

Complications of First Craniotomy for Intra-Axial Brain Tumour

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Abstract: Complications were examined in a single surgeon's series of 207 consecutive adult patients undergoing first craniotomy for intra-axial brain tumour. The study group consisted of 114 gliomas, 74 metastatic tumours and 19 miscellaneous lesions. There were 25 infratentorial tumours and 182 supratentorial tumours (39 deep and 143 superficial). The total number of patients sustaining complications was 52 for an overall complication rate of 25.1%; the rate was higher for infratentorial tumours (44.0%) than supratentorial tumours (22.8%) regardless of histology ($p = 0.012$). There were 5 deaths for a mortality rate of 2.4%. Forty-seven patients incurred operative morbidity (22.7%); 7 out of the 47 had multiple complications. Sixteen patients sustained transient worsening due to edema (7.7%) and 6 patients sustained permanent neurological deficit (2.9%). Medical complications were suffered by 17 patients (8.2%). Major complications which significantly altered the quality and/or quantity of survival were suffered by 9 patients overall (4.3%).

Résumé: Complications de la crâniotomie initiale pour tumeur cérébrale intra-axiale. Nous avons examiné 207 patients adultes consécutifs traités par le même chirurgien, qui ont subi une première crâniotomie pour tumeur cérébrale intra-axiale. Dans le groupe étudié, il y avait 114 gliomes, 74 tumeurs métastatiques et 19 lésions variées. Vingt-cinq tumeurs étaient infratentorielles et 182 étaient supratentorielles (39 profondes et 143 superficielles). Le nombre total de patients qui ont eu des complications étaient de 52, pour un taux de complication global de 25.1%; le taux était plus élevé pour les tumeurs infratentorielles (44.0%) que pour les tumeurs supratentorielles (22.8%), quelque soit l'anatomopathologie ($p = 0.012$). Il y a eu 5 décès, soit un taux de mortalité de 2.4%. Quarante-sept patients ont eu une morbidité opératoire (22.7%); 7 d'entre eux ont eu des complications multiples. Seize patients se sont détériorés temporairement à cause de l'oedème (7.7%) et chez 6 patients le déficit neurologique a été permanent (2.9%). Dix-sept patients (8.2%) ont subi des complications médicales. Neuf patients en tout (4.3%) ont eu des complications majeures qui ont diminué significativement la qualité ou la longueur de leur survie.

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Craniotomy is frequently the initial procedure in the management of a patient with an intrinsic (i.e., intra-axial) brain neoplasm. Surgery aims for maximal removal of the tumour without producing new neurological deficit.¹ Adjuvant therapy is then instituted to delay recurrence and prolong survival.² Despite advances in neuroimaging, anesthesia, and surgical instrumentation, there is always the risk of complications attendant upon an operation to remove an intra-axial brain tumour. Early reports on the surgical treatment of intra-axial tumours paid relatively little attention to morbidity because survival was the prime issue of importance in these early series.^{3,4,5,6} The majority of the more contemporary morbidity studies have addressed only one or two specific complications or have included patients undergoing repeat craniotomy. The complication rate of brain tumour surgery depends on factors other than technique and surgical experience alone. Factors such as the patient's preoperative/postoperative overall physical condition (e.g., age, pulmonary and cardiovascular function, existing neurological deficit), the tumour characteristics (e.g., size, location, histology, quantity of associated edema), and the availability of specific resources (e.g., navigational devices) may all influence surgical outcome.⁷ The purpose of the present study was to

rigorously examine all the possible complications encountered within 30 days of first operation in a contemporary series of craniotomy for intra-axial brain tumour. For greater uniformity, the study population was limited to only adult patients operated by one surgeon in one institution all within the modern imaging era (e.g., CT and MRI).

PATIENT DATA AND METHODS

Between January 1985 and November 1993, 207 adult patients of the senior author (M.B.) underwent first craniotomy for an intra-axial neoplasm. The patients' hospital charts and out-patient records were retrospectively reviewed. Patients undergoing repeat craniotomy or first craniotomy for extra-axial tumour (e.g., meningioma) were excluded.

