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Quality indicators and early adverse in surgery for atypical meningiomas: A 16-year single centre study and systematic review of the literature



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ABSTRACT

Introduction: Atypical meningiomas represent approximately 20% of all intracranial meningiomas and are characterized by distinct histopathological criteria and an increased risk of postoperative recurrence. Recently, quality indicators have been introduced to monitor quality of the delivered care.

Research question: Which quality indicators/outcome measures are being applied in patients being operated for atypical meningiomas? What are risk factors associated with poor outcome? How is the surgical outcome and which quality indicators are reported in the literature?

Material and methods: The primary outcomes of interest were 30-days readmission-, 30-day reoperation-, 30-day mortality-, 30-day nosocomial infection- and the 30-day surgical site infection (SSI) rate, CSF-leakage, new neurological deficit, medical complications, and lengths of stay. The secondary aim was the identification of prognostic factors for the mentioned primary outcomes. A systematic review of the literature was performed screening studies for the mentioned outcomes.

Results: We included 52 patients. 30-days outcomes in terms of unplanned reoperation were 0%, unplanned readmission 7.7%, mortality 0%, nosocomial infection 17.3%, and SSI 0%. Any adverse event occurred in 30.8%. Preoperative C-reactive protein over 5 mg/l was independent factor for the occurrence of any postoperative adverse event (OR: 17.2, p = 0.003). A total of 22 studies were included into the review.

Discussion and conclusion: The 30-days outcomes at our department were comparable with reported outcomes in the literature. Currently applied quality indicators are helpful in determining the postoperative outcome but mainly report the indirect outcome after surgery and are influenced of patient, tumor and treatment related factors. Risk adjustment is vital.

1. Introduction

Meningiomas are the most common primary brain tumors and account for one third of all primary brain tumors (Ostrom et al., 2019). Today, approximately 20% of all intracranial meningiomas represent atypical meningiomas (WHO grade 2) and are characterized by distinct histopathological criteria and an increased risk of postoperative recurrence after primary treatment (Louis et al., 2016; DiMeco et al., 2004). The overall incidence of atypical meningiomas was of 0.268 (95%CI, 0.260–0.276) per 100,000 person-years with an annual percent change increase of 5.6% (Recker et al., 2022). First-line treatment is maximum safe resection, followed by adjuvant radiotherapy in case of subtotal resection (Streckert et al., 2019). However, surgery for atypical meningiomas may be challenging as they show more invasiveness into normal brain than grade 1 meningiomas. During the recent decades, surgical management has evolved towards reduction of perioperative mortality and neurologic impairment after surgery (Meling et al., 2019). None-theless, surgery is still associated with complications.

Steady raising costs in health care have shifted the focus towards

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Abbrevi	iations
ACCI	Age-adjusted Charlson-Comorbidity Index
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CCI	Charlson-Comorbidity Index
CI	confidence interval
CRP	C-reactive protein
CSF	cerebrovascular fluid
GTR	gross total resection
ECOG	Eastern Cooperative Oncology Group
EOR	extent of resection
FLAIR	Fluid attenuated inversion recovery
GTR	gross total resection
LOS	Length of stay
MRI	magnetic resonance imaging
OR	Odds ratio
RT	radiotherapy
SRS	Stereotactic radiosurgery
SSI	surgical site infection
STR	subtotal resection
WHO	world health organization

reimbursement concepts that depend on measuring the quality of the delivered care. For that purpose, the implementation of standardized quality indicators has become a central issue in many medical fields, including neurosurgery. Currently suggested quality indicators are 30-day readmission, reoperation and mortality rates, length of stay (LOS), rates of nosocomial infections and surgical site infection (SSI) (Spille et al., 2022; Schipmann et al., 2017, 2019a, 2019b, 2020, 2022; Dasenbrock et al., 2018). Postoperative complications after cranial neurosurgery are closely connected to the mentioned quality indicators (Schipmann et al., 2019a).

So far, data on quality indicators for the subgroup of atypical meningiomas, that have a course that is clearly distinct from that of benign meningiomas, are scarcely available (DiMeco et al., 2004). The objective of this study is the analysis of these currently applied quality indicators and identification of potential other relevant outcome measures in atypical meningioma tumor surgery and identification of factors associated with poor surgical outcome. Our data are complimented by a systematic review of the literature to identify surgical outcome and applied quality indicators used for atypical meningiomas.

2. Methods

2.1. Patient population and data collection

All patients that have been operated between 2004 and 2021 at the Department of Neurosurgery, Haukeland University Hospital Bergen, Norway, and diagnosed with an atypical meningioma WHO grade 2 were retrospectively assessed for this study. Patients with primary and secondary atypical meningioma according to the WHO classification at the time of diagnoses were included.

For patients who had multiple operations for their meningioma only the first operation was subject to analysis.

Tumor resection was indicated for any-space occupying or progressive/symptomatic meningioma in the absence of contraindications against anesthesia or surgery. Maximum safely achievable tumor resection was performed in all cases. Adjuvant radiotherapy was recommended for patients with subtotal resection. According to our local standards, routine postoperative care included clinical and radiological (MRI) follow-up 3 months after surgery and then repeated semiannually.

Patient data were extracted from the digital medical records. Data

included patient's age, sex, BMI, ECOG, ASA score, data on admission, urgency of surgery, laboratory results on admission, further stratified into clinically relevant stages: leukocytosis (>9800 leukocytes/ μ l), and CRP >5 mg/l. Tumor specific characteristics were collected and histopathological diagnoses were performed according to the 2000, 2007 and 2016 WHO criteria as appropriate (Louis et al., 2000, 2007, 2016).

MR images were reviewed and used for volumetric analysis of contrast enhancement (T1-weighted contrast) and edema (FLAIR) using an established semiautomatic technique (Brainlab Elements, Brainlab AG, Munich, Germany).

Secondary diagnoses that were present on admission, were classified according to the 19 items of the Charlson Comorbidity Index (CCI) (Hoefnagel et al., 2014) and supplemented by other relevant diagnoses with possible impact on surgical outcome, such as nicotine, drug and alcohol abuse, use of oral anticoagulation, platelet inhibitors and epilepsy. The age-adjusted CCI (ACCI) was calculated as described before (Horowitz et al., 2011).

In addition, details on surgery were extracted, including extent of resection (EOR) using the Simpson classification (Simpson, 1957) as determined by the surgeon, duration of surgery and presence of brain infiltration. Tumor location was classified into convexity, falx cerebri/parasagittal, skull base and posterior fossa.

The primary outcomes of interest were classical quality indicators: 30-days readmission-, 30-day reoperation-, 30-day mortality-, 30-day nosocomial infection- and the 30-day surgical site infection (SSI) rate. Other outcomes of interest were CSF-leakage, new neurological deficit, medical complications, including pulmonary embolism, and lengths of stay. In addition, the variable *any early adverse event* was defined, representing the occurrence of one of the following events: postoperative hemorrhage, CSF-leakage, infection, readmission, reoperation, mortality, and pulmonary embolism. The secondary aim was the identification of prognostic factors for the mentioned primary outcomes.

The study was approved by the local ethic committee (reference number: 513297).

2.2. Statistical analysis

IBM SPSS Statistics 26.0 software (IBM, Armonk, New York, USA) was used for statistical analysis. Data was described by standard statistics, using absolute and relative frequencies for categorical variables and median and mean, and interquartile range for continuous variables. Cases with missing information about one variable were only excluded from the corresponding statistical analyses but not from the entire study. According to the Simpson classification (Simpson, 1957), the EOR was dichotomized into gross total resection (GTR; Simpson grade I and II) and subtotal resection (STR; Simpson grade III and IV) in additional analyses. Univariate logistic regression modeling and chi-square test were used for continuous and categorial variables, respectively. All variables that were statistically significant in univariate analysis were entered into a multivariable logistic regression model. Odds ratios (OR) and the corresponding 95% confidence intervals (CIs) were obtained. A probability value less than 0.05 was considered statistically significant throughout the whole analyses. All reported p values are two-sided.

