14.84)	< 0.001
Mean overall satisfaction score	27	8.04 (7.28–8.79)	242	8.01 (7.78–8.23)	0.823
Anxiety in patients prior to procedure	27	4.59 (3.39–5.79)	243	6.16 (5.77–6.54)	0.020
Anxiety in patients after procedure	27	4.26 (3.17–5.35)	237	4.70 (4.33–5.08)	0.564
Anxiety in relatives prior to procedure	27	7.48 (6.59–8.38)	238	7.92 (7.64–8.21)	0.225
Anxiety in relatives after procedure	27	6.30 (5.23–7.36)	229	6.16 (5.81–6.50)	0.785

Table 5b

Differences between benign and malignant tumors in sum score of quantity and quality of memory, overall satisfaction and preoperative anxiety. A Mann-Whitney *U* test was performed to test for differences between groups.

	AC malignant	GA malignant	P value*	GA benign	P value**
Mean sum score for quantity of memory	16.04 (n = 25)	10.31 (n = 72)	0.001	9.41 (n = 132)	0.194
Mean sum score for quality of memory	23.57 (n = 23)	14.68 (n = 69)	< 0.001	13.62 (n = 125)	0.214
Mean score for pre-operative anxiety	4.84 (n = 25)	6.09 (n = 70)	0.096	6.20 (n = 132)	0.655
Mean satisfaction score	8.00 (n = 25)	8.27 (n = 70)	0.774	7.82 (n = 131)	0.237

* P value for difference between AC malignant vs GA malignant.

** P value for difference between the GA malignant group vs the GA benign group.

operated under general anesthesia, it became evident, that not the malignancy of the tumor, but the anesthesia technique has the highest impact on this difference (Table 5b).

3.2. Correlation analysis

There was a significant positive correlation between the sum scores of the answers related to the quantity of memories and the sum scores of the answers related to quality of memories ($P < 0,001$, Table 6). So, patients who remembered more, experienced the perioperative period in a more positive way than patients who remembered less. There was a significant positive correlation between the sum scores of the answers related to the quality of memories and the overall satisfaction score regarding the perioperative period, independent of the anesthesia technique used.

We performed a correlation analysis between the duration of anesthesia and the quality and quantity of memories and found for both a significant but small negative correlation, meaning that patients undergoing longer procedures have a lower quality and quantity of

Table 6

Correlation analysis.

Correlation	Spearman's rho	P value
Sum score quantity of memory with sum score quality of memory	0.801	< 0.001
Time-q with sum score quantity of memory	–0.019	0.760
Time-q with sum score quality of memory	0.023	0.708
Sum score of quantity of memory with overall satisfaction score	0.066	0.281
Sum score of quality of memory with overall satisfaction score	0.186	0.003
Sum score quantity of memory with age	–0.352	< 0.001
Sum score quality of memory with age	–0.273	< 0.001
Sum score quantity of memory with duration of anesthesia	–0.143	0.018
Sum score quality of memory with duration of anesthesia	–0.197	0.001
Anxiety prior to surgery with age	0.050	0.417
Anxiety looking back at surgery with age	0.022	0.725

Table 7
Correlation analysis of anxiety with quantity and quality of memories in general anesthesia and awake craniotomy.

