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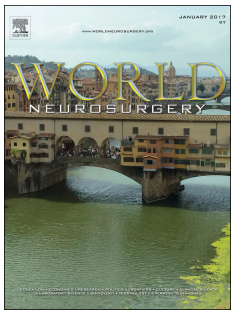

Treatment outcomes of incidental intracranial meningiomas: Results from the IMPACT cohort

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Treatment outcomes of incidental intracranial meningiomas: Results from the IMPACT cohort

Short title: Treatment of incidental meningioma

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Abstract

Background

Incidental findings such as meningioma are becoming increasingly prevalent. There is no consensus on the optimal management of these patients. The aim of this study was to examine the outcomes of patients diagnosed with an incidental meningioma who were treated with surgery or radiotherapy.

Methods

Single-center retrospective cohort study of adult patients diagnosed with an incidental intracranial meningioma (2007-2015). Outcomes recorded were post-intervention morbidity, histopathological diagnosis and treatment response.

Results

Out of 441 patients, 44 underwent treatment. Median age at intervention was 56.1 years (IQR 49.6-66.5); 35 female and 9 males. The main indication for imaging was headache (25.9%). Median meningioma volume was 4.55 cm^3 (IQR 1.91-8.61) and commonest location was convexity (47.7%). Six patients underwent surgery at initial diagnosis. Thirty-eight had intervention (34 surgery and 4 radiotherapy) after a median active monitoring duration of 24 months (IQR 11.8-42.0). Indications for treatment were radiological progression (n=26), symptom development (n=6), and patient preference (n=12). Pathology revealed WHO grade I meningioma in 36 patients and WHO grade II in four. The risk of postoperative surgical and medical morbidity requiring treatment was 25%. Early and late moderate adverse events limiting activities of daily living occurred in 28.6% of patients treated with radiotherapy. Recurrence rate following surgery was 2.5%. All meningiomas regressed or remained radiologically stable following radiotherapy.

Conclusion

The morbidity following treatment of incidental intracranial meningioma is not negligible. Considering most operated tumors are WHO grade I, treatment should be reserved for those manifesting symptoms or demonstrating substantial growth on radiological surveillance.

Introduction

Arising from the arachnoid cap cells in the brain, meningiomas are the commonest primary intracranial tumors.[1] Their management consists of surgery, radiotherapy, radiosurgery, and active clinical-radiological monitoring. Meningiomas presenting with focal neurological deficits and seizures have clear management algorithms; safe maximal resection being first line treatment.[2] In contrast, there remains no clear consensus on the management of asymptomatic meningiomas diagnosed during radiological examination for non-specific symptoms or other diseases, often referred to as "incidental meningiomas".[2, 3] The widespread availability of magnetic resonance imaging (MRI) and computed tomography (CT) has led to an increased reporting of incidental findings, and patients are becoming the so-called Victims Of Modern Imaging Technology (VOMIT).[4, 5] Incidental findings cause significant patient anxiety and distress which are compounded by the uncertainty faced by clinicians in their on-going management.[6]

The IMPACT (***I***ncidental ***M***eningioma: ***P***rognostic ***A***nalysis Using Patient ***C***omorbidity and MRI ***T***ests) study is a longitudinal analysis of clinical and radiological outcomes in a retrospective cohort of patients with incidental intracranial meningioma.[7] Here we report the surgery and radiotherapy outcomes of patients included in the IMPACT study who underwent treatment at initial diagnosis or after a period of active monitoring. We examine post-intervention morbidity, mortality and histopathological diagnosis and investigate the clinical and radiological variables associated with outcomes.

Material and Methods

The Institutional Review Boards at the authors' institutions approved this study, which was conducted and reported based on recommendations of the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.[8]

Study design and baseline characteristics

The IMPACT cohort comprised of adults (age ≥16 y) with a newly identified incidental asymptomatic meningioma between January 2007 and December 2015, with follow-up through to March 2018. Patients with radiation-induced and neurofibromatosis type 2–associated meningiomas were excluded. Specific criteria for inclusion in this study were: patients who (i) had undergone surgery or radiotherapy during the study period, (ii) had adequate documentation in the medical records of tumor pathology, admission, operative and discharge details, and (iii) had pre- and postoperative imaging available. The study setting

was the Walton Centre NHS Foundation Trust, the only specialist stand-alone neuroscience hospital in the UK. It serves a catchment area of 3.5 million people and has service partnerships with 18 other hospitals.

Baseline variables of interest and data sources

Clinical variables included patient age at intervention, sex, the World Health Organization (WHO) performance status (PS) and the age-adjusted Charlson comorbidity index (ACCI),[9, 10] collected retrospectively from electronic and paper medical records.

Imaging factors included (i) calcification on non-contrast CT (diffuse/partial/absent), (ii) tumor signal intensity compared with the contralateral gray matter on T2-weighted or fluid attenuated inversion recovery (FLAIR) MRI (hypo/iso/hyper), (iii) peritumoral signal intensity in relation to tumor volume using the signal change present on T2/FLAIR MRI (0–5%/6–33%/34–66%/67–100%), (iv) meningioma volume using the ABC/2 formula on contrast-enhanced T1-weighted MRI/CT: (A) maximum meningioma diameter on axial plane, (B) diameter perpendicular to (A), and (C) maximum height on coronal/sagittal plane, (v) meningioma location, classed into non–skull base and skull base and further subcategorized according to the International Consortium on Meningioma (ICOM) classification system and (vi) proximity to major dural venous sinuses (separate [≤10 mm]/in direct contact with sinus wall/invading). All factors were recorded using last available pre-intervention radiology apart from calcification status and tumor signal intensity which were noted using initial diagnostic scans.