2.3. Systematic literature review

The systematic literature review followed the PRISMA guidelines (Moher et al., 2009). A computerized search using the Medline/PubMed database was performed to identify relevant articles on quality indicators and 30-day outcome after surgery for atypical meningioma. The search included only articles in English published until February 2022 with no lower date limit. The syntax used was as follows:

The search included one item referring to diagnosis (atypical meningioma, meningioma WHO grade 2) in combination with one referring to outcome (outcome, reoperation, nosocomial infection, surgical site infection, mortality, readmission, quality indicator, neurological deficit, neurological sequelae, adverse event). The search was performed for all possible combinations of search items, both for abstract and title. In addition, the following Mesh terms were used: Diagnosis: atypical meningioma AND outcome: outcome assessment, reoperation, nosocomial infection, mortality, readmission, quality, morbidity. The full syntax can be found in appendix A.

All articles were screened regarding their titles and abstracts independently by three authors (SS, YW and ICR) using EndNote X9 software (Clarivate Analytics, London, UK). We included only articles that presented results on postoperative complications, early surgical outcome and quality indicators. Articles published in other languages than English and without an abstract were excluded from the analysis. Studies that included both patients with WHO grade 1 and grade 2 meningioma were included, however only if more than 10% or more than n = 10 of the included patients were diagnosed with grade 2 meningioma. We aimed at analyzing only the relevant subgroup of patients with atypical meningioma if the data allowed that. If not, all meningioma patients from the study were included. Only studies with patients older than 16 years were included. Relevant articles were retrieved and evaluated independently by the three authors. To ensure that no relevant studies were missed, a cross-reference check of citations of each included relevant study was done. Issues of disagreement regarding inclusion of studies were resolved by discussion and consensus agreement. The following characteristics were extracted from the including studies: study design, setting, time period, number of included patients, number of included patients with atypical meningioma, age, sex, localization of tumor, primary or recurrent tumor, extent of resection according to Simpson grade (Simpson, 1957), length of stay (LOS), CSF-fistula rate, postoperative hematoma rate requiring reoperation, 30-day reoperation, readmission-, nosocomial infection-, surgical site infection (SSI), mortality rate, new neurological deficit, other complications and significant risk factors for outcomes in univariate and multivariate analysis/risk factors.

3. Results

3.1. Baseline characteristics

A total of 52 patients were included in the study, of whom 57.7% were female and 42.3% male. The median age at surgery was 56 years (range 28–83). The majority of patients were admitted in a good general condition as indicated by the ASA and ECOG scores. The median ACCI was 2, ranging from 0 to 9. Most patients were diagnosed primary with an atypical meningioma (n = 40, 85.1%). Less than one third (26.9%, n = 14) were operated for recurrent tumor. Half of all tumors were localized in the convexity, followed by falcine/parasagittal localization in 25%. A Simpson grade I or II resection was achieved in 65.4% (n = 34) of patients.

Baseline characteristics as well as imaging-, tumor- and surgeryspecific details of the analyzed patients are described in detail in Table 1.

3.2. Early adverse events and outcome variables

Outcome variables and quality indicators are summarized in Table 2. Any adverse event occurred in 30.8% of patients. No patient was reoperated within 30 days after index surgery. The 30-day readmission rate was 7.7%. The main reason for unplanned readmission was reduced general condition and was not directly related to surgery (5.8%, n = 3). No patient died in the 30- day postoperative period. The nosocomial infection rate was 17.3% and mainly related to urinary tract infections; no surgical site infections were observed. To patients (3.8%) developed a CSF leakage. A new neurological deficit was documented in 30.8% of patients.

3.3. Prognostic factors for outcome

The results from univariate analysis for risk factors associated with

Table 1

Patients baseline characteristics and information regarding tumor, imaging, and	
surgery.	

PATIENTS BASELINE CHARAC	CTERISTICS	n (%)
Age	mean, range	56.0 (28–83)
Sex	male	22 (42.3)
	female	30 (57.7)
BMI	mean, range	25.99
		(16.3–41.2)
Secondary diagnosis	alcohol abuse	2 (3.8)
	nicotine abuse	17 (32.7)
	Drug abuse	1 (1.9)
	Oral anticoagulation	3 (5.8)
	Platelet inhibitors	8 (15.4)
	Epilepsy	18 (34.6)
Secondary diagnoses	AIDS	0 (0)
according to CCI	Myocardial infarction	3 (5.8)
according to bot	Congestive heart failure	2 (3.8)
	Peripheral vascular disease	2 (3.8)
	CVA/TIA	1 (1.9)
	Dementia	0 (0)
	COPD	3 (5.8)
	Connective tissue disease	2 (3.8)
	Peptic ulcer disease	0 (0)
	Liver disease mild	0 (0)
	Liver disease moderate-severe	0 (0)
	Diabetes mellitus without	4 (7.7)
	complications	
	Diabetes mellitus with end-	1 (1.9)
	organ damage	
	Hemiplegia	0 (0)
	Moderate-severe kidney disease	1 (1.9)
	Solid tumor	7 (13.5)
	Metastatic tumor	2 (3.8)
	Leukemia	1 (1.9)
	Lymphoma	0 (0)
ACCI	Median (range)	2 (0–9)
	-	
Leukocytosis	yes	18 (35.3)
CRP	> 5 mg/l	9 (17.6)
ASA	1	5 (9.8)
	2	38 (74.5)
	3	8 (15.7)
	4	0 (0)
	5	0 (0)
ECOG	0	16 (30.8)
	1	22 (42.3)
	2	10 (19.2)
	3	4 (7.7)
	4	0 (0)
location of admission	home	41 (80.4)
	other hospital	7 (13.7)
	other department within	3 (5.9)
	hospital	5 (0.2)
Jrgency of admission	elective	41 (78.8)
reacted of adminission		41 (78.8) 11 (21.2)
ocation of discharge	emergency	
ocation of discharge	home	25 (48.1)
	other hospital	21 (40.4)
	other department within	3 (5.8)
	hospital	
	care institution	1 (1.9)
	rehabilitation	2 (3.8)
UMOR SPECIFIC CHARACTE	RISTICS	n (%)
rimary vs. recurrent tumor	primary	38 (73.1)
	recurrent	14 (26.9)
Neurosurgical diagnosis	Primary WHO grade 2	40 (85.1)
	Secondary WHO grade 2	7 (14.9)
Localization	Convexity	26 (50)
	Falcine/parasagittal	13 (25)
	Skull base	9 (17.3)
	Posterior fossa	4 (7.7)
Brain invasion pathologically	Yes	8 (15.4)
Classification reg. WHO	Yes	24 (46.2)
-	100	27 (70.2)
2016	Voc	10 (10 2)
Preoperative SRS	Yes	10 (19.2)
Preoperative RT	Yes	1 (1.9)

(continued on next page)

Table 1 (continued)

PATIENTS BASELINE CHARA	CTERISTICS	n (%)
PREOPERATIVE IMAGING CI	ARACTERISTICS	n (%)
Contrast enhancement	homogenous	38 (74.5)
	heterogenous	13 (25.5)
Arachnoidal layer	intact	40 (78.4)
	Not intact	11 (21.6)
Tumor shape	regular	42 (80.8)
	Irregular	10 (19.2)
Intratumoral calcifications	Yes	4 (7.7)
Number of lesions	One	46 (88.5)
	Two	2 (3.8)
	Multifocal (>2)	4 (7.7)
Tumor volume	Mean (range)	43.71
		(4.78–197.2)
Edema volume	Mean (range)	33.03 (0–116.7)
SURGERY CHARACTERISTIC	S	n (%)
Incision-closure time	Median (range)	165 (52–656)
	0–170min	29 (55.8)
	>170min	23 (44.2)
EOR Simpson	Simpson I	5 (9.6)
	Simpson II	29 (55.8)
	Simpson III	6 (11.5)
	Simpson III Simpson IV	6 (11.5) 9 (17.3)
	-	
EOR	Simpson IV	9 (17.3)
EOR	Simpson IV Simpson V	9 (17.3) 3 (5.8)
EOR Visible brain invasion	Simpson IV Simpson V GTR (Simpson I, II)	9 (17.3) 3 (5.8) 34 (65.4)
	Simpson IV Simpson V GTR (Simpson I, II) STR (Simpson > II)	9 (17.3) 3 (5.8) 34 (65.4) 18 (34.6)

BMI: Body Mass Index, CCI: Charlson-Comorbidity Index, ACCI: Age-adjusted Charlson-Comorbidity Index, CVA: cerebrovascular accident, COPD: Chronic obstructive pulmonary disease, TIA: transient ischemic attack, CRP: C-reactive protein, ASA: American Society of Anesthesiologists, ECOG: Eastern Cooperative Oncology Group, SRS: Stereotactic radiosurgery, RT: radiotherapy, EOR: extent of resection, GTR: gross total resection, STR: subtotal resection, ICU: intensive care unit.