Correlation	General anesthesia (Spearman's rho)	P value	N	Awake craniotomy (spearman's rho)	P value	N
Sum score quantity of memory with anxiety prior to operation procedure	-0.161	0.012	243	-0.116	0.564	27
Sum score quantity of memory with anxiety looking back at operation procedure	-0.181	0.005	237	-0.415	0.018	27
Sum score quality of memory with anxiety prior to operation procedure	-0.193	0.003	243	-0.007	0.974	25
Sum score quality of memory with anxiety looking back at operation procedure	-0.217	0.001	237	-0.116	0.581	25
Sum score quantity of memory with anxiety in relatives prior to operation procedure	-0.022	0.736	238	-0.417	0.030	27
Sum score quantity of memory with anxiety in relatives looking back at operation procedure	-0.112	0.092	229	-0.419	0.029	27
Sum score quality of memory with anxiety in relatives prior to operation procedure	0.103	0.122	226	-0.243	0.242	25
Sum score quality of memory with anxiety in relatives looking back at operation procedure	-0.124	0.066	219	-0.226	0.277	25
Anxiety in patients prior to surgery with anxiety in relatives prior to surgery	0.377	< 0.001	238	0.600	0.001	27
Anxiety in patients after surgery with anxiety in relatives after surgery	0.424	< 0.001	229	0.708	< 0.001	27
Anxiety in patients prior to surgery with the overall satisfaction score	-0.128	0.048	243	0.210	0.292	27
Anxiety in patients after surgery with the overall satisfaction score.	-0.217	0.001	235	-0.430	0.832	27

memories (Table 6).

There was a significant negative correlation between age and quantity and quality of the memory ($P = 0.013$ vs $P < 0.001$). Older patients experienced the procedure in a less positive way than patients who were younger. There was no significant correlation between age and anxiety prior to and after surgery ($P = 0.417$ vs $P = 0.725$). There was no significant correlation between the time passed since the procedure (time-q) and the sum score of the answers related to the quality and quantity of memories. A longer interval did not influence the memories in a more positive or more negative way.

To investigate the influence of anxiety on the quantity and quality of the memories, we performed a subgroup analysis for both general anesthesia and awake craniotomy. The sub-group analysis showed significant negative correlations between anxiety prior to the operation procedure and the quantity and quality of the memories in the GA group ($P = 0.012$ for quantity and $P = 0.003$ for quality, Table 7). There were also significant negative correlations between anxiety after the operation procedure and the quantity and quality of the memories in the GA group ($P = 0.005$ for quantity and $P = 0.001$ for quality). In the AC group we found only a significant negative correlation between anxiety after the operation procedure and the quantity of the memories, there was not a significant negative correlation for quality of the memory ($P = 0.018$ for quantity and $P = 0.581$ for quality). There were no significant correlations between anxiety prior to the operation procedure and the quantity and quality of the memories in the AC group.

In both groups (GA and AC) we found a significant positive correlation between anxiety experienced by the relatives and anxiety experienced by the patient prior and after surgery (Table 7).

The mean overall satisfaction score in the studied patient group was 8.01 (S.E. mean 0.110). There were no significant differences in overall satisfaction score between men ($N = 131$) and women ($N = 138$) (8.00 vs 8.02; $P = 0.545$), and patients with complete resection and remnant of tumor (8.06 vs 8.00; $P = 0.336$). The mean overall satisfaction score per diagnosis is shown in Table 8. Three patients did not fill in an overall satisfaction score.

When asked to recall specific events, men ($N = 70$) and women ($N = 70$) experienced different events as most discomfoting. Men experienced the urinary catheterization the most discomfoting (42.9% $N = 30$), followed by pain after surgery (17.1% $N = 12$). Women found the pain after surgery the most discomfoting (24.3% ($N = 17$), followed by the insertion of the intravenous cannula (14.3% $N = 10$).

Anesthesia technique

There was a significant difference in the sum scores of the quantity and quality of the memory between patients who underwent an awake craniotomy and patients who received general anesthesia ($P < 0.001$ and $P < 0.001$, Table 6). The mean of the overall satisfaction score, computed from the satisfaction scores given by the patients, was not different between patients who underwent an awake craniotomy and

Table 8

Mean overall satisfaction score per diagnosis.

Diagnosis	N	Mean score (95% CI)
Glioblastoma	32	8.31 (7.78–8.84)
Astrocytoma	32	8.09 (7.56–8.63)
Oligodendroglioma	13	8.15 (6.64–9.67)
Ependymoma	2	8.50 (0.00–10.00)
Schwannoma	6	7.83 (6.04–9.64)
Lymphoma	7	8.14 (5.91–10.00)
Metastasis	18	8.22 (7.59–8.85)
Craniopharyngioma	4	8.00 (5.40–10.00)
Cyst	7	8.42 (6.51–10.00)
Adenoma	48	7.75 (7.20–8.29)
Meningioma WHO GR I	61	7.98 (7.53–8.43)
Meningioma WHO GR II-III	22	7.54 (6.32–8.77)
Hemangioblastoma	7	8.57 (7.84–9.30)
Other	9	7.88 (6.91–8.86)

patients who received general anesthesia (8.04 vs 8.01; $P = 0.823$).