Intervention details and outcomes

Treatment details included indication for intervention (radiological progression/new symptom development/patient preference) and time to intervention. For patients who underwent surgery, the following was noted: (i) Simpson grade (as recorded by the surgeon in the operative notes), (ii) tumor grade (reclassified according to the WHO 2016 criteria[11]) and histological subtype, (iii) postoperative medical and surgical complications (Landriel-Ibañez Classification[12]), (iv) WHO PS postoperatively and (v) tumor recurrence on MRI. Simpson grades I–III denoted gross total resection (GTR), whilst subtotal resection (STR) was defined as grades IV–V. For patients who underwent stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (*f*SRT), the following was recorded: (i) mode of treatment (primary/adjuvant/salvage), (ii) total dose (Gray [Gy]), (iii) early and late (≥3 months) toxicity (assessed by Common Terminology Criteria for Adverse Events v5.0), (iv) WHO PS

post-intervention and (v) radiological tumor response during follow-up (progression/regression/stable disease). For *f*SRT, number of fractions and fractionated dose were noted.

Statistical analysis

Baseline patient demographics were expressed using descriptive statistics; normally distributed variables as mean (standard deviation [SD]) and skewed variables as median (interquartile range [IQR]). Statistical differences among outcome groups for categorical variables were examined using Chi-squared test, or Fisher's exact test if group sizes were less than five. Normally distributed data were examined using the Student's t-test. Skewed continuous data were assessed using the Mann-Whitney U test. Differences were considered statistically significant at $P<0.05$. The five and 10-year cumulative incidence rates of primary outcome measures (intervention and recurrence) were estimated using life-table statistics. Data were analysed using R v3.5.0.

Neuro-oncology service and incidental meningioma practice

The neuro-oncology service at our center serves a catchment population of 3.5 million peoples and treats over 500 brain tumor patients annually. There are seven subspecialized neuro-oncology surgeons and five radiation neuro-oncologists. Management decisions for meningioma are made by consensus within the neuro-oncology tumor board. Patients are considered for treatment if they become symptomatic, or if they are asymptomatic but showing evidence of meningioma growth on surveillance MRI. Age, performance status and comorbidities are also considered. Patients are informed of the board's recommendation and counselled about each management option (surgery/radiotherapy/active monitoring) before making a shared care decision. Patients with asymptomatic meningioma may express a preference to have the meningioma treated. Surgical removal of meningioma is carried out as an elective procedure by a neuro-oncology surgeon. Post-operative CT is carried out on day 1 to assess the level of cerebral edema and to note the presence of hemorrhage. A baseline MRI is carried out at 3 months post-surgery. Following discharge from hospital, patients are followed-up clinically and radiologically in a specialized neuro-oncology clinic at appropriate intervals based on meningioma grade, extent of resection and clinical status. Radiotherapy parameters are determined by the radiation neuro-oncologists and is delivered using modern Novalis TX® LINAC SRS techniques.

Results

Study population

Figure 1 details the study population selection process. During an overall median follow-up duration of 55.0 months (IQR 37.0-80.0), 10.0% (n=44) underwent an intervention; six at initial presentation (due to patient preference) and 38 after a median active monitoring period of 24.0 months (IQR 11.8-42.0). The five- and 10-year intervention-free survival rates were 90.0 and 87.0% respectively. Patient demographics and clinical characteristics are summarized in Table 1.

Surgical outcomes

Extent of resection, histopathology and recurrence

Gross total resection was achieved in 92.5% (37/40) of patients. The three STRs (Simpson IV) (7.50%) were for superior sagittal sinus invading meningiomas, with two residuals (WHO grade I) treated with adjuvant radiotherapy (Table 4). For 36 (90.0%) patients, surgery revealed WHO grade I meningiomas of the following histological subtypes: meningothelial (n=11), psammomatous (n=8), fibrous (n=8), transitional (n=6), angiomatous (n=1), microcystic (n=1) and lymphoplasmacyte-rich (n=1). The remaining four (10.0%) were WHO grade II atypical meningioma with increased mitotic activity in three cases and microscopic brain invasion in one case. The five-year recurrence free survival rate was 97.0% (median follow-up 35.5 months [IQR 23.0-44.8]). An atypical meningioma had early recurrence five months following GTR (Simpson III), which was treated with fractionated radiotherapy (54 Gy/30 fractions). The patient was followed-up for 37 months following radiation with no evidence of further recurrence before dying from a hospital-acquired pneumonia that was unrelated to their meningioma.

Postoperative morbidity and performance status

Neurosurgical complications requiring treatment (grades Ib-IIIb) occurred in 15.0% (6/40) of patients within 30 days of treatment (Table 2). Two patients had permanent neurological complications – both had meningioma invading the superior sagittal sinus. Five (12.5%) patients experienced grade Ia complications, which did not necessitate further medical or surgical intervention. Surgical complications occurred in six of 10 (60.6%) patients with peritumoral signal change compared to five out of 30 (16.7%) with no signal change (P=0.014). Nine (22.5%) patients experienced postoperative medical complications (grades

Ia-Ib), four of which required medical treatment (grade Ib). The two outcome groups (complications vs. no complications) did not statistically differ in baseline clinical characteristics (Table 3).

