

Preoperative Machine-Learning Models for Predicting Postoperative Morbidity after Anterior Clinoidal Meningioma Surgery: Development and External Validation

Noa Ben Dor

noa.bendorziv@studio.unibo.it

Istituto delle Scienze Neurologiche di Bologna

Gal Ziv

Istituto delle Scienze Neurologiche di Bologna

Filippo Friso

Istituto delle Scienze Neurologiche di Bologna

Carlo Bortolotti

Istituto delle Scienze Neurologiche di Bologna

Diego Mazzatenta

Istituto delle Scienze Neurologiche di Bologna

Matteo Zoli

Istituto delle Scienze Neurologiche di Bologna

Matteo Martinoni

Istituto delle Scienze Neurologiche di Bologna

Filippo Badaloni

Istituto delle Scienze Neurologiche di Bologna

Giulia Casulli

Istituto delle Scienze Neurologiche di Bologna

Vittoria Rosetti

Istituto delle Scienze Neurologiche di Bologna

Luca Zanuttini

Istituto delle Scienze Neurologiche di Bologna

Lorenzo Faccin

Istituto delle Scienze Neurologiche di Bologna

Francesco Travaglini

Ospedale "M. Bufalini" di Cesena

Luigino Tosatto

Ospedale "M. Bufalini" di Cesena

He-ming Wu

Nanjing First Hospital

Catherine Elizabeth Gilkes

The Walton Centre NHS Foundation Trust

Cathal John Hannan

The Walton Centre NHS Foundation Trust

Michael D. Jenkinson

The Walton Centre NHS Foundation Trust

Marcello D'Andrea

Ospedale "M. Bufalini" di Cesena

Alfredo Conti

Istituto delle Scienze Neurologiche di Bologna

Research Article

Keywords: Anterior Clinoid Meningioma, Machine Learning, Neurological Deficits, Postoperative Morbidity, Risk Prediction, Surgical Outcomes

Posted Date: October 11th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11173701/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Purpose

Anterior clinoidal meningiomas (ACMs) are surgically challenging because of their proximity to critical neurovascular structures. Existing classifications address resectability but do not provide validated estimates of postoperative complications. We aimed to develop and validate preoperative machine learning (ML) models and translate them into an online risk calculator.

Methods

We retrospectively analyzed data of 241 adults who underwent first-time microsurgical ACM resection at four tertiary centers in three countries between 2010 and 2025. Complications were classified as medical (systemic), surgical (regional), or neurological. Ridge-penalized logistic regression and gradient boosting used routine preoperative data to model each category, evaluated by internal and internal–external (geographical) cross-validation.

Results

Medical complications occurred in 36 patients (14.9%), predicted by tumor diameter, vessel encasement, comorbidity burden, age, and lower performance status, with an internal area under the curve (AUC) of 0.755 (95% CI 0.667–0.838) and 0.768 across centers. Surgical complications (21, 8.7%) were not reliably predicted (cross-center AUC 0.686). Neurological deficits (68, 28.2%) were poorly predicted as a composite (AUC 0.696) and were modelled by domain. Motor deficits (30, 12.4%) were predicted by tumor diameter, carotid siphon and cavernous sinus involvement, and preoperative motor symptoms (AUC 0.729; 0.711 across centers). Cognitive decline (28, 11.6%) was predicted by age, preoperative motor symptoms, and lower performance status (external AUC 0.731). New visual deficits (19, 7.9%) resolved by 12 months and could not be predicted.

Conclusion

Preoperative data predicted medical complications, motor deficits, and cognitive decline. The models were translated into an investigational online calculator; external validation in independent cohorts is warranted.

INTRODUCTION

Anterior clinoidal meningiomas (ACMs), first described by Cushing and Eisenhardt in 1938 as “inner sphenoid wing meningiomas,”[1] arise from the dura of the anterior clinoid process (ACP) and account for approximately 34–43.9% of all sphenoid wing meningiomas[2–5]. [2–5] Owing to their close relationship with critical neurovascular structures, including the optic nerve, oculomotor nerve, and internal carotid artery (ICA), ACMs remain among the most surgically challenging skull base meningiomas (SBMs). [2–4, 6–10]

Several classification systems have been proposed to guide surgical decision-making for ACMs. The systems developed by Al-Mefty and Goel incorporate factors such as tumor origin, size, ICA involvement, and visual impairment[6, 7]. However, these classifications were designed to predict resectability based on anatomical characteristics, without accounting for patient-level vulnerability. More recent studies of surgical outcomes in ACMs have identified older age, particularly > 60 years, as a predictor of less favorable outcomes [11–15]. Nevertheless, chronological age alone may not adequately capture patient vulnerability, which may also be influenced by cardiovascular, metabolic, psychiatric, and other systemic comorbidities.

Furthermore, existing evidence is largely derived from regression-based analyses, and machine learning (ML)-based risk stratification remains unexplored in ACMs. Therefore, we developed preoperative ML risk models and implemented them in a web-based calculator to support individualized risk estimation and future external validation.

METHODS

Study Design and Setting

We conducted a retrospective multicenter cohort study of consecutive patients who underwent first-time microsurgical resection of anterior clinoid meningioma (ACM) at four tertiary referral centers in three countries between 2010 and 2025. ACM was defined as a meningioma arising predominantly from the lesser wing of the sphenoid bone with a tumor epicenter or adjacent hyperostosis involving the ACP.[3] The study investigators reviewed all radiographs to confirm anatomical diagnostic consistency. Meningiomas from locations other than the ACP or with less than 12 months of clinical and radiographic follow-up were excluded. The research adhered to the Declaration of Helsinki, the STROBE guidelines[16], and the TRIPOD + AI guidelines[17]. Approval for the study was granted by our ethics committee, which waived the requirement for informed consent due to the retrospective nature of the study (CE-AVEC; approval no. 19029).

Data Collection

Data were collected from prospectively maintained institutional databases. The preoperative variables collected were age, sex, cardiovascular, endocrinological, oncological, and psychiatric comorbidities; Charlson Comorbidity Index (CCI)[18]; ASA class[19]; baseline KPS[20]; presenting symptoms; and tumor characteristics on preoperative MRI. Operative data included surgical approach, use of neuronavigation, neurophysiological monitoring, intraoperative ultrasound, performance of anterior clinoidectomy and optic canal unroofing, and intraoperative neurovascular findings. The extent of resection was documented according to the Simpson grade and postoperative MRI classification as gross-total resection (GTR) or subtotal resection (STR), defined by the presence of ≥ 2 mm of nodular enhancement at the resection site.[21] Postoperative complications were recorded and classified according to the

Landriel–Ibáñez system as mild-to-moderate or severe based on the type of complication and treatment required.[22] Non-neurological complications and new or exacerbated motor, visual, and neuropsychological impairments were recorded at discharge, four weeks post-surgery, and at the final available follow-up.

Imaging

Radiological characteristics were assessed using standardized contrast-enhanced T1-weighted and T2-weighted MRI sequences, together with MR angiography. The evaluated features included the maximum tumor diameter and involvement of the internal carotid artery (ICA), carotid siphon, and adjacent major cerebral arteries (ACA, MCA, and PCA). Circumferential vessel involvement was graded as 0, absent; 1, < 90°; 2, 90° to < 180°; 3, 180° to 270°; and 4, > 270°. Additional features included optic canal involvement, cavernous sinus (CS) infiltration, peritumoral edema, midline shift, calcification, dural tail, hyperostosis, and bone invasion. MRI-based estimates of tumor consistency, perforator involvement, and distal dural ring involvement were not systematically recorded at all centers.

Descriptive statistics

Continuous variables are presented as mean $\pm$ standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for non-normally distributed data. Categorical variables are reported as absolute and relative frequencies (%).

Machine Learning Workflow

Ten patients from one center were excluded from the modelling because no complication of any type had been recorded (0 of 10 versus 40.3% elsewhere; Fisher exact $p = 0.008$) and their records were otherwise not comparable with the cohort (Online Resource 1, Table S1); 231 patients were included in the model.

