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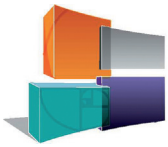

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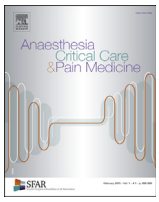

Original Article

Postoperative complications after craniotomy for brain tumor surgery

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ABSTRACT

Introduction: After elective craniotomy for brain tumour surgery, patients are usually admitted to an intensive care unit (ICU) for monitoring. Our goal was to evaluate the incidence and timing of neurologic and non-neurologic postoperative complications after brain tumour surgery, to determine factors associated with neurologic events and to evaluate the timing and causes of ICU readmission.
Patients and methods: This prospective, observational and analytic study enrolled 188 patients admitted to the ICU after brain tumour surgery. All postoperative clinical events during the first 24 hours were noted and classified. Readmission causes and timing were also analysed.
Results: Twenty-one (11%) of the patients were kept sedated after surgery; the remaining 167 patients were studied. Thirty one percent of the patients presented at least one complication (25% with postoperative nausea and vomiting (PONV), 16% with neurologic complications). The occurrence of neurological complications was significantly associated with the absence of preoperative motor deficit and the presence of higher intraoperative bleeding. Seven patients (4%) were readmitted to the ICU after discharge; 43% ($n = 3$) of them had a posterior fossa surgery.
Conclusion: Postoperative complications, especially PONV, are frequent after brain tumour surgery. Moreover, 16% of patients presented a neurological complication, probably justifying the ICU postoperative stay for early detection. The absence of preoperative motor deficit and intraoperative bleeding seems to predict postoperative neurologic complications. Finally, patients may present complications after ICU discharge, especially patients with fossa posterior surgery, suggesting that ICU hospitalization may be longer in this type of surgery.

1. Introduction

Following intracranial tumour surgery, admission to an intensive care unit (ICU) is considered a common practice. Management in an ICU during the postoperative period allows a rapid detection of neurologic deterioration and maintenance of systemic and neurologic homeostasis [1]. Major complications after intracranial surgery occur in 13–27% of patients [2]. These complications may be neurologic, haemodynamic, metabolic or respiratory in nature. Major neurologic complications include postoperative haematomas, cerebral oedema and seizures, and should be differentiated from minor events, such as postoperative nausea and vomiting (PONV), pain and hyperglycaemia. However, there is a possible relationship between events. An event considered as moderate and easily treatable may precede a more severe one. Hypertension may lead to postoperative haematoma [3]. Acute physiological changes during anaesthesia recovery (sympathetic activation, increase in cerebral blood flow and intracranial pressure, shivering and coughing) may be responsible for intracranial complications [2].

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Nevertheless, criteria for admission to the ICU remain unclear. ICU resources are scarce and expensive, and postoperative admissions may limit the availability for emergency admissions [4]. The careful selection of patients admitted to the ICU for postoperative care may reduce hospital lengths of stay and costs [5].

We performed a prospective, observational study involving patients admitted to the ICU after craniotomy for brain tumour surgery. Our first aim was to determine the incidence and timing of neurologic and non-neurologic complications during the first 24 hours. Our second goal was to determine factors associated with a neurologic event. Finally, our study evaluated the incidence, timing and causes of readmission to the ICU.

2. Patients and methods

2.1. Study participants

This prospective observational analytic study was conducted between January 2011 and January 2012 in a University Hospital in France. This study was approved by our local ethics committee (Number: 29-0611), who decided that no written consent was needed for participation given the observational nature of the study. All patients aged 18 years and above who underwent craniotomy for intracranial tumour surgery were enrolled in this study, including emergent (defined by patients receiving preoperative osmotherapy) and elective procedures. All were admitted to a 12-bed neuro-ICU for monitoring during the first 24 hours. Patients aged less than 18 years old were not included.

2.2. Perioperative management

For surgery under general anaesthesia, patients were anaesthetised using sufentanil, propofol and cisatracurium; and anaesthesia was maintained with sevoflurane and sufentanil, except for emergent procedures (total intravenous anaesthesia). Mechanical ventilation was adjusted to obtain an end-tidal carbon dioxide level between 30 and 35 mmHg and an arterial pulse oximetry above 95%. For awake surgery, patients were anaesthetized by using propofol and sufentanil or remifentanil in order to maintain spontaneous breathing with an oxygen facemask at 6 to 8 L/min to maintain arterial pulse oximetry above 95%.