4. Discussion

The primary goal of this study was to investigate the link between preoperative anxiety, the perioperative experience and the quantity and quality of postoperative memories in patients who underwent intracranial tumor surgery.

The results show that patients who remembered more, experienced the perioperative period in a more positive way than patients who remembered less. This suggests that more (positive) memories are better for coping with such a major life event. Further research is necessary to confirm this correlation and to identify possible mechanisms. Future research should focus on psychological outcomes in relation to the memory about the event to identify the role of memory on coping with a major life event.

29 of the GA-patients indicated that they remembered at least something from the moment of intubation. We did not ask for further specification of these memories, but considering the reported quality of the memories it can be supposed, that these patients remember (parts of) anesthesia induction, but not really the performance of the endotracheal intubation. Due to our study design this was not further explored.

The contrast in our study between patients who received GA who stated to remember at least something from moments they were (supposed to be) under anesthesia and patients who underwent an awake craniotomy but stated to remember nothing from moments they were obviously awake and cooperative is noteworthy. We were not able to find an appropriate explanation for this contrast except some memory blockade due to the initial sedation with propofol in the AC group.

For the patients who underwent an awake craniotomy, our results

confirm the findings of our previous study in a different population of patients [6]. In the current study an even larger group of patients in the awake craniotomy group answered that they had no memories at all of the consecutive perioperative steps. The quality of the memories was in both studies mostly positive.

These findings also confirm earlier studies by other authors, showing that patient's acceptance and satisfaction for awake craniotomies is relatively high [7–11] and that an awake craniotomy is absolutely not more (and maybe even less) stressful than general anesthesia [12]. Our findings when comparing malignant and benign tumors (Table 5b) support this hypothesis: even patients undergoing an awake craniotomy for a malignant tumor have a higher quality of memories and a tendency to less anxiety and more satisfaction than patients undergoing resection of a (benign) tumor under general anesthesia.

Our findings about anxiety in the patients and their relatives and the negative correlation between anxiety and the memories especially in the GA group raises the question, what role the experienced anxiety (by the relatives) plays in coping with such a major life event for the patient? Interestingly, the mean scores for the experienced anxiety in the relatives were higher than the mean scores for anxiety in the patient preoperatively and remain higher postoperatively. A possible explanation for this finding could be the experienced inability to help the patient for the relatives. The relatives of the patient have to watch how the patient is dealing with his disease, with only limited options to provide help. This can be very stressful for the relatives of the patient, whilst the patient can sense this stress. Our findings concerning anxiety are in line with an earlier study of Petruzzi et al. [13], who showed that caregivers of patients diagnosed with a brain tumor experience more symptoms of anxiety, than the patient himself. Therefore, it is important to pay attention to the anxiety in the relatives of the patient, and how they are coping with the situation, too.

As far as we could find in the available literature, our findings of a decreased quality and quantity of memories in case of longer lasting procedures have not yet been described before. In opposite, for colonoscopies evidence was found that lengthy procedures were not remembered as particularly aversive [14].

Our results concerning the correlation between age and anxiety and differences in experienced anxiety between men and women are in line with Ruis et al [15]. However, we found a lower pre-operative mean anxiety score, which might be due to the difference in the used questionnaires. The questions in our questionnaire were about the general experience of anxiety and inconveniences, whilst Ruis et al. asked about specific anxieties patients may have about the procedure. This could be helpful in expectation management in patients undergoing brain tumor surgery, too.