Predictors and Outcomes

All predictors were recorded preoperatively and were available at the time of surgical consultation. The variables included demographics, comorbidities, preoperative functional and neurological status, and radiological tumor characteristics (Online Resource 1, Table S2). Postoperative complications were assigned to three domains following the neurological, regional, and systemic classification of craniotomy morbidity, hereafter termed neurological, surgical, and medical complications[23, 24]. Medical complications included systemic infection, deep vein thrombosis, acute respiratory insufficiency, and heart failure; surgical complications included postoperative hematoma, seizure, wound infection, CSF leak, and hydrocephalus; and new ischemic stroke was assigned to the neurological domain. Each category was defined as a separate outcome and ascertained at discharge. For the neurological domain,

we modelled the composite of any new or worsened deficit and each of its components: motor deficit, cognitive decline, and visual deterioration. New psychiatric syndromes were not modelled because only three occurred. Cognitive decline was not recorded in Cesena; therefore, the cognitive model was developed in Bologna and validated in Liverpool. The pooled non-neurological composite was retained for sensitivity analysis.

Model Development

Two prediction analyses were performed independently so that the findings would not depend on a single method: a histogram gradient boosting classifier (HGBC) and logistic regression with ridge (L2) penalization. Gradient boosting was chosen because it accommodates non-linear effects and interactions among many candidate variables without prior specification[25], while ridge regression was chosen because it remains stable when events are few and yields an explicit equation for a calculator[26]. Both analyses used constrained settings because the outcome events were few relative to the variables: gradient-boosting hyperparameters were preset without tuning, and training was stopped when performance ceased to improve; the ridge penalty was selected within each training fold by minimizing the log-loss after standardization. Data from held-out centers were withheld from predictor specification, penalty selection, and all model fitting (Online Resource 1, Fig. S1).

Validation and Performance Assessment

Internal validation used repeated stratified five-fold cross-validation for gradient boosting, during which a high-sensitivity operating threshold was estimated and frozen before external testing, and nested 10-fold cross-validation was repeated five times with 200-replicate bootstrap optimism correction for the ridge models. Transportability was assessed by internal–external cross-validation, each center held out in turn, and the held-out AUCs pooled by random-effects meta-analysis[27, 28] and by geographical external validation; details are given in Online Resource 1. Performance was evaluated using the AUC, calibration slope and intercept, Brier score, threshold-based sensitivity, specificity, predictive values, and decision curve analysis. Specifications, confidence interval methods, and sample size handling are provided in Online Resource 1 (Tables S3–S7).

Software and use of Large Language Models

Analyses were performed using Python 3.11.15 with scikit-learn 1.8.0, NumPy 2.4.4, pandas 3.0.2, and SciPy 1.17.1; figures were drawn with matplotlib 3.10.9 (Table S7). A fixed random seed (2026) was used throughout the study. Claude Opus 5 (Anthropic) was used to accelerate code development and to improve the readability and language of the manuscript. All code was reviewed, tested, and approved by a software engineer (G.Z.), and the authors take full responsibility for the content of the manuscript and the correctness of the analyses.

RESULTS

Cohort Characteristics

Two hundred forty-one patients were included (115, 68, 48, and 10 from the four centers); baseline characteristics are summarized in Table 1 and Online Resource 2 (Table S8). The pterional approach[29] was used in 237 patients (98.3%), and the subfrontal approach[30] was used in four (1.7%); anterior clinoidectomy was performed in 59 (24.5%), Simpson grade I–II resection was achieved in 165 (68.5%), and the radiographic extent of resection was GTR in 152 (63.1%) and STR in 89 (36.9%). Most tumors were WHO grade 1 (84.6%), whereas 15.4% were WHO grade 2[31] (Online Resource 2, Table S8).

Table 1
Patient baseline characteristics and preoperative presentation, overall and by center

Characteristic	Overall (N = 241)	Bologna (n = 115)	Cesena (n = 68)	Liverpool (n = 48)	China (n = 10)
DEMOGRAPHICS					
Age, years — mean ± SD	60.3 ± 12.3	61.0 ± 12.7	60.4 ± 10.6	59.8 ± 13.9	55.0 ± 12.4
Sex					
Female	168 (69.7)	81 (70.4)	47 (69.1)	36 (75.0)	4 (40.0)
Male	73 (30.3)	34 (29.6)	21 (30.9)	12 (25.0)	6 (60.0)
COMORBIDITY BURDEN					
Charlson Comorbidity Index — mean ± SD	2.4 ± 1.6	2.8 ± 1.7	2.2 ± 1.6	2.1 ± 1.4	0.2 ± 0.4
≤ 2	133 (55.2)	50 (43.5)	41 (60.3)	32 (66.7)	10 (100.0)
≥ 3	108 (44.8)	65 (56.5)	27 (39.7)	16 (33.3)	0 (0.0)
ASA class III–IV	120 (49.8)	50 (43.5)	55 (80.9)	15 (31.2)	0 (0.0)
Cardiorespiratory disease	119 (49.4)	69 (60.0)	25 (36.8)	21 (43.8)	4 (40.0)
Hyperlipidemia	40 (16.6)	20 (17.4)	14 (20.6)	6 (12.5)	0 (0.0)
Other neoplasms	38 (15.8)	23 (20.0)	11 (16.2)	4 (8.3)	0 (0.0)
Diabetes mellitus	28 (11.6)	17 (14.8)	4 (5.9)	5 (10.4)	2 (20.0)
PREOPERATIVE FUNCTIONAL STATUS					
Karnofsky Performance Status — median [IQR]	80 [70–90]	80 [70–90]	90 [80–90]	80 [70–80]	90 [82–98]
< 70	22 (9.1)	12 (10.4)	2 (2.9)	7 (14.6)	1 (10.0)
Values are n (%) unless otherwise indicated; percentages are calculated within each column. Categories are not mutually exclusive except where presented as complete groupings (sex, Charlson Comorbidity Index, Karnofsky Performance Status and vessel encasement grade). ICA / carotid siphon involvement and the vessel encasement grade are the variables used in the prediction models. The ten patients from China were excluded from modelling (see Methods). ASA, American Society of Anesthesiologists; ACA, anterior cerebral artery; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; PCA, posterior cerebral artery; SD, standard deviation.					

Characteristic	Overall (N = 241)	Bologna (n = 115)	Cesena (n = 68)	Liverpool (n = 48)	China (n = 10)
DEMOGRAPHICS					
≥ 70	219 (90.9)	103 (89.6)	66 (97.1)	41 (85.4)	9 (90.0)
CLINICAL PRESENTATION					
Cognitive or psychiatric disorder	74 (30.7)	36 (31.3)	19 (27.9)	19 (39.6)	0 (0.0)
Headache	58 (24.1)	28 (24.3)	11 (16.2)	12 (25.0)	7 (70.0)
Motor deficit	56 (23.2)	32 (27.8)	12 (17.6)	12 (25.0)	0 (0.0)
Seizures	54 (22.4)	28 (24.3)	11 (16.2)	15 (31.2)	0 (0.0)
Visual loss	54 (22.4)	20 (17.4)	25 (36.8)	9 (18.8)	0 (0.0)
Language deficit	21 (8.7)	12 (10.4)	4 (5.9)	5 (10.4)	0 (0.0)
Cranial nerve palsy	16 (6.6)	12 (10.4)	4 (5.9)	0 (0.0)	0 (0.0)
RADIOLOGICAL FINDINGS					
Maximum axial diameter, mm – median [IQR]	35 [25–45]	33 [24–43]	36 [29–49]	40 [28–53]	40 [29–44]
Optic canal invasion	31 (12.9)	14 (12.2)	9 (13.2)	8 (16.7)	0 (0.0)
Optic nerve / chiasm compression	106 (44.0)	44 (38.3)	35 (51.5)	27 (56.2)	0 (0.0)
Midline shift	97 (40.2)	37 (32.2)	27 (39.7)	30 (62.5)	3 (30.0)
Peritumoral edema	150 (62.2)	67 (58.3)	46 (67.6)	34 (70.8)	3 (30.0)
Dural tail	110 (45.6)	61 (53.0)	13 (19.1)	26 (54.2)	10 (100.0)
Hyperostosis	73 (30.3)	55 (47.8)	6 (8.8)	12 (25.0)	0 (0.0)
Bone invasion	25 (10.4)	12 (10.4)	5 (7.4)	8 (16.7)	0 (0.0)
ICA / carotid siphon involvement	131 (54.4)	83 (72.2)	25 (36.8)	23 (47.9)	0 (0.0)
Values are n (%) unless otherwise indicated; percentages are calculated within each column. Categories are not mutually exclusive except where presented as complete groupings (sex, Charlson Comorbidity Index, Karnofsky Performance Status and vessel encasement grade). ICA / carotid siphon involvement and the vessel encasement grade are the variables used in the prediction models. The ten patients from China were excluded from modelling (see Methods). ASA, American Society of Anesthesiologists; ACA, anterior cerebral artery; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; PCA, posterior cerebral artery; SD, standard deviation.					