For all patients, during surgery, ephedrine was used in order to maintain a mean arterial pressure (MAP) above 65 mmHg. Neosynephrine or norepinephrine was started after failure of ephedrine. During anaesthesia, a warming blanket was used to prevent hypothermia. No systematic PONV prophylaxis was administered. Droperidol and ondansetron were given to treat PONV in the postoperative period. If steroids were introduced before surgery, they were continued for the perioperative period. Methylprednisolone at 2 mg/kg was given, even in patients who did not receive steroids before, at the beginning of the procedure, and was continued during the postoperative period. Anticonvulsants (levetiracetam at 1 g twice a day) was started the day before surgery and continued for 7 days, except for posterior fossa tumours. Other anticonvulsants, if the patient was under treatment, were continued at the same dosage. Acetaminophen and tramadol or nefopam were given 30 minutes before the end of surgery, and followed after surgery. After awakening, morphine or nalbuphine was used to reduce pain. According to local protocols, antithrombotic prophylaxis with low molecular weight heparin was introduced 48 hours after the surgery.

Patients were woken early after surgery and extubated in the operating room or in the post-anaesthesia care unit (PACU) as soon as possible, if they were stable. Patients with signs of intracranial hypertension were kept sedated, intubated and transferred to the ICU after a CT scan. CT scans were indicated in cases of unexpected motor deficits, dysphasia, seizures and deterioration of consciousness defined by a decrease in the Glasgow coma score of more than 2. Hospital mortality was evaluated for all procedures. Patients who were kept mechanically ventilated for more than three hours were excluded from the final analysis.

Postoperative complications during the first 24 hours were defined and classified into several groups: neurologic (new motor deficits, dysphasia, seizures and deterioration of consciousness defined by a decrease in the Glasgow coma score of more than 2), haemodynamic (bradycardia < 45 b/min, arterial hypertension defined as MAP > 110 mmHg, arterial hypotension defined as MAP < 60 mmHg, and myocardial ischaemia), respiratory (respiratory failure requiring invasive or non-invasive ventilation, hypopnoea defined as respiratory rate < 8/min, hypoxaemia defined as arterial pulse oximetry $< 90\%$), PONV (early PONV < 4 h, h, late PONV between 4 and 24 h), metabolic (hyperglycaemia > 200 mg/dL, diabetes insipidus, dysnatraemia), haemorrhage (blood loss > 500 mL), hyperthermia (core temperature > 38.5 °C) and pain (> 6 on a visual analogical scale after morphine or nalbuphine administration).

2.3. Data collection

Demographic data, preoperative neurological assessment and treatment (steroids, anticonvulsants), tumour type and location, mass effect on CT scan, peroperative data (length of anaesthesia and surgery, type of anaesthesia, position, vasopressor use, quantity and type of fluids, blood loss) and all complications (type and timing) during the first 24 hours were recorded.

Patients were separated into two groups: patients presenting a neurological complication and patients without a neurological complication. The comparison was made to determine the risk factors for neurological complications. Date and cause of readmission in the ICU after discharge were also reported.

2.4. Statistical analysis

Statistical analysis was performed using STATA statistical software, release 11.2 (STATA Corporation, College station, TX, USA). We described patient characteristics using numbers and frequencies for qualitative data and medians (interquartile range [IQR]) for quantitative data. Qualitative variables were compared between groups (neurological complications versus no neurological complications group) using χ^2-tests (or Fisher's exact tests in the case of small expected numbers). Student's t-tests were used to compare the distribution of quantitative data (or Mann–Whitney's tests when distributions departed from normality or when homoscedasticity was rejected). All reported P-values were two-sided and the significance threshold was < 0.05.

3. Results

During the study period, 188 patients were enrolled, including 178 elective and 10 emergent procedures. Three patients died (1.6%): 2 after non-elective procedures (20%), 1 after an elective procedure (0.5%). Twenty-one patients (11%) were excluded (all patients after non-elective procedures and 11 after elective procedures), because they were still sedated and mechanically ventilated 3 hours after the end of surgery (Fig. 1).