Postoperatively 37 patients were PS 0-1. Three patients (7.5%) had deterioration in performance status after treatment: two patients underwent GTR of parasagittal meningiomas (PS 3 & 4) and one patient (PS 2) underwent GTR of a posterior fossa meningioma in contact with the transverse sinus.

Radiation treatment outcomes

Radiotherapy treatment details and outcomes are summarized in Table 4. Four patients received *f*SRT and three had SRS. Radiation treatment was administered after a period of active monitoring (n=4), following subtotal surgical resection of grade I meningioma (n=2) and at early recurrence of a grade II meningioma within 5 months of surgery (n=1). All seven patients exhibited regression or stable disease during a median follow-up period of 31.0 months (IQR 12.0-37.0). Maximum early toxicities were grade II in two (28.6%) patients. Two late grade II toxicities were also observed. Performance status post-intervention was 0-1 for all patients.

Case vignettes

Case 1

A 62-year old female patient (ACCI 3 and PS 0) was diagnosed with an asymptomatic left posterior parasagittal meningioma during MRI investigation of migraines. Patient was offered treatment (surgery/radiotherapy) or active monitoring and opted for the latter. Meningioma volume increased from 2.47 cm^3 to 5.39 cm^3 over the course of 4 years (Fig. 2). Considering the slow radiological progression and the persistence of headaches, the patient requested surgery. Day one postoperatively, the patient developed right-sided hemiparesis and focal seizures. CT demonstrated a large cerebral hematoma with surrounding oedema causing effacement of the pre- and post-central gyri (Fig. 2C). Pathology revealed a WHO grade I meningothelial meningioma. At the last follow-up appointment 32 months following surgery, there was no evidence of recurrence, and the performance status (PS=3) and hemiparesis were unchanged. Patient continues to be under the care of a neurologist for uncontrolled migraines.

Case 2

A 58-year old female (ACCI 2 and PS 0) was found to have an asymptomatic left posterior fossa meningioma during MRI investigation of vertigo. Volume at initial diagnosis was 3.7 cm^3 and after 12 months of follow-up, volume increased to 6.9 cm^3 with peritumoral edema and left-sided motor symptoms (Fig. 3). A shared decision to operate was made. Pathology revealed a WHO grade I fibrous meningioma. Day 1 post surgery, the patient became drowsy (↓ GCS). A CT revealed a hematoma causing mass effect (Fig. 3D), which required evacuation. At the last follow-up appointment 30 months postoperatively, patient was PS 0 with no evidence of recurrence.

Discussion

Modern radiotherapy techniques and microsurgical resection are treatment options recommended by several authors as first-line for the management of incidentally-discovered intracranial meningiomas.[13-16] In this study, the rate and nature of morbidities using both treatment modalities and the histopathological parameters of these tumors are strong arguments against treatment at initial diagnosis or subsequent 'soft' indicators for treatment such as asymptomatic slow radiological progression.

Post-intervention morbidity

Previous reports have shown old age and co-morbidity to correlate with post-intervention morbidity and worse long-term neurological function.[17, 18] Our cohort of incidental meningioma patients was on average younger and with a low burden of comorbidities, however, the risk of complications observed was higher than expected. Description of outcomes following surgery and radiotherapy for incidental intracranial meningioma is sparse and the limited number of reports on this topic lack systematic classification and reporting of morbidity.[19, 20] The risk of complications in our study requiring treatment was 25%, similar to the risk following treatment of symptomatic meningioma.[21] Therefore, the concept of prophylactic surgery or radiotherapy to avoid future clinical and radiological progression of all patients with incidental meningiomas is a somewhat flawed argument, particularly as only 10-25% of patients will have growth necessitating intervention.[7, 22] A recent study of the English National Cancer Registry also demonstrated that approximately a fifth of patients with 'benign' WHO grade I meningiomas were deceased after 10-years of surgery; over what one would expect without the disease.[23] Moreover, surgical resection of a meningioma may

contribute to a reduced health related quality of life and lead to clinically meaningful impairment in several cognitive domains for up to 10 years following surgery.[24]