Characteristic	Overall (N = 241)	Bologna (n = 115)	Cesena (n = 68)	Liverpool (n = 48)	China (n = 10)
DEMOGRAPHICS					
ICA compression	108 (44.8)	75 (65.2)	16 (23.5)	17 (35.4)	0 (0.0)
ICA encasement	48 (19.9)	15 (13.0)	24 (35.3)	9 (18.8)	0 (0.0)
ACA/MCA/PCA involvement	137 (56.8)	64 (55.7)	38 (55.9)	35 (72.9)	0 (0.0)
Circumferential vessel encasement (grade ≥ 1)	166 (68.9)	88 (76.5)	39 (57.4)	39 (81.2)	0 (0.0)
Grade 1 — $< 90^\circ$	30 (12.4)	15 (13.0)	8 (11.8)	7 (14.6)	0 (0.0)
Grade 2 — 90° to $< 180^\circ$	57 (23.7)	33 (28.7)	14 (20.6)	10 (20.8)	0 (0.0)
Grade 3 — 180° to 270°	43 (17.8)	26 (22.6)	9 (13.2)	8 (16.7)	0 (0.0)
Grade 4 — $> 270^\circ$	36 (14.9)	14 (12.2)	8 (11.8)	14 (29.2)	0 (0.0)
Cavernous sinus invasion	45 (18.7)	20 (17.4)	9 (13.2)	16 (33.3)	0 (0.0)
Cranial nerve involvement	39 (16.2)	13 (11.3)	16 (23.5)	10 (20.8)	0 (0.0)
Values are n (%) unless otherwise indicated; percentages are calculated within each column. Categories are not mutually exclusive except where presented as complete groupings (sex, Charlson Comorbidity Index, Karnofsky Performance Status and vessel encasement grade). ICA / carotid siphon involvement and the vessel encasement grade are the variables used in the prediction models. The ten patients from China were excluded from modelling (see Methods). ASA, American Society of Anesthesiologists; ACA, anterior cerebral artery; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; PCA, posterior cerebral artery; SD, standard deviation.					

Postoperative Course

Ninety-three patients (38.6%) experienced at least one complication (Fig. 1 and Table 2). According to the Landriel–Ibáñez classification[22], complications were mild-to-moderate in 72 (29.9%) and severe in 21 (8.7%) patients, including four deaths (1.7%). Neurologic status worsened in 68 patients (28.2%): motor in 30 (12.4%), cognitive in 28 (11.6%), visual in 19 (7.9%), and psychiatric in three (1.2%). Overall, 36 patients (14.9%) experienced a medical complication and 21 (8.7%) experienced a surgical complication; 50 (20.7%) had at least one non-neurological complication. The most common were systemic infection (21, 8.7%) and deep vein thrombosis (17, 7.1%). Functional deterioration, defined as a ≥ 10 -point reduction in the KPS score from baseline to discharge, occurred in 35 (14.5%) patients. The median length of hospital stay was 10 days (IQR: 7–16). At 12 months, 11 of the 30 motor deficits persisted (4.6%), all 19 new visual deficits had resolved, and five patients (2.1%) reported new psychiatric disturbances that were not present at discharge (Online Resource 2, Table S8).

Table 2
Number and types of postoperative complications

Complication	Overall (N = 241)
NEW OR WORSENED NEUROLOGICAL DEFICITS AT DISCHARGE	
Motor deficit	30 (12.4)
Cognitive impairment	28 (11.6)
Visual deficit	19 (7.9)
Psychiatric disturbance	3 (1.2)
MEDICAL COMPLICATIONS	
Systemic infection	21 (8.7)
Deep venous thrombosis	17 (7.1)
Acute respiratory insufficiency	4 (1.7)
Heart failure	4 (1.7)
SURGICAL COMPLICATIONS	
Hematoma	10 (4.1)
Seizure	8 (3.3)
Wound infection	4 (1.7)
CSF leak	3 (1.2)
Hydrocephalus	2 (0.8)
OTHER EVENTS	
New ischemic stroke	7 (2.9)
Death	4 (1.7)
SEVERITY AND MANAGEMENT	
Single or multiple organ failure	9 (3.7)
KPS decline at discharge	35 (14.5)
Values are n (%). Patients may have experienced more than one complication; categories are not mutually exclusive and percentages do not sum to 100%. Three patients with a recorded complication that had not been assigned a Landriel–Ibáñez grade were classified as mild-to-moderate. Complications are grouped by domain (medical [systemic]; surgical [regional]); new ischemic stroke is assigned to the neurological domain and death is a severity grade rather than a complication type. <i>CSF</i>, cerebrospinal fluid; <i>KPS</i>, Karnofsky Performance Status.	

Complication	Overall (N = 241)
NEW OR WORSENED NEUROLOGICAL DEFICITS AT DISCHARGE	
Reoperation under general anesthesia	12 (5.0)
Prolonged or unplanned intensive care stay	9 (3.7)
Values are n (%). Patients may have experienced more than one complication; categories are not mutually exclusive and percentages do not sum to 100%. Three patients with a recorded complication that had not been assigned a Landriel–Ibáñez grade were classified as mild-to-moderate. Complications are grouped by domain (medical [systemic]; surgical [regional]); new ischemic stroke is assigned to the neurological domain and death is a severity grade rather than a complication type. <i>CSF</i> , cerebrospinal fluid; <i>KPS</i> , Karnofsky Performance Status.	

Machine-learning predictive models

The compositions of the development and external cohorts are summarized in Online Resource 1, Table S1.

Medical complications

Tumor diameter contributed most strongly, followed by vessel encasement grade, comorbidity burden, age, and cardiorespiratory disease, whereas a higher KPS was protective (Fig. 2a). The parsimonious ridge model achieved an internally cross-validated AUC of 0.755 (95% CI, 0.667–0.838; optimism-corrected, 0.772), a pooled cross-center AUC of 0.768 (95% CI, 0.665–0.846), and an external AUC of 0.847 (95% CI, 0.641–0.972) in the geographical split. Gradient boosting achieved a repeated-cross-validation AUC of 0.728 (95% CI, 0.644–0.829), 0.722 across centers, and 0.834 (95% CI, 0.650–0.967) externally. External calibration preserved the risk ranking (slope, 1.25), although absolute risk was over-predicted in Liverpool (calibration-in-the-large, – 0.74). Observed complication rates rose from 3.9% in the lowest tertile of held-out predicted risk to 29.9% in the highest; at a 10% threshold, sensitivity was 77.8% and the negative predictive value was 92.5% (Fig. 2b, c; Online Resource 3, Tables S9–S13 and Fig. S2a).

Surgical complications

With the same predictor set, ACA/MCA/PCA involvement was the strongest predictor, whereas the comorbidity terms fell to unity or below (Online Resource 3, Fig. S2b). Neither algorithm discriminated reliably: the ridge model reached an internal AUC of 0.659 (95% CI, 0.526–0.783) and a pooled cross-center AUC of 0.686 (95% CI, 0.518–0.816), with held-out estimates ranging from 0.565 (Bologna) to 0.759 (Cesena), and gradient boosting performed no better (0.624 internally; 0.601 across centers). Pooling medical and surgical complications with ischemic stroke into a single non-neurological composite (50 events) yielded lower and less consistent discrimination than the medical endpoint alone (ridge, 0.707 internally and 0.700 across centers; gradient boosting, 0.697, 0.674) (Online Resource 3, Table S9 and Fig. S2a).