The remaining 167 patients were therefore evaluated. Demographic data are reported in Table 1. Eighty-six (51%) patients were male, with a median age of 57 years. It was the first surgery for 124 (74%) patients. The most encountered tumour types were malignant glioma (31%) and meningioma (28%). In the preoperative setting, 49 (29%) patients had seizures and 42 (25%) a motor

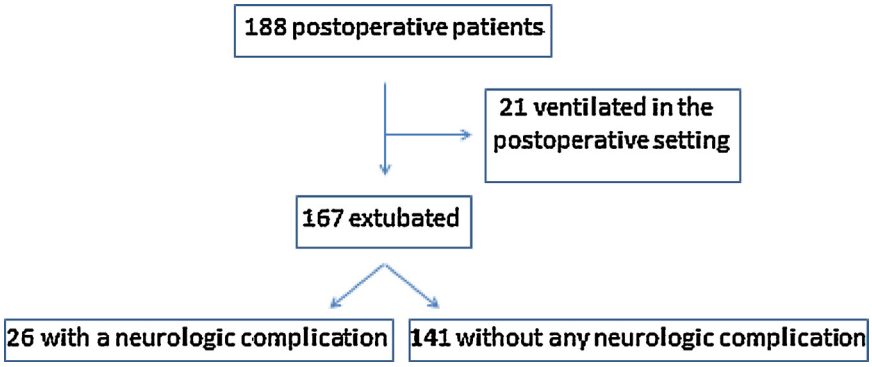

Fig. 1. Study diagram.

deficit. Ninety-two (55%) patients did not experience any complications. Fifty-one (31%) had one complication, 17 (10%) two complications and 7 (4%) more than two complications. PONV was most encountered postoperative complication [42 (25%) patients, especially in the early postoperative period], before neurologic and cardiovascular events. Twenty-six patients (16%) had at least one neurologic complication: 12 (7%) patients had a new motor deficit, 10 (6%) a deterioration of consciousness, 6 (4%) a dysphasia and 2 (1%) had seizures. Twenty-two patients (85%) had their neurologic complication during the first two hours after surgery. Fifteen (9%) patients had a haemodynamic complication: 10 (6%) had a MAP > 110 mmHg. Hyperglycaemia was found in 10 (6%) patients and pain in 11 (7%). No respiratory complication occurred. The incidence of each complication is reported in Table 2.

No delayed awakening was observed; all patients were weaned from mechanical ventilation less than one hour after the end of anaesthesia. Ten (6%) patients required an emergent CT scan. Of these, 3 (2%) had a cerebral haematoma, whereas the brain CT indicated normal postoperative findings in 7 (4%) patients. No surgical evacuation of haematoma was performed. Hydrocephalus was not observed. No patient died during their stay in the ICU.

Table 1
Patient characteristics and preoperative data.

Number of patients (*n*)	167
Male, *n* (%)	86 (51%)
Age (years), median [IQR]	57 [44–66]
ASA status, *n* (%)	
I	19 (11.3%)
II	74 (44.3%)
III	74 (44.3%)
Body mass index, mean [95% CI]	25.1 [24.4–25.9]
First surgery, *n* (%)	124 (74%)
Type of tumour, *n* (%)	
Meningioma	47 (28%)
Malignant glioma	51 (31%)
Brain metastasis	21 (13%)
Cavernous angioma	9 (5%)
Pituitary adenoma	3 (2%)
Unknown	35 (21%)
Preoperative neurologic assessment[a], *n* (%)	
Motor deficit	42 (25%)
Dysphasia	25 (15%)
Seizure	49 (29%)
Trouble of consciousness	17 (10%)
Cerebellar syndrome	9 (5%)
Headache	21 (13%)
Cranial nerve	6 (4%)
Normal examination	30 (18%)

Values are expressed as numbers (percentage) or median values (interquartile range: IQR).
[a] Total percentage exceeds 100% because a subject may have several preoperative neurologic signs.

Predictive criteria for neurologic complications are analysed in Table 3.