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There were 114 gliomas, 74 metastatic tumours and 19 miscellaneous tumours (e.g., lymphoma, choroid plexus papilloma, hemangioblastoma). Patient age ranged from 16 to 83 years old with a mean of 53 years. For patients with metastases, the age ranged from 23 to 77 years and the mean was 56.2 years. For patients with gliomas age ranged from 17 to 83 years and the mean was 51.5 years. The astrocytic tumours were classified pathologically as: astrocytoma, malignant astrocytoma, or glioblastoma (glioblastoma is distinguished from malignant astrocytoma by the presence of necrosis). There were 6 astrocytomas, 26 malignant astrocytomas, and 70 glioblastomas; the other glial tumours were 7 oligodendrogliomas, 3 gangliogliomas, and 2 mixed gliomas.

There were 182 tumours located in the cerebrum (108 gliomas, 57 metastatic, 17 miscellaneous) and 25 in the cerebellum (6 gliomas, 17 metastatic, 2 miscellaneous). Among the cerebral tumours, 39 were deep (i.e., subcortical or deeper) and 143 were superficial (17 tumours were in eloquent cortex).

All but 7 patients were neurologically intact or had mild to moderate neurological deficit only at the time of surgery and were operated electively. Eleven patients had preoperative stereotactic biopsy for tissue diagnosis. For the other 196 patients, the clinical history and imaging studies were highly suggestive of an intra-axial neoplasm. All patients received prophylactic antibiotics and perioperative anticonvulsant and steroid therapy; deep vein thrombosis prophylaxis was not routinely given. Twenty-three patients underwent awake craniotomy with cortical mapping. Ultrasound localization was used routinely for subcortical tumours. The operating microscope and ultrasonic aspirator were used to facilitate excision when indicated. Gross total resection was performed for every metastatic tumour as there is usually a well-defined macroscopic plane between tumour and brain. However subtotal resection only was performed for the majority of the gliomas because these tumours consistently have microscopic (and often macroscopic) tumour invasion of surrounding normal-appearing brain⁸ and the oncological value of macroscopic total removal of gliomas has not been definitively demonstrated.⁹

All complications including death occurring within 30 days of surgery were identified. Complications were divided into 6 major categories: medical (e.g., pneumonia, deep vein thrombosis); wound (e.g., frontalis nerve palsy); seizures; problems in intra-operative localization; hematoma; and neurological. Neurological complications were subclassified into transient neurological worsening and permanent neurological worsening.

COMPLICATIONS

Overall Complication Rate

There were 52 patients who incurred complications within 30 days of surgery; 5 patients died and 47 patients had operative morbidity for an overall complication rate of 25.1%. There were 58 complications (including the 5 deaths) because seven patients had multiple complications (Table 1).

Histology

The complication rate following surgery for the two major tumour types, metastases and gliomas, was the same at 24.3%

and 26.3% respectively regardless of location ($p = 0.5$; logistic regression with maximum likelihood analysis of variance) (Table 2).

Location

The complication rate was higher for infratentorial tumours (44.0%) than supratentorial tumours (22.5%) regardless of histology ($p = 0.012$; logistic regression with maximum likelihood analysis of variance) (Table 2). Ten of the 29 patients with deep cerebral tumours (25.6%) suffered a complication as compared to 31 out of the 143 patients (21.7%) with superficial cerebral tumours; this difference is not statistically significant ($p = 0.503$; Chi square test) (Table 2).

Mortality

There were five deaths for a mortality rate of 2.4%. Two of the patients succumbed to intractable brain edema, on the 1st day and 16th day after surgery for a cerebellar and a deep cerebral glioblastoma respectively. Another patient had a post-operative tumour bleed following resection of a cerebellar metastasis; immediate hematoma evacuation was performed but the patient never regained consciousness. There was also a case of refractory hydrocephalus despite multiple shunting procedures in a patient with a thalamic malignant astrocytoma. An elderly patient died on the 10th post-operative day due apparently to the progressive growth of a deep midline malignant astrocytoma.