Neurological complications

The composite of any new or worsened neurological deficit was mainly informed by cavernous sinus involvement, preoperative motor symptoms, and vessel encasement grade, but it was predicted less well than its components and did not transport across centers: the internal AUC was 0.696 (95% CI, 0.614–0.776) with ridge and 0.652 with gradient boosting, and the held-out AUC ranged from 0.596 in Cesena and 0.623 in Bologna to 0.834 in Liverpool, where calibration was poor (slope, 2.39) (Online Resource 3, Table S14 and Fig. S3). Each component was therefore modelled separately.

For new or worsened motor deficits, the strongest predictors were tumor diameter (standardized OR 1.28), ICA/carotid siphon involvement (1.18), preoperative motor symptoms (1.18), cavernous sinus involvement (1.13), and vessel encasement (1.09), with a higher preoperative KPS being protective (0.78) (Fig. 3a). Performance was similar inside and outside the development centers (internal AUC, 0.729; 95% CI, 0.639–0.805; optimism-corrected, 0.740; pooled cross-center, 0.711; 95% CI, 0.596–0.803; geographical external, 0.684; 95% CI, 0.481–0.865); removing preoperative motor symptoms barely changed discrimination (0.729 to 0.709); therefore, the model did not simply detect a persistent baseline deficit (Fig. 3b, c; Online Resource 3; Tables S9–S12).

For cognitive decline, age, preoperative motor symptoms, and lower KPS carried the most weight, followed by cavernous sinus involvement, comorbidity burden, and tumor diameter (Fig. 3d; Online Resource 3, Table S15). Internal discrimination was modest (nested cross-validated AUC, 0.592; 95% CI, 0.424–0.757; optimism-corrected, 0.653), whereas the external AUC was 0.731 (95% CI, 0.572–0.871). Predicted risks were under-dispersed and too low on average (calibration slope, 4.03; calibration-in-the-large, 0.71), because the penalty compressed them and the event rate in the validation cohort was higher (25.0% versus 13.9%). Gradient boosting reached 0.579 internally and 0.632 externally, and the nested cross-validated AUC with the two centers pooled was 0.681 (95% CI, 0.575–0.786) (Fig. 3e, f; Online Resource 3, Table S15 and Fig. S3). Visual deterioration was not predictable (AUC 0.420, 95% CI, 0.265–0.497).

DISCUSSION

Over the past decade, surgical management has shifted from radical resection to maximal safe resection tailored to neurovascular risk, with an increasing acceptance of planned subtotal resection followed by adjuvant radiosurgery in selected cases.[3, 4, 32–38] In such tailored strategies, decisions on whether, when, and how to operate rely primarily on preoperative information, and preoperative ML risk-prediction models may support patient selection, anticipatory planning, and perioperative resource allocation. Accordingly, we developed and evaluated preoperative ML models that integrate routinely available patient-level characteristics and tumor–neurovascular features to predict adverse postoperative outcomes after ACM surgery.

Surgical outcomes in our cohort in the context of the most recent literature

Overall morbidity in our cohort was 38.6%: 28.2% of patients had neurological deficits, 20.7% had non-neurological complications, 8.7% had severe complications, and mortality was 1.7%. These figures align with modern series: pooled rates of major vessel injury were 1.0% intraoperatively and 1.9% postoperatively, and the pooled mortality rate was 1.2% (95% CI, 0.6–1.8%).[4, 12, 14, 39] Visual deterioration occurred in 7.9% of our patients, compared with 4.5% in the pooled meta-analytic estimate[4, 40], although all such deficits resolved by 12 months.

A particularly relevant finding was the frequency of postoperative motor deficits, an outcome that has received limited attention in previous studies.[14] Motor impairment occurred in 12.4% of patients; half of these deficits were de novo, and 4.6% of the overall cohort had persistent impairment at 12 months. Notably, intraoperative neurophysiological monitoring was not used in 90% of the affected patients, although the retrospective design precludes conclusions regarding its protective effect. Therefore, motor impairment is a clinically meaningful source of morbidity that warrants careful planning and postoperative surveillance, particularly in large vessel-encasing ACMs.

Predictors of Medical and Neurological Complications

Our study suggests that postoperative risk reflects both anatomical complexity and patient vulnerability. Consistent with previous studies, the principal anatomical correlates were tumor diameter, CS invasion, and the degree of ICA and its major branch encasement.[12, 14, 15, 39, 41, 42] Tumor diameter was the strongest predictor of both medical complications and motor injuries. Baseline KPS informed both outcomes, and comorbidity burden and age additionally informed medical complications, supporting evidence that vulnerability is better characterized by comorbidity burden and functional reserve than by age alone.[43–46] In the cognitive model, age, preoperative deficits, and functional status carried more weight than tumor–vessel relationships, although with 16 development events the ranking of its predictors is imprecise. No reproducible model could be developed for visual deterioration. A recent study identified severe baseline visual impairment, radiographic optic nerve encasement, and abnormal optical coherence tomography findings as predictors of unfavorable visual outcomes.[21] These ophthalmological variables were not systematically available in our cohort, which likely limited the prediction.

Preoperative ML Models for Risk Estimation

We developed three parsimonious preoperative ML models with fixed predictor sets (seven variables for medical complications and eight for neurological outcomes) and evaluated them by internal–external cross-validation across centers and in geographically withheld cohorts. The medical model discriminated consistently in every center (pooled AUC 0.768) and reached 0.847 in the withheld cohort despite its more anatomically demanding tumors (Online Resource 1, Table S1); gradient boosting with 25 candidate variables reached 0.834 in the same cohort. Its clearest use is identifying lower-risk

patients: at a 10% threshold, the negative predictive value was 92.5%, and observed rates rose from 3.9% in the lowest tertile of predicted risk to 29.9% in the highest. The cognitive model, developed in a single center with 16 events, was the least mature; it discriminated modestly on internal validation, and its external AUC of 0.731 came with underestimation of absolute risk, so it requires recalibration before use. No clinically useful preoperative model could be built for surgical complications, consistent with the predominantly intraoperative and technical determinants of hematoma, wound infection, CSF leak, and hydrocephalus [47–49]. The medical and motor models, which were discriminated across centers, and the cognitive model, flagged as exploratory, were implemented in the online calculator.

Strengths and Limitations

The main strengths of our study are the large multinational cohort, the incorporation of a substantial number of patient-related variables to reflect vulnerability, and the development and validation of ML-derived preoperative risk models that have not been applied in this setting. This study had several limitations. The retrospective design, center-specific accrual periods spanning 2010–2025, and differences in case selection, surgical strategy, and perioperative practice introduced heterogeneity, affecting transportability. Event counts were small for the surgical (21) and cognitive (16 in the development center) endpoints, and neurological deficits were recorded unevenly across centers. The domain-specific neurological models were examined after the composite, so their confidence intervals did not account for the number of endpoints evaluated. Limited follow-up granularity and the absence of recurrence, radiotherapy, survival, and nonoperative comparison data preclude the determination of whether conservative resection improves the long-term balance between neurological preservation and tumor control. Given the imprecision and imperfect external calibration, the thresholds and calculators remain investigational and require validation and local recalibration before use.

CONCLUSION

In this multinational cohort study of first-time ACM resections, routinely available preoperative data enabled the prediction of medical complications, motor deficits, and cognitive decline. Shared predictors included tumor diameter, vessel encasement grade, and KPS. Comorbidity burden and age additionally informed medical risk; preoperative motor symptoms and involvement of the carotid siphon and cavernous sinus informed motor risk; and age, preoperative deficits, and functional status informed cognitive risk. The resulting models demonstrated consistent discrimination across geographically independent centers, although further external validation remains necessary. To support clinical translation, the models were incorporated into an investigational web-based calculator (<https://neurosurgpredict.com/anterior-clinoidal-meningioma/>). Subject to further validation and center-specific recalibration, this tool may help clinicians identify patients at increased risk of postoperative morbidity and tailor counseling, preoperative optimization, and surgical planning.