Patient selection for treatment based on imaging parameters

In keeping with the 'meningiomics' approach to personalised management,[25] selection of appropriate patients for early intervention can be better delineated using existing prognostic models.[7, 26] Almost half of meningiomas in this treated cohort demonstrated hyperintensity on MRI and some were associated with peritumoral signal change indicative of vasogenic oedema. Whilst these meningiomas are predisposed to radiological growth and clinical progression,[27, 28] and underwent intervention in our study for such indications, the increased risk of treatment-related morbidity seen in both our series and other studies,[29, 30] would justify continuing active monitoring until definitive progression (i.e. symptoms of severity that need treatment e.g. seizures or focal motor deficit) occurs. Larger meningiomas at presentation are correlated with progression during follow-up and increased operative morbidity risk[26, 31]; however, meningioma volume in our study did not have an impact on morbidity and only a few operated meningiomas (n=9, 21%) were >10 cm^3. This reflects the fact that incidental meningiomas are typically smaller than symptomatic meningiomas and remain so throughout follow-up. Similarly, meningioma location and proximity to critical neuro-vascular structures ought to be considered and this has been incorporated into recent prognostic models of incidental meningioma growth.[7] The treated incidental meningioma in this study were mainly non-skull base (n=30, 68%) and surgical adverse events occurred in 9 cases (30%) compared to only 14% (2/14) in skull bases meningioma. Whilst this initially seems counter-intuitive since skull base meningiomas are more closely approximated to critical neuro-vascular structures, it serves to highlight the challenges associated with apparently straightforward convexity and parasagittal meningiomas. These meningiomas often overlie motor, sensory or language cortex, have intimate relationships to cortical draining veins and the sagittal sinus, and can be prone to idiosyncratic post-operative cerebral edema. A more conservative approach to these meningiomas is advised, and a cost-effectiveness study of early *versus* delayed (on evidence of progression) intervention and the impact on patient outcome and healthcare resources would help aid decision making for this group of patients.

Choice of treatment intervention

Most patients in our study who progressed underwent surgical resection whilst a minority were treated with radiotherapy. The majority of incidental meningiomas have a tumor volume less than 10 cm^3 such that surgery and radiosurgery are both reasonable options to deliver

good control rates [32]. Ultimately, the decision will be based on availability of treatment facilities, physician experience, meningioma location and importantly patient preference. Following SRS, up to 14% of patients experience adverse events including epilepsy and cognitive deficits.[16] These are closely related to the development of post-SRS peritumoral edema, which may be associated with parasagittal and parafalcine location.[33, 34] This is postulated to be due to the breakdown of the tumor-brain interface complicated by venous compression and subsequent congestion.[35, 36] These observations in addition to the surgical morbidity associated with meningioma invading the sinus underlines the importance of including venous sinus invasion as a radiological criterion of disease progression in prognostic studies.[37, 38]

Histopathology and behaviour following treatment

Operated incidental meningiomas in our series were primarily WHO grade I with few tumors fulfilling WHO grade II criteria. There were no misdiagnosed metastatic tumors. Previous studies of incidental meningioma have shown that the vast majority (~94%) are WHO grade I and therefore active monitoring is entirely justified as the first line management.[22] A DNA-methylome based classification of meningioma has recently been developed to stratify symptomatic tumors into six distinct prognostic groups.[39] Although we do not have methylation data for our cases, we postulate that most would fall into the benign methylation classes (e.g. MC ben-1), however, those that grew are more likely to be in the intermediate methylation class.

Study strengths and limitations

This is a single-center retrospective study of treated incidental intracranial meningiomas, which adds to the literature available on post-intervention morbidity and histopathological parameters enabling better decision making. Quality of life assessment could not be performed based on clinical notes available though it should be noted that most patients remained under follow-up with the majority reporting no change in clinical symptoms; this comes in support of the notion that most patients with an incidental meningioma lead normal lives – a supposition supported by the limited quality of life studies [40, 41]. Although we did not investigate patient anxiety it is nevertheless an important factor that merits consideration in agreeing a management and follow up plan with patients. With regards to generalizability, the study cohort having been derived from a tertiary institution, which solely serve a large population of 3.5 million, and the agreement with prior studies on variables associated with postoperative outcomes, adds to the strengths of this study. However, the external validity of

our analysis is limited by its meningioma population with case complexity which may not extrapolate to other centers and clinician and patients bias with determination of treatment options.

Conclusions

Incidental intracranial meningiomas are increasingly common and form a not insubstantial workload for neurosurgeons and neuro-oncologists. Considering the histopathological findings of operated meningiomas and the morbidity associated with surgery and radiation, prolonged active monitoring with MRI surveillance is the recommended management strategy. This is supported by the decrease in need of treatment intervention despite the rise in prevalence of new meningioma diagnoses.[42] Details surrounding duration of observation and interval in-between scans/appointment can be better delineated using prognostic models.

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Figure legends

Fig. 1. Study population and indications for brain CT/MRI

Fig. 2. (A) Coronal FLAIR MRI demonstrating a hyperintense left posterior parasagittal meningioma with a volume of 2.5 cm^3 (blue arrow). (B) Over the course of 4 years of follow-up, volume increased to 5.4 cm^3. (C) Coronal non-contrast CT showing a left cerebral haematoma 1-day postoperatively causing effacement of the surrounding gyri (red arrow). (D) Coronal non-contrast CT 1-week following surgery demonstrating maturation of haemorrhage and surrounding oedema (3 red arrows).

Fig. 3. (A) Axial T1+contrast MRI demonstrating a left squamous occipital meningioma with a volume of 3.7 cm^3 (blue arrow). (B) Over the course of 12 months of follow-up, volume increased to 6.9 cm^3. (C) axial CT showing a left hematoma (red arrow) with significant mass-effect on the left cerebellar hemisphere, fourth ventricle and brainstem. (D) Axial T1+contrast MRI 30 months with no evidence of recurrent or residual meningioma.