Seven (4%) patients were readmitted to the ICU (4 (2%) for a cerebral haematoma, 3 (2%) for a non-neurologic cause). Three (43%) had a fossa posterior tumour, 3 (43%) a temporal tumour and 1 (14%) a frontal tumour. Three patients (43%) had a malignant glioma; two (29%) were operated in the sitting position. All patients had general anaesthesia. They are described in Table 4.

4. Discussion

Following intracranial tumour surgery, admission to an intensive care unit (ICU) is considered a common practice [6]. In neurosurgical patients, no anaesthetic regimen has been demonstrated as superior for the prevention of complications [7,8]. In current practice, rapid extubation following brain tumour surgery is required to detect neurological deterioration. Nevertheless, extubation should be performed only in safe conditions. Emergent weaning depends on the patient's preoperative diseases and postoperative status (haemodynamic, respiratory and metabolic). In unstable patients, the risks of early extubation may outweigh the benefits [9]. In our study, 11% of patients were kept sedated and mechanically ventilated in order to wait for good conditions for awakening. In this cohort, two patients died from intracranial hypertension and one had a decompressive craniectomy. Emergent

Table 2
Incidence of complications during the first 24 hours following surgery.

Complications	Incidence: *n* (%) [95% CI]
Neurologic, *n* (%)	26 (16%) [10–22]
New motor deficit	12
Dysphasia	6
Seizure	2
Deterioration of consciousness	10
Haemodynamic, *n* (%)	15 (9%) [5–14]
Bradycardia (< 45 b/min)	5
Arterial hypertension (MAP > 110 mmHg)	10
Arterial hypotension (MAP < 60 mmHg)	1
Myocardial ischaemia	0
Respiratory, *n* (%)	0 (0%)
PONV, *n* (%)	42 (25%) [19–32]
Early PONV (< 4 h)	35
Late PONV (≥ 4 h)	12
Metabolic, *n* (%)	11 (7%) [3–11]
Hyperglycaemia	10
Diabetes insipidus	1
Dysnatraemia	0
Haemorrhage, *n* (%)	1 (1%) [0–3]
Hyperthermia, *n* (%)	1 (1%) [0–3]
Pain, *n* (%)	11 (7%) [3–11]

Values are expressed as numbers (percentage). PONV: postoperative nausea and vomiting; MAP: mean arterial pressure. One subject may have several complications.

Table 3
Factors associated with neurologic complications.

	No neurologic complication ($n=141$)	Neurologic complication ($n=26$)	P
Age (years), median [IQR]	58[44–66]	57 [45–66]	0.74
Male, *n* (%)	72 (51%)	14 (54%)	0.79
Preoperative assessment, *n* (%)			
Motor deficit	40 (28%)	2 (8%)	0.03*
Dysphasia	22 (16%)	3 (12%)	0.77
Seizure	42 (30%)	7 (27%)	0.77
Trouble of consciousness	14 (10%)	3 (12%)	0.73
Cerebellar syndrome	8 (6%)	1 (4%)	1
Headache	20 (14%)	1 (4%)	0.2
Cranial nerve	5 (4%)	1 (4%)	1
Normal examination	21 (15%)	9 (35%)	0.03*
Preoperative treatment, *n* (%)			
Steroids	70 (50%)	8 (31%)	0.08
Anticonvulsants	74 (52%)	11 (42%)	0.34
First surgery, *n* (%)	103 (73%)	21 (81%)	0.41
Preoperative CT scan, *n* (%)			
Midline shift > 15 mm	47 (33%)	4 (15%)	0.07
Cerebral herniation	35 (25%)	6 (23%)	0.85
Tumour type, *n* (%)			
Meningioma	40 (28%)	7 (27%)	0.88
Malignant glioma	45 (32%)	6 (23%)	0.37
Brain metastasis	15 (11%)	6 (23%)	0.1
Cavernous angioma	8 (6%)	1 (4%)	1
Pituitary adenoma	3 (2%)	0 (0%)	1
Unknown	30 (21%)	5 (20%)	0.81
Location, *n* (%)			
Frontal	49 (35%)	9 (35%)	0.99
Temporal	53 (38%)	11 (42%)	0.65
Parietal	28 (20%)	3 (12%)	0.42
Occipital	11 (8%)	3 (12%)	0.46
Posterior fossa	11 (8%)	3 (12%)	0.46
Intrasellar	3 (2%)	0 (0%)	1
Intraventricular	5 (4%)	1 (4%)	1
Type of anaesthesia, *n* (%)			
General anaesthesia	119 (84%)	23 (88%)	0.77
Awake surgery	22 (16%)	3 (12%)	
Duration (min), median [IQR]			
Anaesthesia	210[180–270]	263[180–300]	0.08
Surgery	150[120–195]	180[120–210]	0.44
Peroperative position, *n* (%)			
Supine	114 (81%)	19 (73%)	0.07
Prone	10 (7%)	1 (4%)	
Lateral	13 (9%)	2 (8%)	
Sitting position	4 (3%)	4 (15%)	
Fluids (mL), median [IQR]			
Crystalloids	1000 [1000–1500]	1375 [1000–1500]	0.13
Colloids	0 [0–500]	0 [0–500]	0.78
Use of ephedrine (mg), median [IQR]	0 [0–6]	0 [0–0]	0.67
Estimated blood loss (mL), median [IQR]	100 [0–250]	200 [100–400]	0.01*