Abbreviations

ACM, anterior clinoidal meningioma; ASA, American Society of Anesthesiologists physical status classification; AUC, area under the receiver operating characteristic curve; CCI, Charlson Comorbidity Index; CI, confidence interval; CN, cranial nerve; CS, cavernous sinus; CSF, cerebrospinal fluid; DVT, deep vein thrombosis; EOR, extent of resection; FLAIR, fluid-attenuated inversion recovery; GTR, gross total resection; HGBC, histogram gradient boosting classifier; ICA, internal carotid artery; IQR, interquartile range; KPS, Karnofsky Performance Status; ML, machine learning; MRI, magnetic resonance imaging; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value; ROC, receiver operating characteristic; SBM, skull base meningioma; SD, standard deviation; STR, subtotal resection; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; TRIPOD+AI, Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis–Artificial Intelligence; WHO, World Health Organization.

Declarations

Funding. The authors declare that no funds, grants, or other support was received during the preparation of this manuscript.

Competing Interests. The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions. Conceptualization: NBD, AC; Methodology: NBD, GZ; Investigation / Data curation: NBD, GZ, FF, CB, DM, MM, MZ, LZ, LF, GC, FB, VR, FT, LT, HW, CJH, CEG, MDJ, MD; Formal analysis: NBD, GZ; Programming, software development, implementation of computer code and supporting algorithms: GZ; Visualization: NBD, GZ, AC; Writing – original draft: NBD; Writing – review and editing: all authors; Supervision: AC. All authors critically reviewed the manuscript for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability. The datasets generated and/or analyzed during the current study, the analysis code, the fitted coefficients, and the calculator equations are available from the corresponding author upon reasonable request.

Consent to Participate. The requirement for informed consent was waived because of the retrospective nature of the study.

Consent to Publish. Not applicable; the manuscript contains no identifiable data or images.

References

1. Cushing H, Meningiomas (1938) *Their Classification, Regional Behavior, Life History and Surgical End Results*. 298–319

2. Attia M, Umansky F, Paldor I, Dotan S, Shoshan Y, Spektor S (2012) Giant Anterior Clinoidal Meningiomas: Surgical Technique and Outcomes: Clinical Article. *JNS* 117, 654–665. 10.3171/2012.7.JNS111675
3. Pamir MN, Belirgen M, Özdoğan K, Kılıç T, Özek M (2008) Anterior Clinoidal Meningiomas: Analysis of 43 Consecutive Surgically Treated Cases. *Acta Neurochir (Wien)* 150:625–636. 10.1007/s00701-008-1594-x
4. Barzaghi LR, Pompeo E, Scudieri C, Albano L, Belladonna A, Mortini P (2024) Clinoidal Meningiomas. In *Neurosurgical Treatment of Central Nervous System Tumors*; Mortini, P., Gagliardi, F., Eds.; Springer Nature Switzerland: Cham, ; pp. 105–124 ISBN 978-3-031-68577-4
5. Ayoubi S, Dunn IF, Al-Mefty O (2012) Meningiomas. In *Brain Tumors*; Elsevier, ; pp. 600–629 ISBN 978-0-443-06967-3
6. GOEL A, GUPTA S, DESAI K (2000) New Grading System to Predict Resectability of Anterior Clinoid Meningiomas. *Neurol Med Chir (Tokyo)* 40:610–617. 10.2176/nmc.40.610
7. Al-Mefty O, Clinoidal, Meningiomas (1990) *J Neurosurg* 73:840–849. 10.3171/jns.1990.73.6.0840
8. Xu T, Yan Y, Evins AI, Gong Z, Jiang L, Sun H, Cai L, Wang H, Li W, Lu Y et al (2020) Anterior Clinoidal Meningiomas: Meningeal Anatomical Considerations and Surgical Implications. *Front Oncol* 10:634. 10.3389/fonc.2020.00634
9. Al-Mefty' F (ed) (2011)
10. Pradhan R, Misra BK, Hosmann A (2024) Quality of Life in Patients with Skull Base Meningiomas Treated with Microsurgery: A Prospective Observational Study. *Acta Neurochir (Wien)* 166:416. 10.1007/s00701-024-06291-9
11. Valencia-Ramos C, Del Arroyo JG, Aragon JF, Eguiluz-Mendez AG, Guinto-Nishimura GY, Sangrador-Deitos MV, Gómez Amador JL (2023) Prognostic Factors in the Surgery of Clinoidal Meningiomas. *Cureus* 10.7759/cureus.40122
12. Kim J-H, Jang W-Y, Jung T-Y, Kim I-Y, Lee K-H, Kang WD, Kim S-K, Moon K-S, Jung S (2017) Predictive Factors for Surgical Outcome in Anterior Clinoidal Meningiomas: Analysis of 59 Consecutive Surgically Treated Cases. *Med (Baltim)* 96:e6594. 10.1097/MD.0000000000006594
13. Chernov SV, Rzaev DA, Kalinovskiy AV, Dmitriev AB, Kasymov AR, Zotov AV, Gormolysova EV, Uzhakova EK (2017) Early Postoperative Results of Surgical Treatment of Patients with Anterior Clinoidal Meningiomas. *Vopr neurokhir* 81:74. 10.17116/neiro201780774-80
14. Giammattei L, Starnoni D, Levivier M, Messerer M, Daniel RT (2019) Surgery for Clinoidal Meningiomas: Case Series and Meta-Analysis of Outcomes and Complications. *World Neurosurg* 129:e700–e717. 10.1016/j.wneu.2019.05.253
15. Nanda A, Konar SK, Maiti TK, Bir SC, Guthikonda B (2016) Stratification of Predictive Factors to Assess Resectability and Surgical Outcome in Clinoidal Meningioma. *Clin Neurol Neurosurg* 142:31–37. 10.1016/j.clineuro.2016.01.005
16. Cuschieri S (2019) The STROBE Guidelines. *Saudi J Anaesth* 13:31. 10.4103/sja.SJA_543_18