Table 2

Quality indicators and complications.

OUTCOME	n (%)
30-day reoperation	0 (0)
30-day readmission	4 (7.7)
CSF leak	1 (1.9)
Reduced general condition	3 (5.8)
30-day mortality	0 (0)
30 nosocomial infection	9 (17.3)
Meningitis	1 (1.9)
Pneumonia	2 (3.8)
Surgical site infection	0 (0)
Urinary tract infection	7 (13.5)
30-day surgical site infection	0 (0)
30-day CSF leak	2 (3.8)
New neurological deficit	16 (30.8)
Pulmonary embolism	3 (5.8)
LOS >7	22 (42.3)
Postoperative hemorrhage	3 (5.8)
Requiring surgery	0 (0)
Any adverse event	16 (30.8%)

Any adverse event comprises the occurrence of one or more of the following events: postoperative hemorrhage, CSF-leakage, infection, readmission, reoperation, mortality, and pulmonary embolism. CSF: cerebrovascular fluid.

our outcome measures are presented in Table 3.

Patients with multiple lesions had a higher risk for 30-day readmission, nosocomial infection, longer LOS and any adverse event in general. Longer incision-closure time was significantly associated with higher risk for new neurological deficit, CSF leakage, and LOS >7 days. The outcome measure that was most effected of preoperative Brain and Spine 3 (2023) 101739

Table 3

Risk factors for the different outcome variables obtained in univariate analysis.

		Readmission n n (%)	No Readmission n (%)	p-valu
CRP > 5 mg/l	yes	3 (33.3%)	6 (66.7%)	0.002
-	no	1 (2.4%)	41 (97.6%)	
Number of lesions	1	2 (4.3%)	44 (95.7%)	0.004
	2	0 (0%)	2 (100%)	
	multifocal	2 (50%)	2 (50%)	
Metastatic tumor	(≥3) yes	1 (50%)	1 (50%)	0.022
wetastatic tullor	no	3 (6%)	47 (94%)	0.022
Primary/	primary	2 (5%)	38 (95%)	0.039
secondary	secondary	2 (28.6%)	5 (71.4%)	
atypical				
meningioma				
30-day nosocomial	infection			
		Nosocomial	No nosocomial	p-
		infection n (%)	infection n (%)	value
Number of lesions	1	5 (10.9%)	41 (89.1%)	0.002
	2	1 (50%)	1 (50%)	
	multifocal	3 (75%)	1 (25%)	
	(≥3)			
New neurological d	eficit			
		New deficit n	No new deficit	р-
		(%)	n n (%)	value
Brain invasion	yes	6 (66.7%)	3 (33.3%)	0.010
(visible under	no	10 (23.3%)	33 (76.7%)	
microscope)		- (22, 22)		
Extent of	GTR	7 (20.6%)	27 (79.4%)	0.029
resection	STR	9 (50%) Madian: 217	9 (50%) Madiany 142	0.014
Incision-closure		Median: 217	Median: 143	0.014
time		(IQR:283)	(IQR: 85)	
CFS leakage				
		CFS leakage n	No CFS leakage	р-
		(%)	n (%)	value
Incision-closure		Median: 484.5	Median: 155	0.005
time (min)		(IQR:)	(IQR: 107)	
Pulmonary embolis	m			
		Pulmonary	No pulmonary	p-
		embolism n	embolism n	value
		(%)	(%)	
Myocardial	yes	1 (33.3%)	2 (66.7%)	0.035
infarction		9 (4 10/)	47 (95.9%)	
	no	2 (4.1%)		
•	no yes	2 (4.1%) 1 (50%)	1 (50%)	0.006
vascular				0.006
vascular disease	yes no	1 (50%) 2 (4%)	1 (50%) 48 (96%)	
vascular disease	yes no yes	1 (50%) 2 (4%) 1 (33.3%)	1 (50%) 48 (96%) 2 (66.7%)	0.006 0.035
vascular disease COPD	yes no yes no	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%)	0.035
vascular disease COPD Primary/	yes no yes no primary	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%)	
vascular disease COPD Primary/ secondary	yes no yes no	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%)	0.035
vascular disease COPD Primary/ secondary atypical	yes no yes no primary	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%)	0.035
vascular disease COPD Primary/ secondary atypical meningioma	yes no yes no primary secondary	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%)	0.035 0.009
vascular disease COPD Primary/ secondary atypical meningioma	yes no yes no primary secondary regular	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%)	0.035
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape	yes no yes no primary secondary	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%)	0.035 0.009 0.032
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape	yes no yes no primary secondary regular irregular	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%)	0.035 0.009 0.032
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT	yes no primary secondary regular irregular yes	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 0 (0%)	0.035 0.009 0.032 <0.00
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX	yes no yes no primary secondary regular irregular yes no yes no	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 0 (0%) 10 (0%)	0.035 0.009 0.032 <0.00 <0.00
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX	yes no yes no primary secondary regular irregular yes no yes no 0	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 0 (0%) 49 (96.1%) 16 (100%)	0.035 0.009 0.032 <0.00
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX	yes no yes no primary secondary regular irregular yes no yes no 0 1	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 22 (100%)	0.035 0.009 0.032 <0.00 <0.00
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX	yes no yes no primary secondary regular irregular yes no yes no yes no 1 2	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 0 (0%) 2 (20%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 0 (0%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%)	0.035 0.009 0.032 <0.00 <0.00
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 0 (0%) 2 (20%) 1 (25%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%)	0.035 0.009 0.032 <0.00 <0.00 0.032
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 2 3 1	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 0 (0%) 2 (20%) 1 (25%) 0 (0%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%)	0.035 0.009 0.032 <0.00 <0.00
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2	$\begin{array}{c} 1 \ (50\%) \\ 2 \ (4\%) \\ \end{array}$ $\begin{array}{c} 1 \ (33.3\%) \\ 2 \ (4.1\%) \\ 1 \ (2.5\%) \\ 2 \ (28.6\%) \\ \end{array}$ $\begin{array}{c} 2 \ (28.6\%) \\ \end{array}$ $\begin{array}{c} 1 \ (2.4\%) \\ 2 \ (20\%) \\ 1 \ (100\%) \\ 2 \ (3.9\%) \\ 1 \ (100\%) \\ 2 \ (3.9\%) \\ 0 \ (0\%) \\ 0 \ (0\%) \\ 2 \ (20\%) \\ 1 \ (25\%) \\ 0 \ (0\%) \\ 1 \ (2.6\%) \\ \end{array}$	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%) 37 (97.4%)	0.035 0.009 0.032 <0.00 <0.00 0.032
disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission ASA score	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2 3 3	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 0 (0%) 2 (20%) 1 (25%) 0 (0%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%)	0.035 0.009 0.032 <0.00 <0.00 0.032
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission ASA score	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2 3 3	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 2 (3.9%) 0 (0%) 2 (20%) 1 (25%) 0 (0%) 1 (2.6%) 2 (25%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%) 37 (97.4%) 6 (75%)	0.035 0.009 0.032 <0.00 0.032 0.042
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2 3 3	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 2 (28.6%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 0 (0%) 0 (0%) 2 (20%) 1 (25%) 0 (0%) 1 (2.6%) 2 (25%) LOS > 7 days n	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%) 37 (97.4%) 6 (75%) LOS 1–7 days n	0.035 0.009 0.032 <0.00 0.032 0.042 P-
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission ASA score	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2 3 3	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 2 (3.9%) 0 (0%) 2 (20%) 1 (25%) 0 (0%) 1 (2.6%) 2 (25%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%) 37 (97.4%) 6 (75%)	0.035 0.009 0.032 <0.00 0.032 0.042
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative CTX ECOG admission ASA score	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 2 (3.9%) 0 (0%) 1 (25%) 0 (0%) 1 (26%) 2 (39%) 1 (26%) 2 (39%) 1 (26%) 2 (39%) 1 (39,1%) 1 (39,1%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 22 (100%) 8 (80%) 3 (75%) 5 (100%) 37 (97.4%) 6 (75%) LOS 1-7 days n (%) 28 (60.9%)	0.035 0.009 0.032 <0.00 <0.00 0.032 0.042 P-
vascular disease COPD Primary/ secondary atypical meningioma Tumor shape Preoperative RT Preoperative RT Preoperative CTX ECOG admission ASA score	yes no yes no primary secondary regular irregular yes no yes no 0 1 2 3 1 2 3 1 2 3 3	1 (50%) 2 (4%) 1 (33.3%) 2 (4.1%) 1 (2.5%) 2 (28.6%) 1 (2.4%) 2 (20%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 1 (100%) 2 (3.9%) 0 (0%) 2 (3.9%) 0 (0%) 1 (25%) 0 (0%) 1 (25%) 0 (0%) 1 (25%) 2 (25%) LOS > 7 days n (%)	1 (50%) 48 (96%) 2 (66.7%) 47 (95.9%) 39 (97.5%) 5 (71.4%) 41 (97.6%) 8 (80%) 0 (0%) 49 (96.1%) 16 (100%) 49 (96.1%) 16 (100%) 3 (75%) 5 (100%) 37 (97.4%) 6 (75%) LOS 1-7 days n (%)	0.035 0.009 0.032 <0.00 0.032 0.042 P- value