In contrast, a study of Milian et al. [16] showed that 44% of the patients who underwent an awake craniotomy had either repetitive recollections or dreams who were related to the surgery, and 2 out of 16 patients were diagnosed to have PTSD. In our center, patients who are planned for an awake craniotomy receive an intensive information and preparation interview, which is done with video and slides by the responsible anesthesiologist who also will provide the care for the patient during the operation. We consider this preparation and the quite active role for the patient during the surgery as crucial factors for the positive results in our population. From our point of view, it would be unethical to proof this by a prospective interventional trial.

Santini et al. identified psychological warning signs like fear of pain, anxiety and the incapability of self-control as predictive for intraoperative monitoring failures [17]. These criteria might be helpful in patient selection.

This links also to the recent findings of Jenkins et al. [18], who showed that patients with brain tumors have more emotional changes, such as depression, and personality disturbances after surgery than a control group that had undergone spinal surgery. Another study by Richter et al. [19] suggests that white matter damage could be a cause

for these psychological symptoms.

In the assessment of factors that might have influenced the appreciation of the patient perception about the perioperative period, the quantity and quality of memories should be taken into consideration. Patients who remember more about the perioperative period may be able to process such a major life event in a better way than patients who remember less.

We studied a relative large group of patients and had a relative large group of responders (> 57%). This provided the opportunity to examine the differences between responders and non-responders. However, we could not identify any structural differences between these groups. In our study population no generalized seizures occurred during AC, local seizures due to stimulation were treated with local ice water application at the surgical field only.

Our data do not confirm previously published evidence [20], that men are more satisfied with the care provided. Almost every patient in our study went to the PACU (Post Anesthesia Care Unit) or ICU after the operation. On the PACU and ICU there is a lower patients/nurse-ratio and therefore a higher and more personal level of care provided to all patients than on a recovery room followed by care on a normal ward.

In contrast to the earlier mentioned study [20], our patients who were older remembered less and gave a lower score for their experience of the perioperative period. We were not able to reveal a convincing cause for this phenomenon; however, with an aging population it deserves special attention in future research.

The sum score for the quantity of memories was surprisingly low in our awake craniotomy group. This was mainly caused by the low score for quantity of memory about the local anesthesia of the operation area and the placement of the head of the patient in the Mayfield clamp whilst both are performed according to our protocol with an awake and cooperative patient. However, we routinely give a bolus of about 50 mcg remifentanyl before the local infiltration, which might influence the memories. We were not able to identify other possible factors that could explain this relative low score for these items.

4.1. Limitations

There are some limitations to this study. This was a retrospective study and although an intracranial surgery is a major life event, this could lead to recall bias in memories about the surgery. "Memory" as a neuropsychological correlate is a multi-location phenomenon. Memory formation might be influenced by location, grade and size of the tumor, too. However, these aspects cannot be clearly attributed to memory formation and therefore, we decided not to perform additional subgroup analyses.

The questionnaire used in this study was based on validated questionnaires, but was by itself not validated before this study. The authors did not find an applicable validated questionnaire for the central question of this study, therefore a new approach had to be chosen. Furthermore, there could be a positive effect on patient satisfaction simply by showing interest in how the patient experienced the perioperative period.

Our questions about the psychological aspects in the used questionnaire are much more general as the often used Hospital Anxiety and Depression Scale (HADS), however, we studied a relative large patient group and our findings are largely in line with studies which used the HADS in patients with a brain tumor.

The anxiety scores for the relatives of the patients were reported by the patient self. This could lead to bias. However, the relationship between brain tumor patients and their family caregivers is an upcoming research topic [21], and our data only show, how intense the patients experienced the anxiety of their relatives. This might be influenced by concerns about an actual or anticipated change in physical and/or cognitive performance of the patients due to the tumor and/or the surgery.

In our study there was a varying time interval between the

operation and the moment the patients received our questionnaire. This might influence the results; however, we did not find any significant correlation between the time interval (time-q) and the quantity nor the quality of the memories.