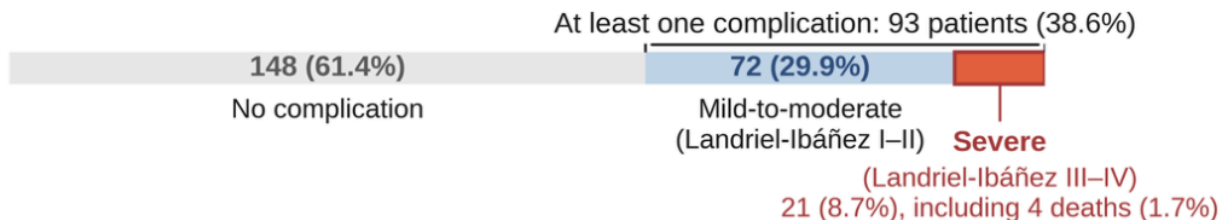
17. Collins GS, Moons KGM, Dhiman P, Riley RD, Beam AL, Van Calster B, Ghassemi M, Liu X, Reitsma JB, Van Smeden M et al (2024) TRIPOD + AI Statement: Updated Guidance for Reporting Clinical Prediction Models That Use Regression or Machine Learning Methods. *BMJ* e078378. 10.1136/bmj-2023-078378
18. Ening G, Osterheld F, Capper D, Schmieder K, Brenke C (2015) Charlson Comorbidity Index: An Additional Prognostic Parameter for Preoperative Glioblastoma Patient Stratification. *J Cancer Res Clin Oncol* 141:1131–1137. 10.1007/s00432-014-1907-9
19. Daabiss M (2011) American Society of Anaesthesiologists Physical Status Classification. *Indian J Anaesth* 55:111–115. 10.4103/0019-5049.79879
20. Karnofsky DA, Abelmann WH, Craver LF, Burchenal JH (1948) The Use of the Nitrogen Mustards in the Palliative Treatment of Carcinoma. With Particular Reference to Bronchogenic Carcinoma. *Cancer* 1:634–656. 10.1002/1097-0142(194811)1:4%3C634::AID-CNCR2820010410%3E3.0.CO;2-L
21. Cohen-Cohen S, Graffeo CS, Botello-Hernandez E, Carlstrom LP, Perry A, Tooley AA, Link MJ (2024) Anterior Clinoid Meningiomas: Surgical Results and Proposed Scoring System to Predict Visual Outcomes. *J Neurosurg* 140:1295–1304. 10.3171/2023.8.JNS23894
22. Ibañez FAL, Hem S, Ajler P, Vecchi E, Ciralo C, Baccanelli M, Tramontano R, Knezevich F, Carrizo A (2011) A New Classification of Complications in Neurosurgery. *World Neurosurg* 75:709–715. 10.1016/j.wneu.2010.11.010
23. Gozal YM, Aktüre E, Ravindra VM, Scoville JP, Jensen RL, Couldwell WT, Taussky P (2020) Defining a New Neurosurgical Complication Classification: Lessons Learned from a Monthly Morbidity and Mortality Conference. *Journal of Neurosurgery* 132, 272–276. 10.3171/2018.9.JNS181004
24. Sawaya R, Hammoud M, Schoppa D, Hess KR, Wu SZ, Shi W-M, Wildrick DM (1998) Neurosurgical Outcomes in a Modern Series of 400 Craniotomies for Treatment of Parenchymal Tumors. *Neurosurgery* 42:1044–1055. 10.1097/00006123-199805000-00054
25. Nhat-Duc H, Van-Duc T (2023) Comparison of Histogram-Based Gradient Boosting Classification Machine, Random Forest, and Deep Convolutional Neural Network for Pavement Raveling Severity Classification. *Autom Constr* 148:104767. 10.1016/j.autcon.2023.104767
26. Pavlou M, Ambler G, Seaman S, De Iorio M, Omar RZ (2016) Review and Evaluation of Penalised Regression Methods for Risk Prediction in Low-Dimensional Data with Few Events. *Stat Med* 35:1159–1177. 10.1002/sim.6782
27. Steyerberg EW, Harrell FE (2016) Prediction Models Need Appropriate Internal, Internal–External, and External Validation. *J Clin Epidemiol* 69:245–247. 10.1016/j.jclinepi.2015.04.005
28. Takada T, Nijman S, Denaxas S, Snell KIE, Uijl A, Nguyen T-L, Asselbergs FW, Debray TPA (2021) Internal-External Cross-Validation Helped to Evaluate the Generalizability of Prediction Models in Large Clustered Datasets. *J Clin Epidemiol* 137:83–91. 10.1016/j.jclinepi.2021.03.025
29. Luzzi S, Giotta Lucifero A, Bruno N, Baldoncini M, Campero A, Galzio R (2022) Pterional Approach. *Acta Biomed* 92:e2021346. 10.23750/abm.v92iS4.12775

30. Subfrontal (2020) and Bifrontal Craniotomies with or without Orbital Osteotomy. In *Core Techniques in Operative Neurosurgery*; Elsevier, ; pp. 79–82 ISBN 978-0-323-52381-3
31. Torp SH, Solheim O, Skjulsvik AJ (2022) The WHO 2021 Classification of Central Nervous System Tumours: A Practical Update on What Neurosurgeons Need to Know-a Minireview. *Acta Neurochir (Wien)* 164:2453–2464. 10.1007/s00701-022-05301-y
32. Starnoni D, Tuleasca C, Levivier M, Daniel RT (2022) Surgery for Clinoidal Meningiomas with Cavernous Sinus Extension: Near-Total Excision and Chiasmopexy. *Acta Neurochir* 164:2511–2515. 10.1007/s00701-022-05281-z
33. Goldman MJ, Teh BS, Lo SS, Butler EB, Baskin DS (2024) Radiosurgery for Intracranial Meningiomas: A Review of Anatomical Challenges and an Update on the Evidence. *Cancers* 17. 10.3390/cancers17010045
34. Akyoldaş G, Hergünel ÖB, Yılmaz M, Şengöz M, Peker S (2020) Gamma Knife Radiosurgery for Anterior Clinoid Process Meningiomas: A Series of 61 Consecutive Patients. *World Neurosurg* 133:e529–e534. 10.1016/j.wneu.2019.09.089
35. Acker G, Kluge A, Lukas M, Conti A, Pasemann D, Meinert F, Anh Nguyen PT, Jelgersma C, Loebel F, Budach V et al (2019) Impact of 68Ga-DOTATOC PET/MRI on Robotic Radiosurgery Treatment Planning in Meningioma Patients: First Experiences in a Single Institution. *NeuroSurg Focus* 46:E9. 10.3171/2019.3.FOCUS1925
36. Conti A, Pontoriero A, Salamone I, Siragusa C, Midili F, La Torre D, Calisto A, Granata F, Romanelli P, De Renzis C et al (2009) Protecting Venous Structures during Radiosurgery for Parasagittal Meningiomas: Technical Note. *FOC* 27, E11. 10.3171/2009.8.FOCUS09-157
37. Raffa G, Picht T, Scibilia A, Rösler J, Rein J, Conti A, Ricciardo G, Cardali SM, Vajkoczy P, Germanò A (2020) Surgical Treatment of Meningiomas Located in the Rolandic Area: The Role of Navigated Transcranial Magnetic Stimulation for Preoperative Planning, Surgical Strategy, and Prediction of Arachnoidal Cleavage and Motor Outcome. *J Neurosurg* 133:107–118. 10.3171/2019.3.JNS183411
38. Minutoli F, Amato E, Sindoni A, Cardile D, Conti A, Herberg A, Baldari S (2014) Peptide Receptor Radionuclide Therapy in Patients with Inoperable Meningiomas: Our Experience and Review of the Literature. *Cancer Biotherapy Radiopharmaceuticals* 29:193–199. 10.1089/cbr.2013.1599
39. Bassiouni H, Asgari S, Sandalcioglu IE, Seifert V, Stolke D, Marquardt G (2009) Anterior Clinoidal Meningiomas: Functional Outcome after Microsurgical Resection in a Consecutive Series of 106 Patients. *JNS* 111:1078–1090. 10.3171/2009.3.17685
40. Arnautovic KI, Lasica N (2025) Update on Anterior Clinoid Process Removal in Anterior Clinoid Meningioma Surgery: Literature Review, and a New Didactical Concept. *Acta Neurochir* 167:335. 10.1007/s00701-025-06742-x
41. Czernicki T, Kunert P, Nowak A, Marchel A (2015) Results of Surgical Treatment of Anterior Clinoidal Meningiomas – Our Experiences. *Neurol Neurochir Pol* 49:29–35. 10.1016/j.pjnns.2015.01.003
42. Chen L-H, Xia Y, Wei F, Sun K, Huang H-Z, Xu R-X (2023) The Factors Influencing Postoperative Efficacy of Anterior Clinoidal Meningioma Treatment and an Analysis of Best-Suited Surgical