Tables

Table 1. Baseline clinical and imaging variables for the IMPACT cohort and patients who received intervention				
			IMPACT cohort (N=441)	Intervention cohort (N=44)
Age	Median (IQR)		64.0 (55.0-72.5)	56.1 (49.6-66.5)
Sex, N (%)	Female		348 (78.9)	35 (79.5)
	Male		93 (21.1)	9 (20.5)
ACCI	Median (IQR)		4 (3-6)	2 (1-4)
	0-2		103 (23.4)	23 (52.3)
	3-5		212 (48.1)	18 (40.9)
	≥6		126 (28.6)	3 (6.80)
PS	Median (IQR)		0 (0-1)	0 (0-0)
	0-1		387 (87.8)	44 (100)
	2-4		54 (12.2)	0 (0)
Indication for treatment, N (%)	Radiological progression		26 (5.9)	26 (59.1)
	New symptom development		6 (1.4)	6 (13.6)
	Patient preference		12 (2.7)	12 (27.3)
Meningioma count, N (%)				
Single			426 (96.6)	44 (100)
Multiple	2		13 (2.9)	0 (0)
	3		1 (0.2)	0 (0)
	4		1 (0.2)	0 (0)
Volume*	Median (IQR)		1.6 (0.6-4.0)	4.55 (1.9-8.6)
	≤10 cm^3		420 (91.5)	35 (79.5)
	>10 cm^3		39 (8.5)	9 (20.5)
Location, N (%)*	Non-skull base	Convexity	183 (39.9)	21 (47.7)
		Parasagittal	77 (16.8)	5 (11.4)
		Parafalcine	36 (8.2)	2 (4.50)
		Tentorial	21 (4.6)	2 (4.50)
		Intraventricular	5 (1.1)	0 (0)
	Skull base	Sphenoid wing	45 (9.8)	6 (13.6)
		Posterior fossa – lateral & posterior	42 (9.2)	4 (9.1)
		Anterior Midline	34 (7.4)	3 (6.8)
		Posterior fossa – midline	16 (3.5)	1 (2.3)
Calcification, N (%)*	Diffuse		81 (17.6)	1 (2.3)
	Partial		74 (16.1)	5 (11.4)
	Absent		109 (23.7)	13 (29.5)
	NA		195 (42.5)	25 (56.8)
Tumor signal intensity, N (%)*	Hypo		75 (16.3)	3 (6.80)
	Iso		210 (45.8)	18 (40.9)
	Hyper		119 (25.9)	23 (52.3)
	NA		55 (12.0)	0 (0)

Peritumoral signal intensity, N (%)*	0-5%		373 (81.3)	34 (77.3)
	6-33%		16 (3.5)	2 (4.50)
	34-66%		13 (2.8)	5 (11.4)
	67-100%		2 (0.4)	3 (6.80)
	NA		55 (12.0)	0 (0)
Venous sinus involvement, N (%)*	No		291 (63.6)	20 (45.5)
	Yes	Separate	49 (10.5)	4 (9.10)
		In direct contact	98 (21.4)	12 (27.3)
		Invaded	21 (4.6)	8 (18.2)
Venous sinuses involved, N (%)†	SSS		95 (56.5)	14 (58.3)
	CS		35 (20.8)	4 (16.7)
	SS		21 (12.5)	3 (12.5)
	TS		15 (8.9)	3 (12.5)
	Torcula		2 (1.2)	0 (0)

Abbreviations: NA=not available; CS=cavernous sinus; SSS=superior sagittal sinus; SS=sigmoid sinus; TS=transverse sinus
Imaging parameters for the IMPACT cohort are at presentation, however they were recorded using last available pre-intervention radiology (apart from calcification status and tumor signal intensity) for the intervention cohort
*The IMPACT cohort imaging parameters are for 459 meningiomas in 441 patients
†For meningiomas in proximity of venous sinuses

Table 2. Details of postoperative surgical complications

Patient number	ICOM category	Sub-category	Extent of resection-Simpson grade	WHO grade	Postoperative radiology	Clinical manifestation (yes/no)	If yes, manifestation	Persisted beyond 30 days of treatment? (yes/no)	Landriel-Ibañez Classification
1	Parasagittal	Anterior	GTR-II	I	Haemorrhage	Yes	Motor deficit, dysphasia	Yes	IIIb-P
2	Convexity	Anterior	GTR-II	I	Subdural empyema	Yes	Seizure	No	IIIa-T
3	Posterior fossa – lateral & posterior	Squamous occipital	GTR-III	I	Haemorrhage	Yes	Decreased level of consciousness (↓Glasgow Coma Scale)	No	IIIa-T
4	Parasagittal	Posterior	STR-IV	I	Haemorrhage	Yes	Motor deficit, seizure	Yes	IIa-P
5	Sphenoid wing	Lateral	GTR-II	I	-	Yes	Seizure	No	Ib-T
6	Convexity	Posterior	GTR-II	I	Cerebral abscess	Yes	Motor deficit	No	Ib-T
7	Convexity	Posterior	GTR-II	I	-	Yes	Visual deficit	Yes	Ia-P
8	Parasagittal	Posterior	STR-IV	I	-	Yes	Motor deficit	Yes	Ia-P
9	Convexity	Anterior	GTR-I	I	CSF accumulation	No	NA	No	Ia-T
10	Convexity	Anterior	GTR-III	II	Haemorrhage	No	NA	No	Ia-T
11	Parafalcine	Posterior	STR-IV	I	Haemorrhage	No	NA	No	Ia-T