(continued on next page)

Table 3 (continued)

30-day readmission	L			
		Readmission n	No Readmission	p-value
		n (%)	n (%)	
	multifocal	4 (100%)	0 (0%)	
	(≥3)			
Intact	yes	13 (32.5%)	27 (67.5%)	0.016
arachnoidal layer	no	8 (72.7%)	3 (27.3%)	
Tumor shape	regular	14 (33.3%)	28 (66.7%)	0.007
•	irregular	8 (80%)	2 (20%)	
Preoperative SRS	yes	8 (80%)	2 (20%)	0.007
•	no	14 (33.3%)	28 (66.7%)	
Incision-closure		Median: 231	Median: 141	0.011
time (min)		(IQR: 228)	(IQR: 67)	
	0-170	8 (27.6%)	21 (72.4%)	0.016
	> 170	14 (60.9%)	9 (39.1%)	
ECOG admission	0	2 (12.5%)	14 (87.5%)	0.002
	1	9 (40.9%)	13 (59.1%)	
	2	9 (90%)	1 (10%)	
	3	2 (50%)	2 (50%)	
Admission	emergency	8 (72.7%)	3 (27.3%)	0.021
	elective	14 (34.1%)	27 (65.9%)	
Any adverse event				
		Adverse event	No adverse	p-
		n (%)	event n (%)	value
COPD	yes	3 (100%)	0 (0%)	0.007
	no	13 (26.5%)	36 (73.5%)	
Number of lesions	1	11 (23.9%)	35 (76.1%)	0.006
	2	1 (50%)	1 (50%)	
	multifocal	4 (100%)	0 (0%)	
	(≥3)			
CRP > 5 mg/l	yes	6 (66.7%)	3 (33.3%)	0.012
-	no	10 (23.8%)	32 (76.2%)	

Variables that are presented in Table 1 were subject to analysis. In this table only significant results (p < 0.05) are shown.

CRP: C-reactive protein, GTR: gross total resection, STR: subtotal resection, RT: radiotherapy, CTX: chemotherapy, ASA: American Society of Anesthesiologists, ECOG: Eastern Cooperative Oncology Group, SRS: Stereotactic radiosurgery, LOS: length of stay.

comorbidities (myocardial infarction, peripheral vascular disease, COPD) the patient's condition (ASA and ECOG score), and preoperative tumor treatment was pulmonary embolism. CRP >5 mg/l on admission was a risk factor for both early readmission and any adverse event.

Multivariate analysis revealed number of lesions \geq 3 (OR: 24.6, 95% CI: 2.131–283.9, p = 0.010) as independent risk factor for the manifestation of a nosocomial infection. Incision-closure time was significantly associated with CSF-leakage (OR: 1.008, 95% CI: 1.0–1.016, p = 0.040). Emergency admission (OR: 15.307 95% CI: 1.166–200.874, p = 0.038), higher ECOG of 3 (OR: 54.379, 95% CI: 1.315–2249.415, p = 0.035), and incision-closure time (OR: 1.007, 95% CI: 1.00–1.013, p = 0.049) were independent risk factors for LOS >7 days. The only independent risk factor for the occurrence of any adverse event was preoperative elevated CRP >5 mg/l (OR: 17.222, 95% CI: 2.686–110.440, p = 0.003).

No significant correlations were seen for 30-day readmission, new neurological deficit, pulmonary embolism.

3.4. Systematic literature review

Our search initially identified 2744 possible citations. After excluding duplications, 1523 studies were retrieved for abstract evaluation. Screening and titles identified 155 articles for full-text evaluation. After full-text screening, 22 studies met the inclusion criteria. The reasons for exclusion are shown in Fig. 1. The most common reasons for exclusion were the absence of surgical relevance, followed by lack of quality indicator evaluation and the lack of included patients with WHO grade 2 meningiomas. All included studies evaluated 30-day outcome, post-operative complications and quality measures. Baseline characteristics of

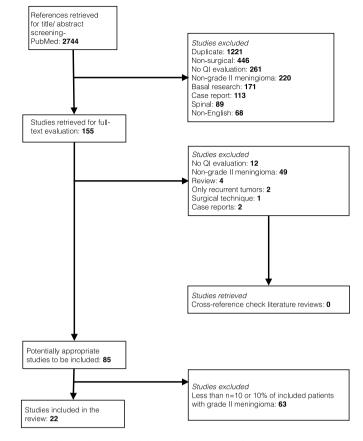


Fig. 1. Flow chart of the study screening and selection process.

the included studies and the patient collectives are presented in Table 4. The included studies were published between 2004 and 2021 and included a total of 4569 patients operated on for intracerebral meningioma between 1986 and 2018. Of those, 1014 patients were diagnosed with atypical meningioma (22%). The median number of included patients with atypical meningioma was 18 patients with a range of 10–199 patients and a rate ranging from 10 to 36%. All studies were of retrospective nature. Meningioma localization varied between the studies, there were four studies (18%) that only included meningiomas localized next to a major venous sinus. Together, the studies covered all most common localizations. The studies included both primary operated patients (n = 2342 (95%)) and patients with tumor recurrence (n = 125 (5%)) (not reported in the remaining 2102 (46%) patients). Gross total resection (Simpson I, II) was achieved in 2540 of the 3065 (83%) patients were EOR was reported.

The outcome data and quality indicators of the included studies from the literature review are summarized in Table 5. None of the studies reported all the included outcome measures. The 30-day reoperation rate was reported in five (23%) studies and ranged from 2.2% to 15.4%. The main reported reason for reoperation was postoperative hematoma. None of the studies allowed extraction of data regarding the 30-day readmission rate. The 30-day mortality rate varied from 0 to 7%. A surgical site infection was reported in 1.5–9%. A CSF-leakage occurred in 0.7–10%. Length of stay was reported in four (18%) studies and the median days of stay were between 5 and 11 days. Many studies analyzed the rate of venous thromboembolism, reporting a rate of up to 7.2%. Several studies reported risk factors regarding the outcome measures. Tumor location, surgical approach, higher age, high BMI, preoperative KPS, and Simpson grade I resection were significantly associated with higher risk for complications.

Table 4

Baseline characteristics of the included studies (literature review).