- Strategies. *Front Neurol* 14:1097686. 10.3389/fneur.2023.1097686
43. Muhlestein W, Akagi D, Chotai S, Chambless L (2017) The Impact of Presurgical Comorbidities on Discharge Disposition and Length of Hospitalization Following Craniotomy for Brain Tumor. *Surg Neurol Int* 8:220. 10.4103/sni.sni_54_17
44. Quinn TJ (2025) Assessing the Tools for Assessing Frailty. *JACC Asia* 5:811–813. 10.1016/j.jacasi.2025.03.006
45. Giaccherini L, Galaverni M, Renna I, Timon G, Galeandro M, Pisanello A, Russo M, Botti A, Iotti C, Ciammella P (2019) Role of Multidimensional Assessment of Frailty in Predicting Outcomes in Older Patients with Glioblastoma Treated with Adjuvant Concurrent Chemo-Radiation. *J Geriatr Oncol* 10:770–778. 10.1016/j.jgo.2019.03.009
46. Ben Dor N, Friso F, Ziv G, Bortolotti C, Martinoni M, Badaloni F, Corazzelli G, Rustici A, Balestrini D, Scibilia A et al (2026) Machine Learning–Enhanced Prognostic Modelling in Elderly Glioblastoma Isocitrate Dehydrogenase-Wildtype: A Multidimensional Single-Center Cohort Study. *World Neurosurg* 206:124754. 10.1016/j.wneu.2025.124754
47. Palermo M, Zeoli F, Rastegar V, Sturiale CL, Signorelli F (2025) Risk Factors for Postoperative Cerebrospinal Fluid Fistulas After Craniotomy and Craniectomy: A Systematic Review and Meta-Analysis. *Acta Neurochir (Wien)* 167:264. 10.1007/s00701-025-06685-3
48. Lemée J-M, Corniola MV, Da Broi M, Schaller K, Meling TR (2019) Early Postoperative Complications in Meningioma: Predictive Factors and Impact on Outcome. *World Neurosurg* 128:e851–e858. 10.1016/j.wneu.2019.05.010
49. Burkhardt J-K, Zinn PO, Graenicher M, Santillan A, Bozinov O, Kasper EM, Krayenbühl N (2011) Predicting Postoperative Hydrocephalus in 227 Patients with Skull Base Meningioma. *FOC* 30, E9. 10.3171/2011.3.focus117

Figures

a



b

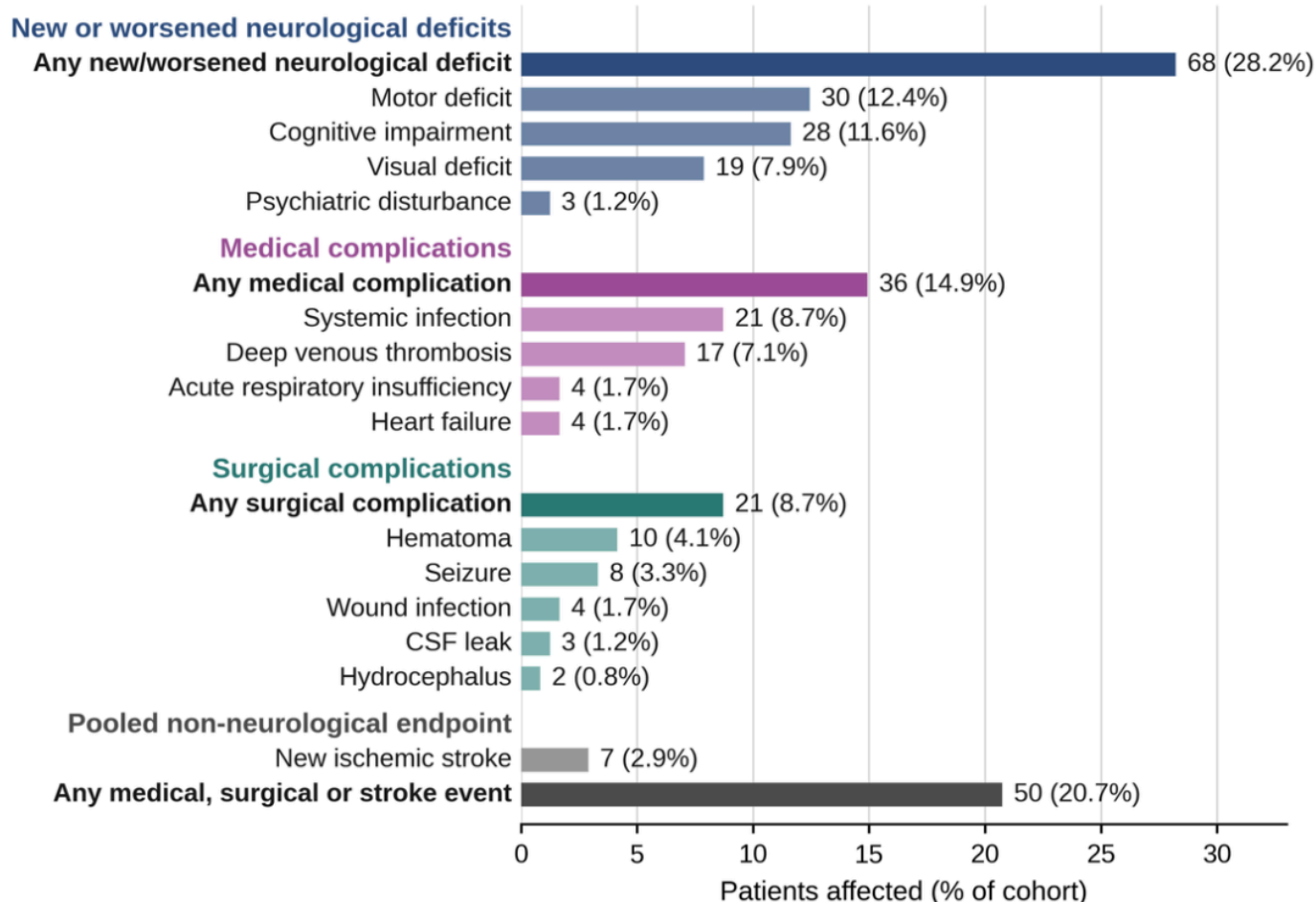


Figure 1

Postoperative complications in the pooled cohort (N = 241). a, Overall complication burden and maximum severity per patient graded by the Landriel-Ibáñez classification. b, Type and frequency of new or worsened neurological deficits at discharge, medical and surgical complications, new ischemic stroke (assigned to the neurological domain), and the pooled non-neurological endpoint. Bold bars indicate composite endpoints; categories are not mutually exclusive; therefore, components do not sum to the composite, and percentages do not total 100%. The severity and management outcomes are presented in Table 2. Three patients with recorded complications but no assigned Landriel-Ibáñez grade were classified as mild-to-moderate. CSF, cerebrospinal fluid