Another limitation of this study is the fact, that we do not have any information about the ethnic-cultural background and educational level of the patients, whilst coping mechanisms most probably will be influenced by these factors. Interestingly, literature for brain tumor patients on this aspect is lacking.

This is a mono-center study, which might make it difficult to extrapolate our results to other centers working in a different way. Nevertheless, many aspects of brain tumor surgery show a world-wide uniformity which makes this limitation less relevant.

Our study interval is too short to come to a conclusion whether the quality and quantity of memories have any link with patients' outcome. Future studies will address this question.

5. Conclusions

The quantity of memories of the perioperative period in patients undergoing brain tumor surgery is low and the quality of these memories is quite positive. Patients who underwent an awake craniotomy had a higher quantity and quality of memory about the procedure than patients undergoing general anesthesia.

We found selective aspects of unpleasant memories like the urinary catheter especially in men and pain in both sexes, which should be addressed better in pre-operative consulting and postoperative management to further increase patient satisfaction.

However, the total quantity of memories after an awake craniotomy is much lower than one would expect considering the fact that the patients are literally awake and fully cooperative for long parts of the procedure. Planned intraoperative awareness does not seem to be traumatizing for the patients.

Patients who remembered more about the perioperative period, experienced the perioperative period in a more positive way than patients who remembered less. This is independent of the anesthesia technique used. A possible explanation of these findings is that patients who remember more are better able to cope with their perioperative experiences.

Patients in the GA group, who experienced more anxiety prior to and looking back at the operation procedure had a lower quantity and quality of their memories. Furthermore, patients in this group who experienced more anxiety prior to and when looking back at the operation procedure had less patient satisfaction.

In the AC group only patients who experienced more anxiety in the days after the operation procedure had a lower quantity of their memories. Patients in this group who experienced more anxiety had not less patient satisfaction.

Declaration of interests

None.

Sources of support

Departmental funding only.

Acknowledgments

We are grateful to Ms. G. De Jonge, M. Sc., Biomedical Information

Specialist, Medical Library, Erasmus University Medical Centre, Rotterdam, The Netherlands for her support with the literature search.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.clineuro.2018.05.013>.