Study	Years	Setting	Number of included patients (total)	Number of patients with grade II meningioma (%)	Age at surgery in years	Sex	Localization of meningioma	Primary or recurrent tumor	Extent of resection
Amano et al., 2018 (Amano et al., 2018)	2008–2017	Japan	138	28 (20%)	NR	F: 99 (71.7%) M: 39 (28.3%)	Convexity: 31 (22.5%) Posterior fossa: 31 (22.5%) Parasagittal: 25 (18.1%) Falx: 14 (10.1%) Skull base anterior/ middle: 28 (20.3%) Other: 9 (6.5%)	P: 138 (100%)	S I: 56 (40.6%) S II: 60 (43.5%) S III: 18 (13%) S IV: 4 (2.9%)
Anthofer et al., 2017 (Anthofer et al., 2017)	2000–2012	Germany	141	16 (11.3%)	Mean: 57.7 Range: 24- 89	F: 109 (77.3%) M: 32 (22.7%)	Meningiomas located within 20 mm of a major venous sinus	P: 141 (100%)	S I: 82 (58.2%) S II: 25 (17.7%) S III: 4 (2.8%) S IV: 30 (21.3%)
DiMeco et al., 2004 (DiMeco et al., 2004)	1986–2001	Italy	108	16 (14.8%)	Mean: 56.2 Median: 57.5 Range: 22- 83	F: 73 (67.6%) M: 35 (32.4%)	Parasagittal tumors invading the superior sagittal sinus: 108 (100%)	P: 100 (92.6%) R: 8 (7.4%)	S I: 63 (58.3%) S II: 37 (34.2%) S III: 0 (0%) S IV: 8 (7.4%)
Elkady et al., 2020 (Elkady et al., 2020)	2012–2017	Egypt	101	14 (13.9%)	Mean: 55.1 ± 5 Range: 35- 62	F: 63 (62.3%) M: 38 (37.7%)	Only infratentorial CPA: 41 (40.6%) Tentorial: 17 (16.8%) Petroclival: 15 (14.8%) Foramen magnum: 14 (13.9) Convexity: 14 (13.9)	NR	S I: 63 (62.4%) S II: 15 (14.8%) S III: 23 (22.8%)
Gousias et al., 2016 (Gousias et al., 2016)	1996–2008	Germany	901	174 (19.3%)	Mean: 59.9 ± 12.8 Median: 60.8 Range: 20- 92	F: 638 (70.8%) M: 263 (29.2%)	Convexity: 214 (23.8%) Parasagittal: 137 (15.2%) Falx: 84 (9.3%) Tentorium: 42 (4.7%) Frontobasal: 142 (15.8%) Ventricles: 13 (1.4%) Middle fossa: 116 (12.9%) Sphenoorbital: 18 (2%) Posterior fossa: 86 (9.5%) Spinal: 46 (5.1%) Other: 3 (0.3%)	P: 901 (100%)	S I: 572 (63.5%) S II: 199 (22.1%) S III: 93 (10.3%) S IV: 37 (4.1%)
Haeren et al., 2021 (Haeren et al., 2021)	2010–2018	Finland	76	18 (23.7%)	Median: 83 Range: 80- 96	F: 52 (68%) M: 24 (32%)	Convexity: 31 (40.8%) Falx: 9 (11.8%) Skull-base: 33 (43.4%) Other: 3 (4%)	P: 76 (100%)	GTR: 70 (92%) STR: 6 (8%)
Hoefnagel et al., 2014 (Hoefnagel et al., 2014)	1997–2009	The Netherlands	581	88 (15.%)	Mean: 56.2 ± 13.5 Range: 16- 89	F: 401 (69%) M: 180 (31%)	Convexity: 140 (24.1%) Sphenoid Ridge: 116 (19.9%) Falx cerebri: 115 (19.8%) Other: 210 (36.2%)	NR	NR
Idowu et al., 2021 (Idowu et al., 2021)	1999–2018	USA	43	10 (23%)	Mean: 54 ± 15.6 Range: 32- 80	F: 35 (81%) M: 8 (19%)	Spheno-orbital: 43 (100%)	P: 35 (81%) R: 8 (19%)	S I,II: 15 (35%) (S III: 6 (14%) S IV: 22 (51%)
Mantovani et al., 2014 (Mantovani et al., 2014)	2005–2013	USA	38	11 (29%)	Mean: 51.58 ± 15.56 Range: 19- 78	F: 25 (66%) M: 13 (34%)	Meningiomas invading the dural venous sinuses 100%	NR	(81%) S I, II: 33 (87%) S III, IV, V 5 (13%)
Monden et al., 2021 (Monden et al., 2021)	2009–2015	Germany	421	153 (36.3%)	Mean: 56.6 Median: 57	F: 287 (68.2%) M: 134 (31.8%)	NR	P: 421 (100%)	NR

(continued on next page)

Table 4 (continued)

Study	Years	Setting	Number of included patients (total)	Number of patients with grade II meningioma (%)	Age at surgery in years	Sex	Localization of meningioma	Primary or recurrent tumor	Extent of resection
	_				Range: 16-				
Morokoff et al., 2008 (Morokoff et al., 2008)	1986–2005	USA	163	16 (10%)	86 Median: 57 Range: 20- 89	F: 120 (72.8%) M: 43 (27.2%)	Convexity: 163 (100%)	NR	S I: 155 (95%) NR: 8 (5%)
Narayan et al., 2017 (Narayan et al., 2018)	1995–2015	USA	80	16 (20%)	Mean: 56.3 ± 16.1 Median: 16 Range: 16- 86	F: 53 (66.3%) M: 27 (33.8%)	Skull base: 57 (71.3%) Convexity: 17 (21.2%) Falx/parasagittal: 6 (7.5%)	NR	S I: 9 (11.3%) S II: 60 (75%) S III: 1 (1.3%) S IV: 10 (12.5%)
Oh et al., 2014 (Oh et al., 2014)	2009–2012	USA	464	79 (17%)	Mean: 58 ± 13 Median: 58 Range: 18- 92	F: 331 (71%) M: 133 (29%)	NR	P: 383 (82%) R: 81 (18%)	NR
Ottenhauset al., 2019 (Ottenhausen et al., 2018)	2000–2017	USA	89	27 (30.3%)	Mean: 58.4 ± 15.8	F: 53 (59.6%) M: 36 (40.4%)	Convexity: 72 (80.9%) Falx: 17 (19.1%) Only tumors near motor cortex (rolandic meningiomas)	NR	S I: 51 (57.3%) S II: 31 (34.8%) S III: 6 (6.7%) S IV: 1 (1.1%)
Rami et al., 2018 (Rami et al., 2018)	2004–2015	Jordan	665	199 (30%)	Mean: 49.6 Range: 22- 87	F: 464 (70%) M: 201 (30%)	Parasagittal.: 263 (39.5%) Convexity: 183 (27.5%) Falx: 41 (6.2%) Anterior/middle fossa: 150 (22.6%) Cerebellar: 15 (2.3%) Intraventricular: 13 (1.9%)	NR	GTR (S I,II): 486 (73.1%) STR: 150 (22.6%) NR: 29 (4.3%)
Sanai et al., 2010 (Sanai et al., 2010)	1997–2007	USA	141	35 (25%)	Median: 48 Range: 18- 95	F: 92 (65%) M: 49 (35%)	Convexity: 141 (100%)	P: 128 (91%) R: 13 (9%)	S I:122 (87%) S II: 19 (13%)
Schneider et al., 2019 (Schneider et al., 2019)	2009–2017	Germany	195	36 (18%)	Mean: 61 ± 13	F: 151 (77%) M: 44 (23%)	Frontal skull base: 195 (100%)	NR	S I: 79 (40%) S II: 88 (45%) S III: 16 (8%) S IV: 11 (6%)
Shapey et al., 2019 (Shapey et al., 2019)	2005–2016	UK	34	11 (32.4%)	Median: 49	F: 22 (65%) M: 12 (35%)	Sphenoorbital: 34 (100%)	P: 19 (56%) R: 15 (44%)	S V: 1 (1%) S I: 4 (11.8%) S II: 4 (11.8%) S III: 21 (61.8%) S IV: 4 (11.8%) NR: 1 (2.9%)
Sughrue et al., 2011 (Sughrue et al., 2011)	1991–2007	USA	135	49 (36.3%)	Mean: 56	F: 83 (61.5%) M: 52 (38.5%)	Parasagittal and falcine: 135 (100%)	NR	(2.9%) GTR: 109 (80.7%)
Zeeshan et al., 2019 (Zeeshan et al., 2019)	2005–2016	USA	55	18 (33%)	Mean: 51.3 Range: 19- 72	(38.3%) NR	meningiomas invading the dural venous sinuses: 55 (100%)	NR	GTR: 48 (87.2%) STR: 7 (12.8%)

All included studies were of retrospective nature. P: primary, R: recurrent, S I–V: Simpson grade I–V, F: female, M: male, NR: not reported, CPA: cerebellopontine angle, GTR: gross total resection, STR: subtotal resection.