Permanent Neurological Deficit

Six patients sustained permanent neurological deficit (2.9%) which included 2 cases of hemiplegia, 2 hemianopsia, one dysphasia, and one bulbar dysfunction. The histology was metastatic in 4, one glioblastoma and one lymphoma. There were 5 deep cerebral tumours and one cerebellar vermian tumour.

Transient Neurological Worsening

Sixteen patients (7.7%) sustained transient neurological worsening after operation but gradually improved to pre-operative status or better. These complications were attributed to edema and all were documented with post-operative CT scan and treated with steroids. Recovery period ranged from 7 days to 60 days. Worsening included 11 cases of increased motor

Table 1. 30-day complications of intra-axial tumour surgery (seven patients had multiple complications).

Complications	No. of cases	case incidence (%)
Neurological Worsening		
Transient	16	7.7
Permanent	6	2.9
Medical	17	8.2
Intra-operative localization	6	2.9
Wound	4	1.9
Hematoma	2	1.0
Seizures	2	1.0
Death	5	2.4

Table 2. Complication rate by histology and tumour location.

	Metastasis	Glioma	Miscellaneous	TOTAL
Supratentorial ^a				
superficial	21.6% (11/51)	25.0% (20/83)	00.0% (0/9)	21.7% (31/143) ^c
deep	00.0% (0/5)	32.0% (8/25)	25.0% (2/8)	25.6% (10/39) ^c
Infratentorial ^a	41.2% (7/17)	33.3% (2/6)	100.0% (2/2)	44.0% (11/25)
TOTAL	24.3% (18/74) ^b	26.8% (30/114) ^b	21.1% (4/19)	25.4% (52/207)

a statistically significant difference ($p = 0.012$; maximum likelihood analysis of variance)

b no significant difference ($p = 0.503$; maximum likelihood analysis of variance)

c no significant difference ($p = 0.503$; Chi square test)

weakness, 4 dysphasia, 2 diabetes insipidus, 2 hemianopsia, one dysmetria, and one drowsiness (the total is greater than 15 as some patients deteriorated in more than one sphere). Fourteen tumours were gliomas and 2 were metastatic. Tumour location was cerebral in 15 (11 deep and 4 superficial) and one tumour was in the cerebellar vermis.

Problems with Intra-operative Localization

Problems in localization were encountered in 6 patients (2.9%); this was associated with transient neurological worsening due to edema in three patients and these three patients are included in the group of 16 described above. Three tumours were in the cerebrum (1 deep and 2 superficial) and 3 were in the cerebellum.

Post-operative Hematoma

One intracerebral and one epidural hematoma were encountered post-operatively. Both patients had superficial cerebral glioblastomas and both underwent emergency evacuation of the clot. There was also a post-operative cerebellar hematoma following removal of a metastasis; this patient is included in the mortalities (see above).

Seizures

A patient operated for a choroid plexus papilloma had a complex partial seizure with secondary generalization one month after surgery. Another patient had increased seizure frequency after excision of a superficial cerebral glioma. All remaining patients experienced no worsening in their seizure pattern following surgery.

Wound Complications

Four patients had wound complications (1.9%). Two patients had temporary pain on chewing presumably due to inflammation of the temporo-mandibular joint. The other wound complications were one pseudomeningocele and one case of superficial cellulitis.

Medical Complications

Medical complications were suffered by 17 patients (8.2%); 2 patients had multiple medical complications. There were 5 cases of deep venous thrombosis with one progressing to pulmonary embolism, 4 cases of urinary tract infection, 5 post-op psychoses, two cases of pneumonia, and one case of electrolyte imbalance. The tumour histology was metastatic in 10, glioma

in 6, and one hemangioblastoma. Thirteen tumours were located in the cerebrum and 4 were in the cerebellum.