References

- [1] D.H. Kraus, Living in a patient-centric universe, *JAMA Otolaryngol. Head Neck Surg.* 142 (2016) 1231–1232, <http://dx.doi.org/10.1001/jamaoto.2016.3168>.
- [2] S. Honeybul, G.R. Gillett, K. Ho, Futility in neurosurgery: a patient-centered approach, *Neurosurgery* 73 (2013) 917–922, <http://dx.doi.org/10.1227/NEU.000000000000014>.
- [3] A. Palese, M. Skrap, M. Fachin, et al., The experience of patients undergoing awake craniotomy: in the patients' own words. A qualitative study, *Cancer Nurs.* 31 (2008) 166–172, <http://dx.doi.org/10.1097/01.NCC.0000305699.97625.dc>.
- [4] I.R. Whittle, S. Midgley, H. Georges, et al., Patient perceptions of "awake" brain tumour surgery, *Acta Neurochir. (Wien)* 147 (2005) 275–277, <http://dx.doi.org/10.1007/s00701-004-0445-7> discussion 7.
- [5] R.A. Danks, M. Rogers, L.S. Aglio, et al., Patient tolerance of craniotomy performed with the patient under local anesthesia and monitored conscious sedation, *Neurosurgery* 42 (1998) 28–34 discussion 6.
- [6] M. Klimek, P.H. van der Horst, S.E. Hoeks, et al., Quality and quantity of memories in patients who underwent awake brain tumor resection, *World Neurosurg.* 109 (2018) e258–64, <http://dx.doi.org/10.1016/j.wneu.2017.09.158>.
- [7] H. Joswig, D. Bratelj, T. Brunner, et al., Awake craniotomy: first-year experiences and patient perception, *World Neurosurg.* 90 (2016), <http://dx.doi.org/10.1016/j.wneu.2016.02.051> pp. 588–96 e2.
- [8] K.H. Wrede, L.H. Stieglitz, A. Fiferna, et al., Patient acceptance of awake craniotomy, *Clin. Neurol. Neurosurg.* 113 (2011) 880–884, <http://dx.doi.org/10.1016/j.clineuro.2011.06.010>.
- [9] K.J. Khu, F. Doglietto, I. Radovanovic, et al., Patients' perceptions of awake and outpatient craniotomy for brain tumor: a qualitative study, *J. Neurosurg.* 112 (2010) 1056–1060, <http://dx.doi.org/10.3171/2009.6.JNS09716>.
- [10] M. Milian, M. Tatagiba, G.C. Feigl, Patient response to awake craniotomy - a summary overview, *Acta Neurochir. (Wien)* 156 (2014) 1063–1070, <http://dx.doi.org/10.1007/s00701-014-2038-4>.
- [11] P.H. Manninen, M. Balki, K. Lukitto, et al., Patient satisfaction with awake craniotomy for tumor surgery: a comparison of remifentanyl and fentanyl in conjunction with propofol, *Anesth. Analg.* 102 (2006) 237–242, <http://dx.doi.org/10.1213/01.ANE.0000181287.86811.5C>.
- [12] J.W. Hol, M. Klimek, M. van der Heide-Mulder, et al., Awake craniotomy induces fewer changes in the plasma amino acid profile than craniotomy under general anesthesia, *J. Neurosurg. Anesthesiol.* 21 (2009) 98–107, <http://dx.doi.org/10.1097/ANA.0b013e318192d4aa>.
- [13] A. Petrusi, C.Y. Finocchiaro, A. Lamperti, et al., Living with a brain tumor. Reaction profiles in patients and their caregivers, *Support. Care Cancer* 21 (2013) 1105–1111, <http://dx.doi.org/10.1007/s00520-012-1632-3>.
- [14] D.A. Redelmeier, D. Kahneman, Patients' memories of painful medical treatments: real-time and retrospective evaluations of two minimally invasive procedures, *Pain* 66 (1996) 3–8.
- [15] C. Ruis, I. Huenges Wajer, P. Robe, et al., Anxiety in the peroperative phase of awake brain tumor surgery, *Clin. Neurol. Neurosurg.* 157 (2017) 7–10, <http://dx.doi.org/10.1016/j.clineuro.2017.03.018>.
- [16] M. Milian, R. Luerding, A. Ploppa, et al., "Imagine your neighbor mows the lawn": a pilot study of psychological sequelae due to awake craniotomy: clinical article, *J. Neurosurg.* 118 (2013) 1288–1295, <http://dx.doi.org/10.3171/2013.2.JNS121254>.
- [17] B. Santini, A. Talacchi, F. Casagrande, et al., Eligibility criteria and psychological profiles in patient candidates for awake craniotomy: a pilot study, *J. Neurosurg. Anesthesiol.* 24 (2012) 209–216, <http://dx.doi.org/10.1097/ANA.0b013e3182464aec>.
- [18] L.M. Jenkins, K.J. Drummond, D.G. Andrewes, Emotional and personality changes following brain tumour resection, *J. Clin. Neurosci.* 29 (2016) 128–132, <http://dx.doi.org/10.1016/j.jocn.2015.12.007>.
- [19] A. Richter, C.M. Woernle, N. Krayenbuhl, et al., Affective symptoms and White matter changes in brain tumor patients, *World Neurosurg.* 84 (2015) 927–932, <http://dx.doi.org/10.1016/j.wneu.2015.05.031>.
- [20] M.A. Caljouw, M. van Beuzekom, F. Boer, Patient's satisfaction with perioperative care: development, validation, and application of a questionnaire, *Br. J. Anaesth.* 100 (2008) 637–644, <http://dx.doi.org/10.1093/bja/aen034>.
- [21] P.R. Sherwood, M. Cwiklik, H.S. Donovan, Neuro-oncology family caregiving: review and directions for future research, *CNS Oncol.* 5 (2016) 41–48, <http://dx.doi.org/10.2217/cns.15.43>.