4. Discussion

Surgical outcome after meningioma surgery has improved during the last years as a result of advances in surgical treatment and perioperative management (Meling et al., 2019; Sicking et al., 2018). Undoubtfully, complications still do occur especially within the first 30 days after surgery. This time period has become the focus of attention in health-care economics. As a result, several quality indicators that are closely linked to postoperative complications have been developed and are being increasingly used in various medical fields, also for financial reimbursement purposes (Schipmann et al., 2019a; Kim et al., 2017; Joynt and Jha, 2013).

In a recently published clinical study on quality indicators in meningioma, the applicability of the mentioned quality indicators has been discussed with regard to meningioma surgery in general (Spille et al., 2022).

This study and review aim to focus on the subgroup of atypical meningiomas, which account for approximately 20% of all meningiomas and have been a raising entity due to changes in pathological classification during the last years (Louis et al., 2016). Atypical meningiomas tend to invade the brain and thus complicate surgery, encompass a higher tumor related mortality and higher recurrence rates (Sanai et al., 2010; Mantovani et al., 2014).

Applicability, usefulness and limitations of the classical quality indicators (30-day readmission, reoperation, nosocomial- and surgical site infection rate, mortality rate and length of stay), and the need for adequate risk adjustment strategies have been extensively discussed before (Spille et al., 2022; Schipmann et al., 2016, 2017, 2019a, 2019b, 2020, 2022; Dasenbrock et al., 2018).

4.1. The 30-day readmission rate

The 30-day readmission rate in our collective was 7.7%, with most of these patients having been readmitted due to reduced general condition not directly related to surgery. Report of readmission rates is lacking in the studies included in the review. James et al. showed that patients with atypical meningiomas did not have a higher risk for readmission compared to patients with grade 1 histology (James et al., 2019). Readmission rates in general for meningioma patients range from 3.8 to 34% in the literature with postoperative infection being the main reason (Spille et al., 2022; Lin et al., 2020; James et al., 2019).

We found CRP at admission, operation for recurrent tumor and underlying metastatic tumor disease as being significantly associated with a higher risk for readmission. Except preoperative elevated CRP that can potentially be lowered by treatment of an underlying infection, all other associated factors are patient-related. Most documented factors that affect the readmission rate cannot be modified by the surgeon (Lin et al., 2020; Fischer et al., 2014) and the lack of consistent risk factors impedes the development of adequate risk adjustment models for benchmarking purposes. These aspects render a limitation in using readmission as a quality indicator.

However, the analysis of reasons for readmission might help identifying patients at higher risk that might benefit from a modified follow-up setting.

4.2. The 30-day reoperation rate

Unplanned reoperations prolong length of stay, increase mortality, can be easily extracted from administrative data, and are consequently an attractive quality measure (Spille et al., 2022; Schipmann et al., 2017; Morris et al., 2007).

The reoperation rate in our collective was 0%. Reported rates for 30day reoperation from the systematic literature review range from 2.2% to 15.4% (Haeren et al., 2021; Mantovani et al., 2014; Monden et al., 2021; Shapey et al., 2019; Sughrue et al., 2011). No separate outcome rates for atypical meningiomas were reported. Patients with underlying comorbidities undergoing complex surgery have been are at higher risk for reoperation (Oh et al., 2014; Spille et al., 2022; Suero Molina et al., 2020). This highlights the necessity for adequate risk adjustment when using the 30-day reoperation rate as a quality indicator. The main reported reasons for reoperation were hematoma and postoperative edema (Monden et al., 2021; Shapey et al., 2019; Sughrue et al., 2011). In both cases, indications for reoperation are strongly based on internal decision-making and guidelines, which affects rates and impedes the generalizability.

The postoperative hemorrhage rate with the need of surgical ranged from 0% to 9.2% (Amano et al., 2018; DiMeco et al., 2004; Haeren et al., 2021; Hoefnagel et al., 2014; Mantovani et al., 2014; Morokoff et al., 2008; Narayan et al., 2018; Sanai et al., 2010; Shapey et al., 2019; Sughrue et al., 2011). The highest rate was observed by Haeren et al. in patients older than 80 years being operated for a giant (>5 cm) meningioma. They also showed that the reoperation rate for postoperative hemorrhage was higher in atypical meningiomas than benign meningiomas (17% vs. 6%) (Haeren et al., 2021).

4.3. Nosocomial infection rate

The nosocomial infection rate in our study was 17.3%, mainly due to a high prevalence of uncomplicated urinary tract infection. There were no surgical site infections. The only risk factor we could find for infection was the presence of a multifocal meningioma, which presumably is accompanied by reduced patient mobility demanding urinary catheter insertion and higher prevalence of neurological deficits, predisposing for the development of infections.

Our literature review demonstrated that higher age, intraoperative blood loss and procedure duration were risk factors for pneumonia (Monden et al., 2021; Oh et al., 2014). Nosocomial infections are a significant source of patient mortality and morbidity and prevention of such complications is imperative (Bueno-Cavanillas et al., 1994; O'Keeffe et al., 2012; Oh et al., 2014). It is well known that meningioma surgery inherits a higher risk for SSI (James et al., 2019), ranging from 1.5% to 9.6% (Amano et al., 2018; DiMeco et al., 2004; Idowu et al., 2021; Monden et al., 2021; Morokoff et al., 2008; Ottenhausen et al., 2018; Sanai et al., 2010; Sughrue et al., 2011; Zeeshan et al., 2019). Most studies focus on the first 30 days after surgery when evaluating SSIs. However there are data that indicate that SSI also tend to occur later with a median of 42 days after index surgery (Schipmann et al., 2016) and cause later readmissions (James et al., 2019), suggesting to extent the observation time.

4.4. 30-day mortality rate

The 30-day mortality rate in our cohort was 0%, rates in the literature vary between 0% and 7% (Amano et al., 2018; DiMeco et al., 2004; Elkady et al., 2020; Gousias et al., 2016; Haeren et al., 2021; Mantovani et al., 2014; Monden et al., 2021; Morokoff et al., 2008; Narayan et al., 2018; Ottenhausen et al., 2018; Rami et al., 2018; Sanai et al., 2010; Shapey et al., 2019; Zeeshan et al., 2019). Studies that revealed higher mortality rates were performed in a developing country (Elkady et al., 2020), analyzed only elderly patients (Haeren et al., 2021; Monden et al., 2018), indicating that case complexity strongly affects mortality rates. No study showed an association between underlying pathology (grade 1 vs. grade 2 meningioma) and mortality, although it is known from the literature that surgical mortality for meningiomas is lower due to the mainly benign nature compared to malignant brain tumors (Lassen et al., 2011).

Several studies have raised concerns regarding the reliable use of this rate as a quality measure (Dimick et al., 2004; Wahba et al., 2022), due to the fact that low procedure numbers might impede the detection of poor performance and the corresponding lack of statistical power. The department's caseload must be high enough to detect raising in mortality rates (Dimick et al., 2004), this remains difficult when focusing only on

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Outcome measures and quality indicators of the included studies (literature review).