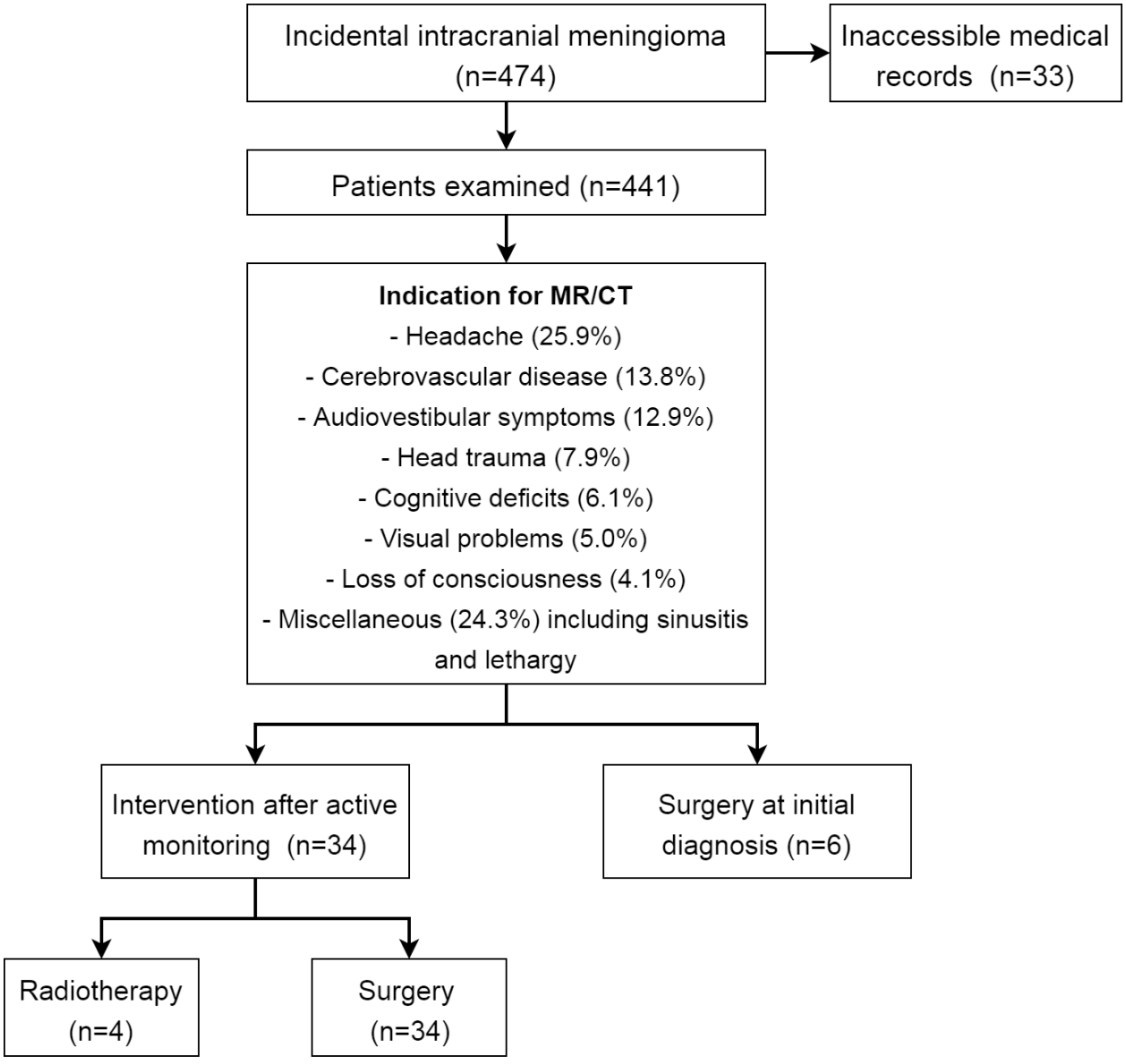
Abbreviations: P=permanent; T=transient; NA=not applicable