Overall Major Complications

Major complications which significantly altered the quality and/or quantity of survival were incurred by 9 of the above-described patients (4.3%); 4 patients had metastases and 5 had gliomas. These 9 patients included the 5 mortalities, as well as one post-operative hematoma, one massive pulmonary embolus, and two patients with significant permanent post-operative neurological deficit.

DISCUSSION

Histology

Glial and metastatic brain tumours comprise the majority of intracranial tumours requiring intervention by a neurosurgeon. Previous reports had generally studied these two major tumours separately because of their difference in origin, behavior, patient population and prognosis. However, the anticipated complication rate for surgery of gliomas and metastases would be expected to be similar due to the simple fact that both tumour types are located within the brain parenchyma which requires the same surgical techniques of corticotomy, and the requisite retraction and manipulation of the surrounding brain to facilitate removal of the lesion. There appears to be no significant difference in complication rates for surgery of gliomas and metastases from selected series published since 1980 (Table 3), and our findings confirm this observation.¹⁰⁻²⁷

Location

Surgical complication rate appears to be more dependent on the location of the tumour than the histology (i.e., infratentorial vs. supratentorial). Posterior fossa tumour surgery was found to carry significantly higher complication rates than supratentorial tumour surgery in the current series; perhaps this obtains because of the small margin of error the surrounding vital structures will tolerate. For supratentorial tumours, as the operation proceeds deeper into the brain, the risk of damaging the surrounding viable tissue should increase because of the compactness of vital pathways in the deep white matter and also the attendant retraction and manipulation on the surrounding superficial brain. This has been reported by others²⁸ although we observed no statistically significant difference in complication

Table 3. Complication rates for intra-axial tumour surgery in selected series.

Series	Year	Collection interval	n	Mortality rate (%)	Morbidity rate (%)
Metastasis					
Winston KR et al. ²⁷	1980	1967-77	96	10.0	3.1
Sundaresan N et al. ²⁵	1983	1978-81	35	3.0	14.3
Galicich JH et al. ¹⁴	1985	1977-80	75	9.0	^a
Sundaresan N et al. ²⁴	1985	1978-82	125	6.0	27.0
Kelly PJ et al. ¹⁸	1988	1980-87	44 ^b	^a	11.4
Guazzo EP et al. ¹⁵	1989	1978-87	29	^a	24.0
Brega K et al. ¹¹	1990	1983-89	13	0	30.0
Patchell RA et al. ²²	1990	1985-88	25	4.0	0.0 ^c
<i>Mean</i>				5.3	16.9
Present study	1993	1985-93	74	1.4	23.3
Glioma					
Ammirati M et al. ¹⁰	1987		31	0	16.1
Ciric I et al. ¹²	1987		42	0	21.4
Kelly PF et al. ¹⁷	1989	1984-88	28 ^{b,d}	3.6	14.3
Vecht CJ et al. ²⁶	1990	1975-84	66 ^e	20.9	23.9
			177 ^f	22.5	19.1
Höllerhage HG et al. ¹⁶	1991	1978-86	80 ^{f,g}	20.0	9.0
			38 ^{f,h}	3.0	10.0
Paoletti P et al. ²¹	1991	1973-80	145	7.6	27.2
	1981-89		194	2.6	(overall)
McCormack BM et al. ²⁰	1992	1977-88	44 ⁱ	2.3	13.6
Devaux BC et al. ¹³	1993	1984-88	78 ^b	0	20.3
			25 ^j	0	(overall)
Kreth FW et al. ¹⁹	1993	1986-91	57	^k	15.8
Philippon JH et al. ²³	1993	1978-87	199 ⁱ	5.0	^a
<i>Mean</i>				6.7	17.3
Present study	1993	1985-93	114	3.6	23.2