Study	LOS in days	CSF fistula	Postoperative hemorrage	30-day reoperation	30-day nosocomial infection	30-day SSI	30-day mortality	New neurological defict	Other complications	Risk factors associated with outcome rates	Comments
Amano et al., 2018 (Amano et al., 2018)	NR	1 (0.7%)	0 (0%)	NR	NR	2 (1.5%)	0 (0%)	Hemiparesis: 7 (5%) Cranial nerve palsy: 15 (10.9%)	NR	Age not risk factor for adverse outcome	Study compared patients > and <75 years
Anthofer et al., 2017 (Anthofer et al., 2017)	NR	NR	NR	NR	NR	NR	NR	Neurological deficit: 8 (5.6%) T 6 (4.2%) P New epilepsy: 4 (2.8%)	NR	NR	
DiMeco et al., 2004 (DiMeco et al., 2004)	NR	11 (10%) (2 required reoperation)	2 (1.85%)	NR	NR	3 (2.7%), all required reoperation	2 (1.85%) (1 PE; 1 postoperative hematoma)	New or worsened neurological deficit: 12 (11.1%) New seizure: 3 (7.7%)	Morbidity: 31 (28.7%) Brain swelling: 9 (8.3%) DVT: 3 (2.7%) PE: 1 (0.9%)	NR	
ilkady et al., 2020 (Elkady et al., 2020)	NR	3 (3%)	NR	NR	Pneumonia: 9 (8.9%) Meningitis: 1 (1%)	NR	6 (5.9%) (3 chest infections, 1 PE, 2 failure to recover postoperatively)	Cranial nerve pasly: 43 (42.6%) T P: 27 (28.4%) Motor weakness: 32 (31.7%) T 13 (13.7%) P Ataxia: 4 (4%) T 2 2.1% P	Overall complication rate: 56 (55.4%) T P: 33 (32.6%) Hydrocephalus: 17 (16.8%) DVT: 4 (4%) PE: 1 (1%)	Preoperative KPS and peritumor edema were significantly associated with complications in univariate analysis Location (highest_ petroclival, foramen magnum) and surgical approach (lowest suboccipital apporach) independent risk factors for development of complications	Only patients in developing countries without advanced intraoperative techniques like CUSA; navigation, MRI, US, Mapping
Gousias et al., 2016 (Gousias et al., 2016)	NR	NR	NR	NR	NR	NR	7 (0.8%)	84 (9.3%)	NR	Predictors for worse outcome (mulivariate): higher age (over 61), preoperative KPS, location (better: convexity, worse: petroclival) Not: EOR	
Haeren et al., 2021 (Haeren et al., 2021)	Median: 6.5 Range: 5- 8	2 (2.6%)	7 (9.2%) requiring surgical intervention Minor ICH without need for surgery: 14 (18.4%)	8 (10.5%)	Pneumonia: 4 (5.3%) UTI: 13 (17.1%) Other infection: 7 (9.2%)	NR	5 (7%)	Hemiparesis: 2 (2.6%) Other neurological deficit: 9 (11.85%) New seizure: 8 (10.5%)	Overall complication rate: 43 (56.6%) Hydrocephalus: 1 (1.3%) PE/DVT/SVT: 4 (5.3%)	Giant meningioma showed trend towards increased likelihood to develop major complications Higher rate for occurrence of postoperatiev ICHs requiring reoperation (17% in atypical meningiomas vs. 6%	compared giant meningiomas >5 cm diameter and non-giant meningiomas in pasients 80 years old and older

Study	LOS in days	CSF fistula	Postoperative hemorrage	30-day reoperation	30-day nosocomial infection	30-day SSI	30-day mortality	New neurological defict	Other complications	Risk factors associated with outcome rates	Comments
Hoefnagel et al., 2014 (Hoefnagel et al., 2014)	NR	NR	17 (2.9%) requiring surgery	NR	NR	NR	NR	NR	VTE: 41 (7.2%) DVT: 20 (3.5%), PE: 26 (4.6%)	in benign meningioms) For VTE: high BMI, weight, bedridden postoperatively No relation between	
dowu et al., 2021 (Idowu et al., 2021)	NR	NR	NR	NR	NR	3 (7%) Hardware infection (titanium- mesh): 1 (2%)	NR	Reduction of vision: 1 (2.3%) Trochlear palsy: 2 (5%) Reactive strabismus: 2 (5%) Aponeurotic blepharoptosis: 1 (2%) (strabismus treated with corrective surgery)	NR	tumor grade and VTE NR	
Mantovani et al., 2014 (Mantovani et al., 2014)	NR	NR	1 (2.6%)	2 (5.3%)	NR	CSF or wound related complications: 9 (23.7%)	0 (0%)	New onset seizures: 3 (7.9%) New neuological deficit (inkl. seizures); 5 (13.1%)	Overall complication rate: 15 (39.5%)	NR	
Vonden et al., 2021 (Monden et al., 2021)	>70 y: median 11 Range: 4-44 <70y median: 8, Range: 2–124 (p = 0.03)	NR	NR	>70 y: 11 (15.4%) <70: 51 (14.7%) (edema/ hematom) p = n.s.	Pneumonia: >70: 7 (10%) <70: 11 (3.2%) p = 0.02 Sepsis >70: 0 (0%) <70: 2 (0.58%) p = n.s.	>70: 6 (8.9%) <70: 33 (9.6%) p = n.s.	>70: 2 (2.8%) <70: 1 (0.3%) p = n.s.		PE: >70: 9 (12.7%) <70: 21 (6%) p = 0.02	Older age: longer LOS, higher risk for pneumonia, PE	Compared patients over and under 70 years
Morokoff et al., 200 (Morokoff et al., 2008)8	NR	NR	1 (0.6%)	NR	n.s. Total: 5 (3%) UTI: 1 (0.6%) SSI: 4 (2.5%)	4 (2.5%)	0 (0%)	worsening of hemiparesis: 3 (1.8%) Seizure 2 (1.2%)	Overall complication rate: 9.4% Cardiac complications: 2 (1.2%) DVT: 2 (1.2%) Hydrocephalus: 2 (1.2%)	NR	
Narayan et al., 2017 (Narayan et al., 2018)	Mean: 5.9 ± 6.2	1 (1.2%)	2 (2.5%)	NR	NR	NR	4 (5%)	NR	NR	NR	Only giant meningiomas >5 cm diameter
Ch et al., 2014 (Oh et al., 2014)	Mean: 7 ± 7	NR	NR	NR	Pneumonia: 6 (1.3%)	NR	NR	NR	NR	Independent risk factors for pneumonia:	

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Study	LOS in days	CSF fistula	Postoperative hemorrage	30-day reoperation	30-day nosocomial infection	30-day SSI	30-day mortality	New neurological defict	Other complications	Risk factors associated with outcome rates	Comments
	Median: 5 Range: 1- 90									higher age, blood loss, procedure duration	
Ottenhausen al., 2019 (Ottenhausen et al., 2018)	NR	NR	NR	NR	Pneumonia: 2 (2.2%)	7 (7.9%)	0 (0%)	New or worsend neurological defict: 22 (24.7%) New seizures: 5 (5.6%)	Total complication rate: 15 (16.9%) Venous infarction: 1 (1.1%) Postoperative ischemia: 1 (1.1%)	Predictors for motor decline: preoperative embolization, minor preoperative weakness, existence of a preoperative motor defict	
Rami et al., 2018 (Rami et al., 2018)	NR	NR	NR	NR	NR	NR	11 (1.6%)	16 (2.4%)	NR	NR	
et al., 2018) Sanai et al., 2010 (Sanai et al., 2010)	NR	2 (1.4%)	2 (1.4%) EDH	NR	NR	5 (3.5%) Only two required reoperation	0 (0%)	0 (%)	Total complication rate: 14 (10%) DVT: 6 (4.2%) PE: 2 (1.4%)	NR	
Schneider et al., 2019 (Schneider et al., 2019)	NR	Simpson I: 8 (10%) Simpson II: 2 (2%)	NR	NR	NR	NR	NR	New cranial nerve deficit: 44 (22.6%) T 35 (18%) P	NR	Simpson grade I resection higher risk for cranial nerve deficit and CSF leakage	
Shapey et al., 2019 (Shapey et al., 2019)	NR	2 (6%)	2 (6%)	5 (14.7%) 2 hematoma, 2 edma/ raised ICP	Meningitis: 3 (8.8%)	NR	1 (3%)	New cranial nerve palsy: 2 (6%) Worse visual outcome: 4 (11.8%) Seizure: 4 (11.8%)	Overall complication rate: 14 (41.2%)	No difference in complications between primary and repeat surgery or between different surgical approaches	
Sughrue et al., 2011 (Sughrue et al., 2011)	NR	N = 4 (3%)	2 (1.5%) (ASDH)	3 (2.2%) (2 ASDH, 1 edema)	Pneumonia: 1 (0.7%) UTI: 1 (0.7%)	2 (1.5%)	NR	New or worsend neurological deficit: 4 (3%) New seizures: 3 (2.2%)	Overall complication rate: 26 (19%) Medical complications: 10 (7.4%) HC: 4 (3%) DVT: 1 (0.7%) Venous infarction: 1 (0.7%)	NR	
Zeeshan et al., 2019 (Zeeshan et al., 2019)	NR	3 (5.5%)	1 (1.8%) (intraventricular, not requiring surgery)	NR	NR	5 (9%)	0 (0%)	New neurological deficit: 3 (5.5%) Seizures: 2 (3.6%)	DVT: 1 (1.8%)		