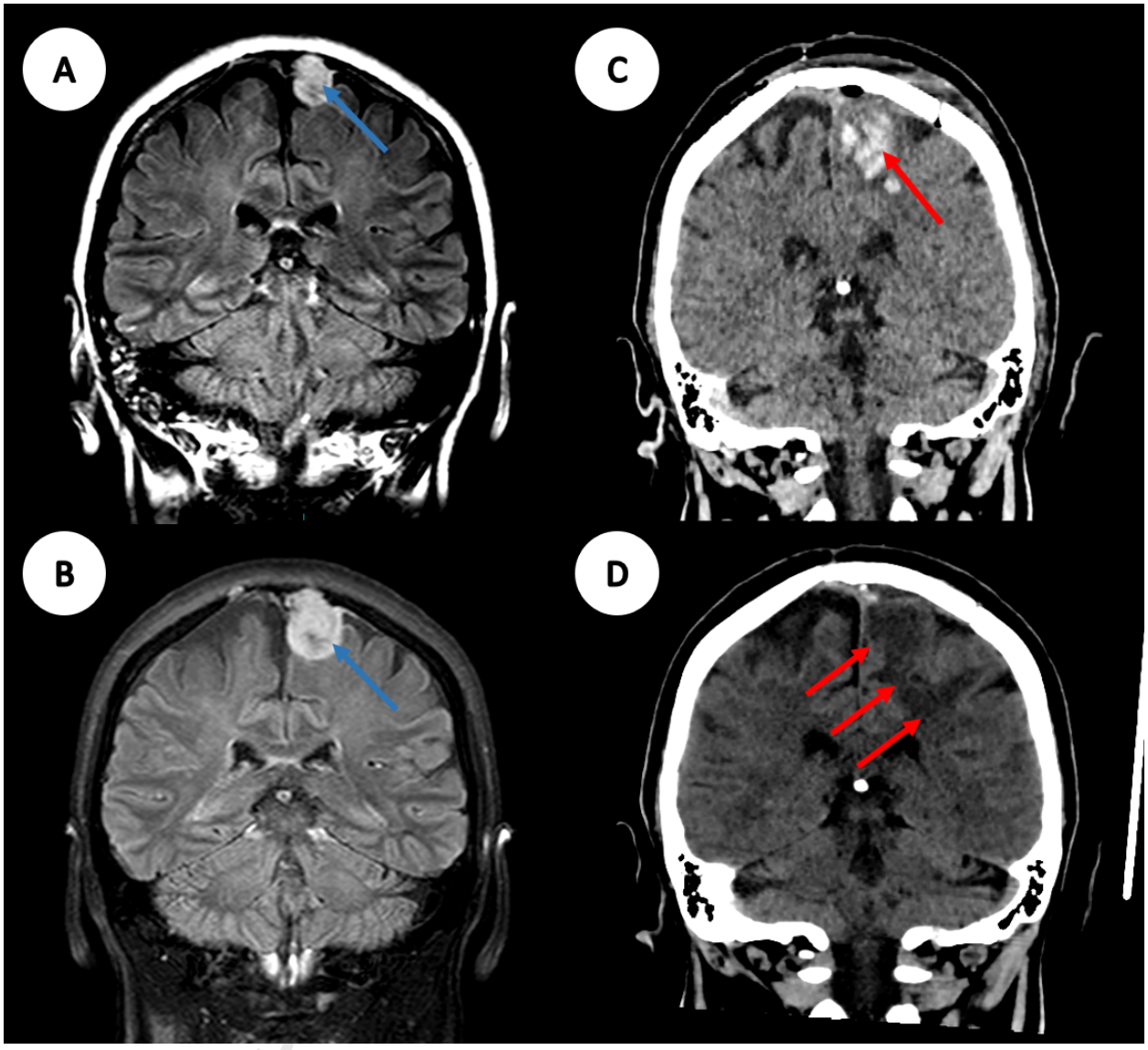
Table 3. Difference in clinical and radiological characteristics among the postoperative complication groups				
		Overall postoperative complications		**P**
		Yes (N=15)	No (N=25)	
Age	Median (IQR)	59.0 (49.5-66.8)	53.5 (49.0-64.8)	0.670
Sex, N (%)	Female	12 (36.4)	21 (63.6)	0.769
	Male	3 (42.9)	4 (57.1)	
ACCI	Median (IQR)	2 (1-3)	2 (2-4)	0.431
		Postoperative surgical complications		
		Yes (N=11)	No (N=29)	
Meningioma volume	Median (IQR)	7.84 (5.33-21.6)	3.68 (1.92-7.33)	0.077
Meningioma location, N (%)	Non-skull base	9 (31.0)	20 (69.0)	0.694
	Skull base	2 (18.2)	9 (81.8)	
Peritumoral signal intensity, N (%)	0-5%	5 (16.7)	25 (83.3)	0.014
	6-100%	6 (60.0)	4 (40.0)	
Venous sinus involvement, N (%)	No	3 (15.8)	16 (84.2)	0.163
	Yes	8 (38.1)	13 (61.9)	

Table 4. Radiation treatment details and outcomes

Patient number	Age at treatment, sex	ICOM category	Sub-category	Meningioma volume (cm^3)	Mode	Modality	Duration of treatment (days)	Dose/fraction (Gy)	Follow-up (months)	Treatment Response	Early CTCAE toxicity-(0-4)	Late CTCAE toxicity-(0-4)
1	56, F	Convexity	Anterior	0.50	Primary	SRS	1	12.5	70	Regression	Fatigue-1 Headache-1	Neuralgia-1
2	49, M	Posterior fossa - midline	Petro-clival	0.26	Primary	SRS	1	12.5	12	Stable	Vomiting-1	Paresthesia-1
3	45, M	Anterior midline	Tuberculum sellae	3.20	Primary	*f*SRT	42	54/30	33	Stable	Nausea-1	Headache-2
4	67, F	Sphenoid wing	Medial	0.56	Primary	*f*SRT	42	54/30	8	Regression	Nausea-1 Fatigue-2	TN disorder-2
5	56, F	Parasagittal	Posterior	NM	Adjuvant	SRS	1	12.5	31	Stable	Fatigue-1 Paresthesia-1	NR
6	52, F	Parafalcine	Posterior	NM	Adjuvant	*f*SRT	42	54/30	24	Stable	Nausea-1 Fatigue-1 Alopecia-2	NR
7	68, M	Convexity	Anterior	NM	Salvage	*f*SRT	42	54/30	37	Stable	Fatigue-1	Phantom pain-1