* $P < 0.05$.

Table 4
Description of patients readmitted to the ICU.

	Tumour location and type	Duration of surgery (min)	Position	Estimated blood loss (mL)	Early complication (during the first 24 hours)	Type and timing of complication (cause of readmission)
Patient 1	Frontal Malignant glioma	195	Supine	150	None	ACS Day 1
Patient 2	Posterior fossa Malignant glioma	225	Sitting position	150	None	Respiratory distress Day 2
Patient 3	Posterior fossa Brain metastasis	165	Sitting position	400	Late PONV Hypertension	Intracerebral haematoma Day 4
Patient 4	Temporal Meningioma	390	Supine	1200	Early PONV	Intracerebral haematoma Day 2
Patient 5	Temporal Unknown	195	Supine	100	Dysphasia	Epidural haematoma Day 2
Patient 6	Posterior fossa Unknown	300	Prone	< 100	Late PONV	Cardiac arrest (brain herniation) Day 4
Patient 7	Temporal Malignant glioma	150	Supine	< 100	Hyperglycaemia	Intracerebral haematoma Day 13

ACS: acute coronary syndrome. All patients received general anaesthesia.

surgery, use of osmotherapy before and/or during surgery, longer surgery duration and larger tumour sizes were factors limiting early awakening.

In our study, 45% of patients had at least one complication during the first 24 hours following surgery. PONV was the most frequent complication and was found in 25% of patients in our study. During the study period, PONV was not systematically prevented in our unit; preventive measures were taken only in patients at risk based on the Apfel Score. In a study by Manninen et al. [10], PONV occurred in 38% of patients and also represented the most frequent early postoperative complication. For the prevention of PONV, 5-HT3 receptor antagonists have shown their efficacy to reduce emesis, but they failed to control nausea [11]. Neurologic and cardiovascular events are respectively the second and third most frequent complications. Hypertension is the most frequent cardiovascular complication, preceding bradycardia and hypotension. Acute pain occurred in 7% of patients. Pain after craniotomy has often been underestimated, and its severity can be managed via a multimodal approach [12]. Interestingly, no respiratory complication was noted during the first 24 hours following surgery.

Neurologic complications are the most feared. In our study, only 2 patients had postoperative seizures. Early postoperative seizures are rare after supratentorial neurosurgery [13]. The routine use of antiepileptic drugs has recently been shown to provide no benefit [14]. Seizures are not linked to metabolic abnormalities or intracranial haematomas [15]. For known epileptic patients, the incidence of postoperative seizure is higher, even if a prophylactic anticonvulsant, associated with the continuation of the preexisting medication, is given [16]. These patients should probably be closely monitored.