None of the studies reported separate outcome for atypical meningiomas. There were no data regarding the 30-day readmission rate.

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LOS: length of stay, CSF: cerebrospinal fluid, NR: not reported, KPS: Karnofsky performance scale, VTE: Venous thromboembolism, BMI: body mass index, PE: pulmonary embolism, DVT: deep venous thrombosis, T: transient, P: permanent, y: year.

certain subdiagnoses, e.g. atypical meningioma, compared to tumor craniotomy procedures in general.

4.5. Postoperative neurological outcome

Surgery for meningiomas bears an inherent risk of neurological deterioration, this might even be higher when operating for atypical meningiomas due to brain invasion (Sanai et al., 2010; Mantovani et al., 2014). Rates for new neurological deficits vary significantly between the in the review included studies and heterogeneity in definition of a new deficit impedes benchmarking purposes. In addition, the most critical factor defining the type of a new neurological deficit is tumor localization (Schneider et al., 2019) (Ottenhausen et al., 2018).

Our data revealed visible brain invasion, subtotal resection and higher incision-closure time as risk factors. Ottenhausen et al. showed that patients with preoperative existence of a motor deficit were more likely to deteriorate after surgery (Ottenhausen et al., 2018). Studies on meningiomas showed that the presence of a large peritumoral edema exposes the patient to higher risk of postoperative new neurological deficit, a finding that might be also of relevance for atypical meningiomas that tend to present with surrounding edemas (Spille et al., 2022; Idowu et al., 2021).

Compared to the already discussed quality indicators, affects neurological outcome directly the patient's quality of life (Kim et al., 2016). This emphasizes the importance of neurological deficit as a potential quality indicator; however, more data regarding risk adjustment, type of deficit, homogenous definitions and time aspects are required to evaluate its role as a quality indicator.

4.6. Length of stay (LOS)

There are many efforts to reduce the LOS to increase cost efficiency. Thus, the LOS has been suggested as a potential quality measure (Schipmann et al., 2017).

The median LOS in our study of 7 days was in accordance with the reports from the literature (Haeren et al., 2021; Monden et al., 2021; Narayan et al., 2018; Oh et al., 2014). None of the included studies indicated longer LOS in patients diagnosed with atypical meningioma compared to benign meningioma. We found multifocal meningioma, irregular tumor shape, destroyed arachnoidal layer, preoperative SRS, longer incision-closure time, tumor, higher ECOG and emergency admission as being associated with longer LOS. From the literature, older age was a risk factor for prolonged LOS (Monden et al., 2021). These documented associations show that prolonged LOS is mainly attributed to tumor and patient-inherent factors that cannot be modified by the surgeon. In addition, LOS is strongly affected by local treatment guide-lines, bed capacity and reimbursement schemes, therefore limiting its use as a general quality indicator (Schipmann et al., 2017).

4.7. CSF-leakage

We observed a CSF leak in 3.8% of patients and CSF leak was the only surgery related reason for readmission in our collective. CSF-leakage rates reported in the literature range from 0.7% to 10% (Amano et al., 2018; DiMeco et al., 2004; Elkady et al., 2020; Haeren et al., 2021; Narayan et al., 2018; Sanai et al., 2010; Schneider et al., 2019; Shapey et al., 2019; Sughrue et al., 2011; Zeeshan et al., 2019). Schneider et al. showed in their series with frontal skull base meningiomas that CSF leak was significantly higher after Simpson I resection compared to Simpson II resection (10 vs. 2%) (Schneider et al., 2019). Our own data revealed longer incision-closure time as associated risk factor, indicating that case complexity is of relevance. CSF-leakage can be relevant as a quality measure as it is associated with higher postoperative mortality (Horowitz et al., 2011). Again, homogenous definitions lack and strategies for risk adjustment are lacking.

4.8. Any adverse event

The any adverse event rate is subject to definition and therefore not comparable between the included studies. Special attention should be paid to thromboembolic complications as patients with meningiomas are at higher risk for thromboembolic complications (Anthofer et al., 2016) with a rate of pulmonary embolism reported in the literature ranging from 0.9% to 12.7% (DiMeco et al., 2004; Elkady et al., 2020; Haeren et al., 2021; Hoefnagel et al., 2014; Monden et al., 2021; Sanai et al., 2010). Typical risk factors are related to the patient's comorbidities and special precautions should be considered when operating on those patients. Hoefnagel et al. showed that the tumor grade does not influence the risk for thromboembolic complications (Hoefnagel et al., 2014).

An interesting aspect that was not scope of this study is the estimation of long-term outcome and recurrence as atypical meningiomas inherit a higher risk of recurrence with a 5-year recurrence rate of 41% (Perry et al., 1997). Extent of resection influences the risk of recurrence and especially in atypical meningiomas the risk of an aggressive surgical strategy for lowering the risk of recurrence must be weighed against increased tumor related mortality (Mantovani et al., 2014). The mentioned quality indicators should therefore all be evaluated in the light of the achieved extent of resection.

4.8.1. Limitations

Despite the fact that the study adds novel data to the literature for quality measures in atypical meningioma surgery, there are some limitations that deserve mention.

The number of included subjects was small and the study is of retrospective nature which limits drawing conclusions on a wider level. We included both patients and studies over a long time period and within this period the pathological definition for atypical meningioma has changed. Changes of staff and surgical indications in face of an increasing role of radiosurgery might have confounded the results.

We did not follow up readmissions to other hospitals. In addition, the included studies present a heterogenous collective with both grade 1 and grade 2 meningiomas and different tumor localizations that impede drawing conclusions for the subgroup of atypical meningiomas and comparison of outcome measures. Most of the studies from the literature review were not performed with the intention of evaluating quality indicators, which might lead to underreported outcome measures.

5. Conclusions

Atypical meningiomas have a course that is clearly distinct from that of benign meningiomas (DiMeco et al., 2004) and surgery faces potentially higher risks for complications (Haeren et al., 2021), thus special attention should be turned on this subgroup when evaluating postoperative quality indicators.

Our study provides data on quality indicators and short-term outcome for surgery of atypical meningiomas, supplemented by a systematic review of the literature. The data show that it is difficult to compare outcome mainly due to differences in the patients' underlying comorbidities and case complexity. Risk adjustment is therefore vital. Most factors that lead to worse outcome are not modifiable by the surgeon. CRP >5 mg/l on admission was a risk factor for both early readmission and any adverse event and might be modified prior to surgery.

There is a need for large and multicenter databases that enable proper risk adjustment and consider disease-specific variables for atypical meningioma surgery. Future studies and registries should also include quality of life and patient-related outcomes in addition to currently applied quality indicators.

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Declaration of competing interest

The authors have no relevant financial or non-financial interests to disclose.

Appendix A. Supplementary data

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