Abbreviations: NM=not measured; NR=none reported


Incidental intracranial meningioma (n=474)
Inaccessible medical records (n=33)
Patients examined (n=441)
Indication for MR/CT
- Headache (25.9%)
- Cerebrovascular disease (13.8%)
- Audiovestibular symptoms (12.9%)
- Head trauma (7.9%)
- Cognitive deficits (6.1%)
- Visual problems (5.0%)
- Loss of consciousness (4.1%)
- Miscellaneous (24.3%) including sinusitis and lethargy
Intervention after active monitoring (n=34)
Surgery at initial diagnosis (n=6)
Radiotherapy (n=4)
Surgery (n=34)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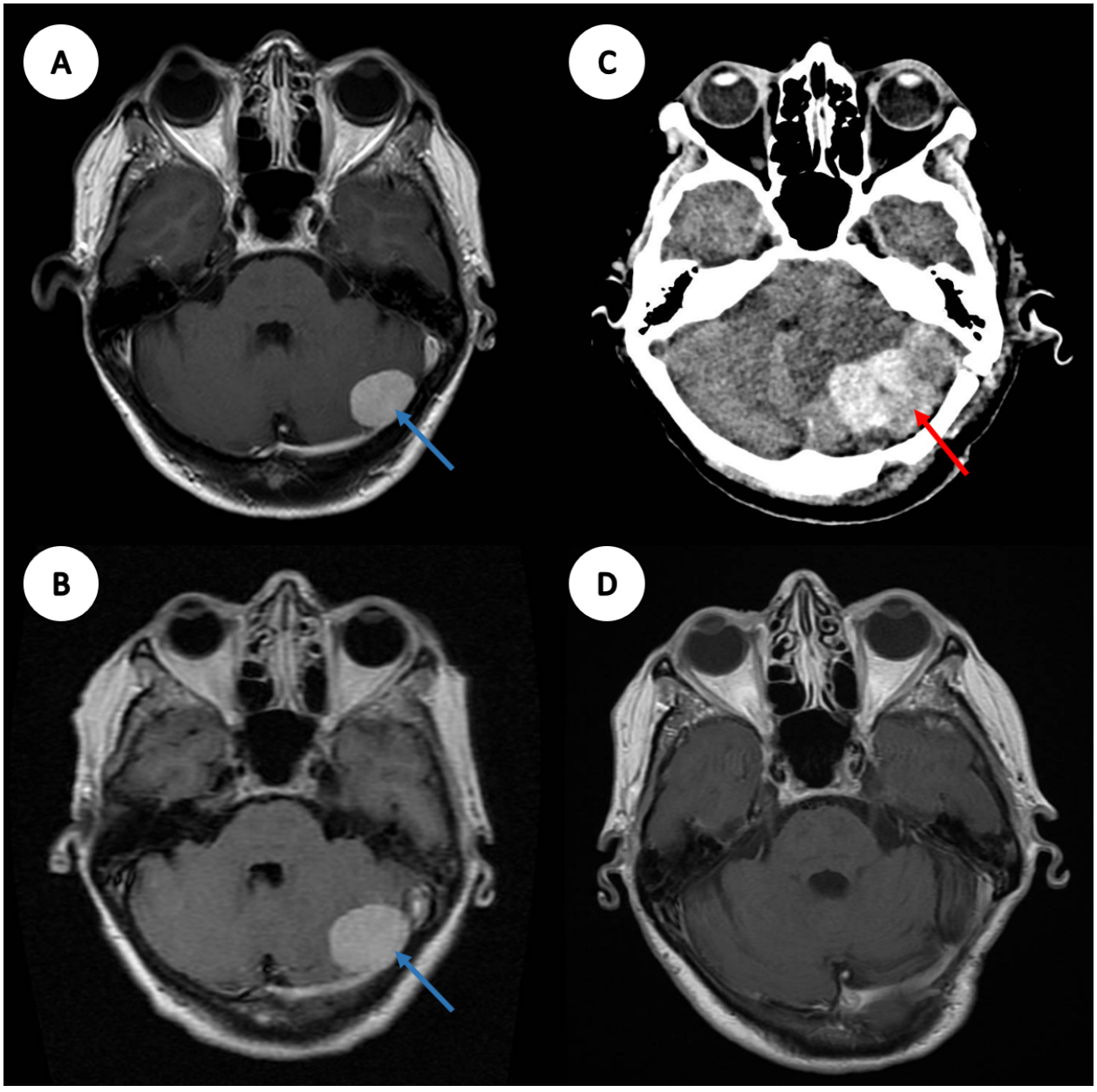
A
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Abbreviations

ACCI, Age adjust Charlson comorbidity index

CT, Computed tomography

fSRT, Fractionated stereotactic radiotherapy

GTR, Gross total resection

Gy, Gray

IMPACT, Incidental meningioma: prognostic analysis using patient comorbidity and MRI tests

IQR, Interquartile range

MRI, Magnetic resonance imaging

PS, Performance status

SD, Standard deviation

SRS, Stereotactic radiosurgery

STR, subtotal resection

STROBE, Strengthening the reporting of observational studies in epidemiology

VOMIT, Victims of modern imaging technology

WHO, World Health Organization

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