Twelve patients had a new motor deficit and the absence of neurological deficit before surgery was associated with a higher probability of developing a new neurological deficit in the postoperative period and therefore a neurological complication. This could only be related to the fact that when neurological deficits were already present in the preoperative period, probably due to a mass or tumour effect, the neurosurgery by itself is unlikely to induce a new deficit in another region, whereas in patients without neurological deficits, the surgery by itself could have induced a neurological deficit due to surgical removal of the tumour. Ten patients had a deterioration of consciousness and had an emergency CT scan. Postoperative intracranial haematoma was found in only 3. Though this results in an incidence of less than 10%, this complication clearly affects clinical outcome. The type of tumour (intracranial meningiomas), high intraoperative blood loss and coagulation disorders are associated with postoperative haematomas [17–19]. Clinical deterioration linked to a postoperative haematoma occurred principally within 6 hours of surgery [20], but intracranial haematoma can be detected later [3,19]. In the present study, factors significantly associated with a neurologic complication are: the absence of a preoperative motor deficit (and a normal preoperative neurologic examination) and a higher estimated peroperative blood loss. The absence of a preoperative steroid treatment or a preoperative CT scan with midline a shift of $\leq$ 15 mm, brain metastasis, a longer duration of anaesthesia, sitting peroperative position and a higher amount of crystalloid fluids tended to be associated with neurologic complications, without reaching the significance threshold. Age, sex, first surgery, tumour location, length of surgery, type of anaesthesia and the use of ephedrine were not associated with neurologic complications. In current practice, a small fraction of patients requires prolonged intensive care unit stay after craniotomy for tumour resection [21], but criteria for admission to ICUs remain unclear. Patients with anticipated long operation times, extensive blood loss, and high anaesthetic risks should be selected for postoperative ICU admission [22]. In their study, Hanak et al. [23] found that, in a multivariate analysis, only diabetes and older age predicted the need for an ICU level intervention after elective craniotomy. Rhondali et al. [4] found that the predictors of postoperative complications are: a duration of surgery of more than 4 hours, lateral positioning of the patient during surgery, and mostly the failure to extubate the trachea in the operating room.

Finally, 7 patients (4%) were readmitted to the ICU after discharge. The principal cause was intracranial bleeding (4 cases, between days 2 and 13). One patient presented a cardio-respiratory arrest on day 4 due to an unknown cause (but signs of intracranial hypertension were present before, and he/she probably had a brain herniation leading to the cardiac arrest). One patient, with Parkinson's disease, went into respiratory distress on day 2. One patient, who had coronary artery disease, presented an acute coronary syndrome on day 1, a few hours after leaving the ICU. Interestingly, though posterior fossa surgery concerned only 8% of patients, it was associated with late complications in 3 patients (43% of readmissions). Late PONV (2 cases) must be considered as intracranial hypertension and not classic PONV.

Our study may have certain limitations. We have chosen to mix elective and non-elective procedures in order to evaluate mortality after intracranial tumour surgery. Postoperative complications have therefore not been evaluated for patients who were mechanically ventilated for more than 3 hours, even if major postoperative complications may be expected to be more frequent in this group. The limitations of our study include the relatively small sample size based on only one centre and the reliability of the collected data. Certain complications may have been underestimated. For example, nurses give a prescribed rescue antiemetic drug when the patients feel sick without a call for confirmation. Moreover, some complications have not been studied, such as shivering. Finally, the exclusion of patients who were kept sedated and mechanically ventilated may limit the number of neurologic complications. Because of a relatively small sample size, we could not assess the independent determinants of neurologic complications. Therefore, our results require confirmation via larger cohorts.

5. Conclusion

Our study shows that complications occurring during the first 24 hours following brain tumour surgery are frequent. PONV are the most encountered complications. However, major neurologic complications are also frequent (16% of the patients) and certain criteria may allow us to predict them: the absence of a preoperative motor deficit, heavy intraoperative bleeding, the absence of a preoperative steroid treatment or a preoperative CT scan with a midline shift of $\leq$ 15 mm, brain metastasis, a longer duration of anaesthesia, sitting peroperative position and higher doses of crystalloid fluids. Tumour location, length of surgery and type of anaesthesia are not associated with early neurologic complications in our study. Finally, even if ICU readmission is rare, complications may be observed after 24 hours, especially after a fossa posterior surgery, suggesting that these patients should be monitored for more than 24 hours in the ICU.

Disclosure of interest

The authors declare that they have no competing interest.

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