^a not discussed^b stereotactic resection^c 3 patients excluded from the study because the lesion proved to be non-neoplastic^d thalamic astrocytomas only^e anaplastic astrocytomas only^f glioblastoma multiforme only^g microsurgical technique employed^h microsurgical technique employedⁱ low-grade astrocytomas^j non-stereotactic resection^k deaths excluded outright from the study

rate for deep vs. superficial tumours. Stereotactic techniques can now be used for resection of both deep-seated metastatic and glial tumours to further reduce the complication rate.^{13,17,18}

Mortality

The 30 day mortality of surgery for either metastatic tumour or glioma remained in the range of 20 to 40 percent until the advent of corticosteroids, modern neuroanesthesia and microneurosurgery.^{3,4} Since then, there has been a steady decline in surgical risk (Table 3). The operative mortality rate

for metastatic tumours for most series reported during the last 10 years has been 10% or less.^{11,14,22,24,25,29} Several published series of glial tumour surgery have achieved mortality rates of less than 3% and no mortality for stereotactic resection.^{10,12,13,16,20,21,27} Some of the recent glial tumour series have high mortality rates because of the patients' poor preoperative condition or the use of macrosurgery techniques.²⁶ In the present study, both patients with metastatic and glial tumours were relatively good risk; the majority had mild or no preoperative

neurologic deficit, there was good control of the systemic disease in metastatic tumour patients, and microsurgical excision was done when indicated. The low operative mortality of 1.4% and 3.5% for metastases and gliomas respectively and the low overall mortality rate of 2.4% compare favourably to earlier reported rates.

Morbidity-types

The types of morbidity encountered in the present retrospective review of one surgeon's experience were not unusual. The most important complication seen is neurological worsening; the etiology may be vascular injury (i.e., arterial or venous), increased cerebral edema, and/or post-operative hematoma or abscess; in some cases, the cause is not apparent. Intra-operative attention to vascular structures and to retraction injury, peri-operative steroids and antibiotics, and meticulous surgical hemostasis will help minimize neurological worsening due to the above cited causes.³⁰ Seizures are a common sequela of neurosurgical procedures and are not specific to intra-axial tumour surgery.^{31,32} Peri-operative administration of anticonvulsant medications has become routine in neurosurgical practice. Problems with intra-operative tumour localization should become more uncommon because of excellent available imaging techniques and intra-operative adjuncts such as stereotactic guidance, navigational devices, and ultrasound. Medical complications such as thromboembolic events are easily recognizable sequelae of most types of surgery including craniotomy for intra-axial neoplasm but this and other medical complications are potentially preventable and most are treatable.³³

Morbidity-rate

The morbidity rate in the present series is at the high end of the range of rates reported by others (Table 3); this is partly due to thoroughness of reporting since we included urinary tract infection, electrolyte imbalance, post-operative psychosis, pneumonia, and problems in intra-operative tumour localization which have not been included in many previous reports. Inter-series differences in complication rate may also be partly due to operator judgment, experience and technique all of which are exceedingly difficult to accurately quantitate.

Summary

The morbidity and mortality of first craniotomy for intra-axial tumour does not appear to depend on histology (i.e., glioma vs. metastasis) but does depend on location; surgery of infratentorial tumours appears to have a significantly higher complication rate than surgery of supratentorial tumours. Mortality rate in the present series was 2.4%. The overall complication rate was 25.1%. The quality and/or quantity of survival was made significantly worse by surgery in 9 of our 207 patients (4.3%); (i.e., in the other 43 patients who sustained morbidity, the complication did not impact significantly on the quality or quantity of life). Surgery for intra-axial tumours has a significant complication rate if all complications are rigorously reported. Many of these morbidities (e.g., medical, localization problems) are to some degree preventable and if they do occur, are treatable. Surgical judgment and technical skill play an important role in minimizing complications, but whenever cortex is violated and brain parenchyma retracted and manipulated, the possibility of morbidity exists.

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