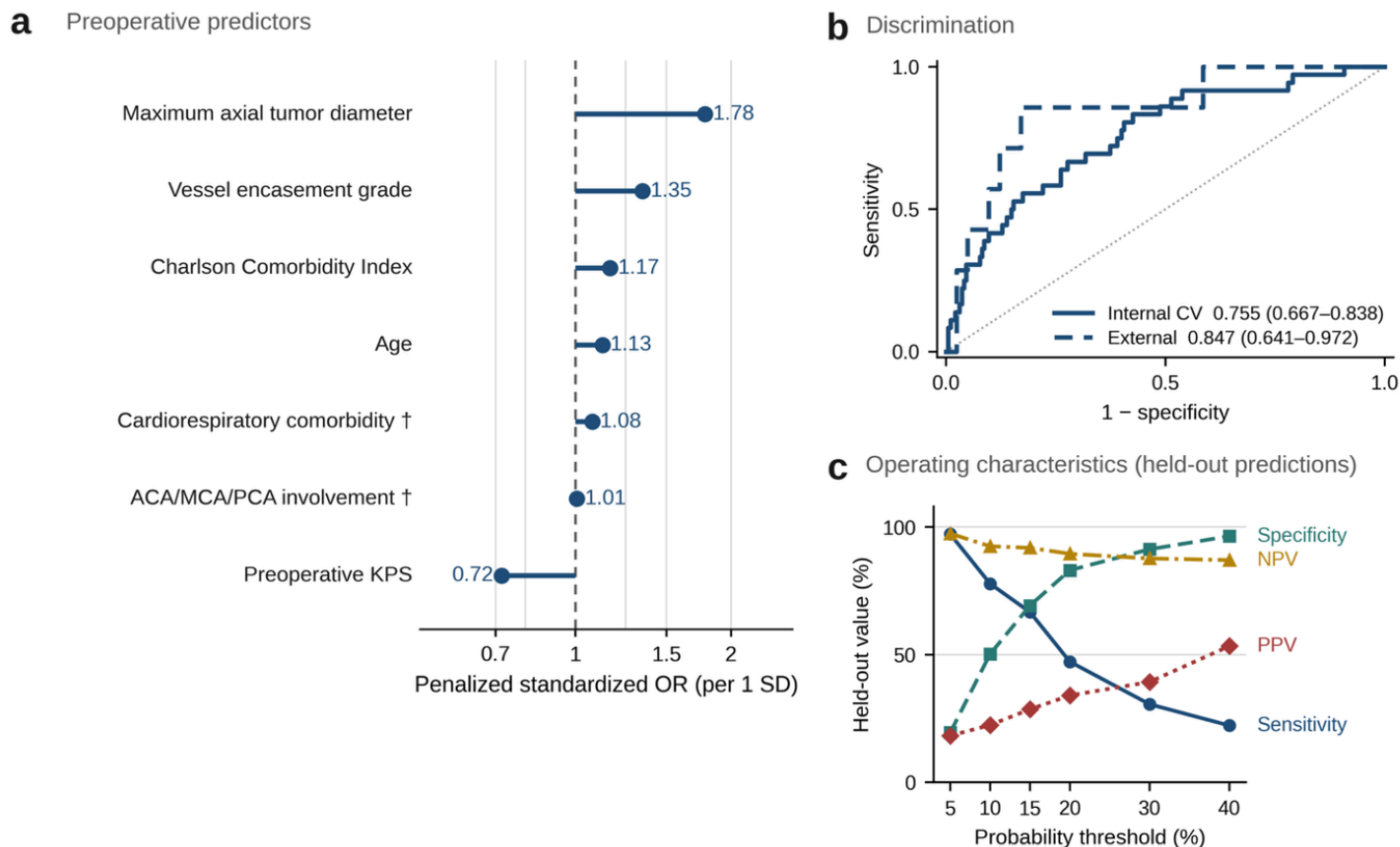


Figure 2

Medical complications ($n = 231$, 36 events): preoperative predictors, discrimination, and operating characteristics of the ridge-penalized model. **a**, Standardized odds ratios per 1-SD increase on a logarithmic scale; the dashed line marks unity. Estimates are ridge-penalized and therefore shrunk toward 1, and confidence intervals are not shown because penalized coefficients have no valid closed-form standard errors. †Binary predictor: the 1-SD scaling is a statistical convention and does not correspond to the presence or absence of a condition. **b**, Receiver operating characteristic curves. The solid line indicates internal cross-validation in all 231 patients (out-of-fold predictions averaged over the five repeats; the AUC given is the mean across repeats); the dashed line indicates geographical external validation in Liverpool (48 patients) of the model fitted in Bologna and Cesena; the dotted diagonal indicates chance. Areas under the curve are given with 95% percentile bootstrap confidence intervals. **c**, Sensitivity, specificity, positive predictive value, and negative predictive value of the held-out predictions from internal–external cross-validation across probability thresholds. AUC, area under the receiver operating characteristic curve; CV, cross-validation; KPS, Karnofsky Performance Status; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value

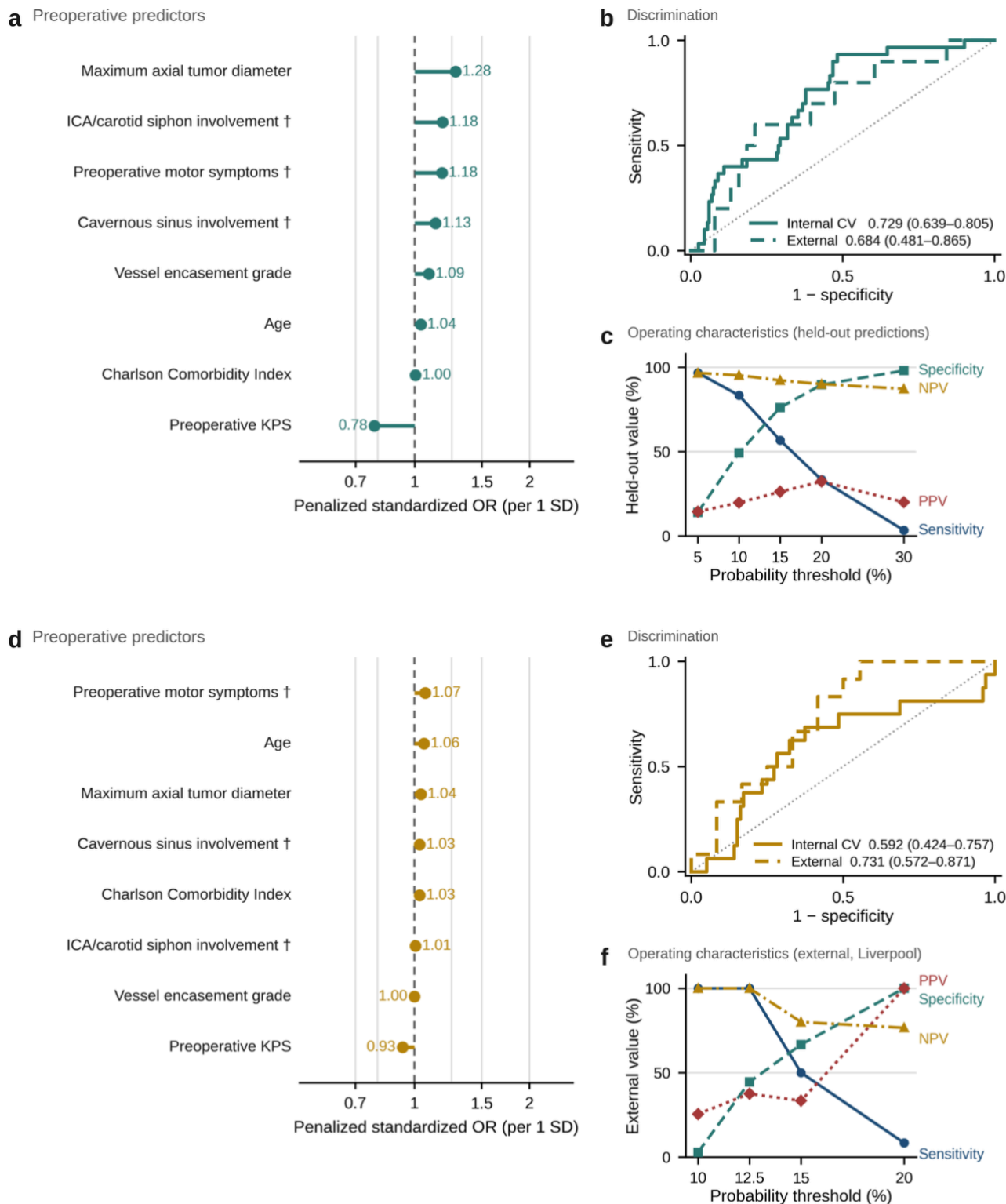


Figure 3

New or worsened motor deficit (a–c; $n = 231$, 30 events) and cognitive decline (d–f; model developed in Bologna, 115 patients, 16 events): preoperative predictors, discrimination, and operating characteristics of the ridge-penalized models. a, d, Standardized odds ratios per 1-SD increase on a logarithmic scale, shown as in Fig. 2a; †binary predictor. b, e, Receiver operating characteristic curves. Solid lines indicate internal cross-validation (out-of-fold predictions averaged over the five repeats; the AUC given is the

mean across repeats), in all 231 patients for the motor model and in Bologna (115 patients) for the cognitive model; dashed lines indicate geographical external validation in Liverpool (48 patients) of models fitted in Bologna and Cesena (motor) or in Bologna alone (cognitive); dotted diagonals indicate chance. Areas under the curve are given with 95% percentile bootstrap confidence intervals. c, Sensitivity, specificity, positive predictive value, and negative predictive value of the held-out predictions from internal–external cross-validation across probability thresholds. f, The same for the external predictions of the cognitive model in Liverpool; because its predicted risks ranged from 9.6% to 20.2%, thresholds are shown within that range. AUC, area under the receiver operating characteristic curve; CV, cross-validation; KPS, Karnofsky Performance Status; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [ESM1.docx](#)
- [ESM2.docx](#)
- [ESM3.docx](#)