



Predictors of Permanent and Temporary Motor Deficits in Patients Undergoing Glioma Resection: A Systematic Review and Meta-Analysis

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■ **OBJECTIVE:** To identify predictors of permanent and temporary motor deficits in patients undergoing glioma resection.

■ **METHODS:** A literature search accessed the databases Ovid Medline, Scopus, Web of Science, Cumulative Index to Nursing and Allied Health Literature/EBSCO, PsychInfo, Cochrane, and Wiley for studies reporting motor outcomes following surgical resection of glioma. Outcomes were stratified by patient/tumor characteristics, preoperative condition, and intraoperative factors for both permanent and temporary motor deficits. Generalized estimating equations were used to generate odds ratios.

■ **RESULTS:** A total of 1332 titles and abstracts were reviewed resulting in the evaluation of 261 full-text articles. Data were extracted from 67 studies including 2616 patients with 371 (14%) developing permanent postoperative motor deficits, 465 (18%) developing temporary deficits, and the remaining 1780 (68%) having no deficit. Preoperative deficit was the most significant predictor of permanent postoperative motor deficit (odds ratio [OR] 6.40, confidence interval [CI] 2.82–14.5, $P < 0.0001$), while high preoperative Karnofsky Performance Scale (OR 0.98, CI 0.97–0.99, $P < 0.001$) and subcortical tumor location (OR 0.14, CI 0.030–0.62, $P = 0.001$) had a lower odds of a permanent deficit. Intraoperative motor-evoked potential

changes was a significant predictor of both permanent (OR 5.18, CI 1.99–13.5, $P = 0.00075$) and temporary (OR 9.44, CI 2.78–32.0, $P = 0.0003$) motor deficits.

■ **CONCLUSIONS:** Preoperative motor deficits were the most significant predictors of persistent or worsening postoperative motor deficits. Intraoperative motor-evoked potential changes were associated with both permanent and temporary deficits. High Karnofsky Performance Scale and subcortical tumor location had lower odds of permanent motor deficits.

INTRODUCTION

Gliomas are the most prevalent primary adult brain tumor with an incidence of 6 per 100,000 people in the U.S.¹ They are associated with profound morbidities such as seizures, aphasia, cognitive impairments, and motor deficits.² Additionally, glioblastoma, the most severe form of glioma, has a 5-year survival rate of only 5%¹ and median survival rate of two years with high treatment compliance.^{3,4} Standard of care treatment starts with maximal safe resection due to its proven survival benefit.⁵ Although achieving gross total resection ($\geq 95\%$ removal radiographically) has been shown to maximize survival,⁵ this may not be possible without causing a neurological deficit

Key words

- Extent of resection
- Glioma
- Karnofsky Performance Scale
- Postoperative motor deficit
- Preoperative motor deficit
- Subcortical tumor

Abbreviations and Acronyms

- CI: Confidence interval
- GEE: Generalized estimating equation
- KPS: Karnofsky Performance Scale
- MEP: Motor-evoked potential
- MRI: Magnetic resonance imaging
- OR: Odds ratio
- SEP: Somatosensory-evoked potential
- SMA: Supplementary motor area

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when tumors invade areas of the brain critical for daily function, such as the primary motor cortex (M1).^{2,6} Unfortunately, causing a permanent motor deficit from surgery has also been demonstrated to negate any survival benefit from extensive resection.⁷

Because of this evidence, preservation of function typically takes precedence over extent of resection in most cases. Prior studies have aimed to determine patient, tumor, and surgical characteristics associated with improved survival.^{8,9} However, current evidence on functional motor outcomes following glioma resection is limited to a small number of case series, retrospective analyses, and reviews.² Thus, in many cases, it can be challenging to determine functional prognosis for patients with gliomas undergoing surgery (i.e., who will recover function and who will not). Moreover, there are mixed results on which neurosurgical practices are associated with either temporary or permanent postoperative deficits.¹⁰

Here we systematically reviewed the literature to generate the first meta-analysis of predictors of motor deficits following glioma resections with the hope that pooling our collective experience will lead to insights potentially unseen in smaller, individual studies. We analyzed published literature from 1986 to the present, as this is the year temozolomide was first introduced in humans, thereby altering the standard of care treatment pathway for gliomas.¹¹ We examined patient and tumor characteristics, preoperative motor status, and neurosurgical practices as potential variables impacting postoperative motor deficits.

MATERIALS AND METHODS

Literature Search

A literature search of the databases Ovid Medline, Scopus, Web of Science, Cumulative Index to Nursing and Allied Health Literature/EBSCO, PsychInfo, Cochrane, and Wiley was performed by a medical sciences librarian to identify relevant articles between 1986 and 2024. Search terms included the MeSH headings and other terms related to gliomas, surgery, motor deficit, sensation disorders, and ataxia (**Supplemental Tables 1–6**). This yielded 1332 titles and abstracts after duplicates were removed, which were examined by two independent reviewers (B.C. and S.A.) for the following inclusion criteria: 1) surgical treatment of intracranial gliomas, 2) motor and/or sensory neurological deficit after surgery of gliomas, 3) publication between 1986 and 2024,¹¹ 4) availability in English language, and 5) patients above the age of 18.¹² Of all titles and abstracts, 261 met criteria for full-text examination for the following exclusion criteria: 1) studies/series with less than five patients reporting outcomes of interest, 2) review articles, 3) insufficient data on motor outcomes of interest, or 4) studies in languages other than English that are not otherwise available in English. Ultimately, 67 studies with a total of 2616 patients were identified and included in the analyses (**Figure 1**).^{13–79} In cases when one of the studies included patients with gliomas as well as other tumors (e.g. meningioma, metastasis), the non-glioma patients were excluded when it was possible to determine their postoperative motor outcome. The literature search and study design were guided by preferred reporting items for systematic reviews and meta-analyses guidelines.⁸⁰

Data Collection

Full text-manuscripts were reviewed and outcomes following surgical resection of gliomas were classified as permanent motor deficit, temporary motor deficit, or no motor deficit based on manual muscle testing data (e.g. 3/5) or qualitative descriptions of deficits (e.g., upper extremity hemiparesis). A permanent motor deficit was defined as any sort of motor deficit present three months postoperatively or later, and it was considered temporary if it resolved by three months or sooner. To investigate predictors of motor deficits, data for the following variables were extracted as available: sex, age, tumor size, histological grade (WHO classification), tumor cell type, hemisphere, tumor lobe location, tumor depth (subcortical or superficial), Karnofsky Performance Scale (KPS), preoperative motor deficit, preoperative sensory deficit, intraoperative motor-evoked potential (MEP) changes, intraoperative somatosensory-evoked potential (SEP) changes, use of intraoperative MEP monitoring, use of any intraoperative monitoring, craniotomy type, extent of resection, and supratotal resection.

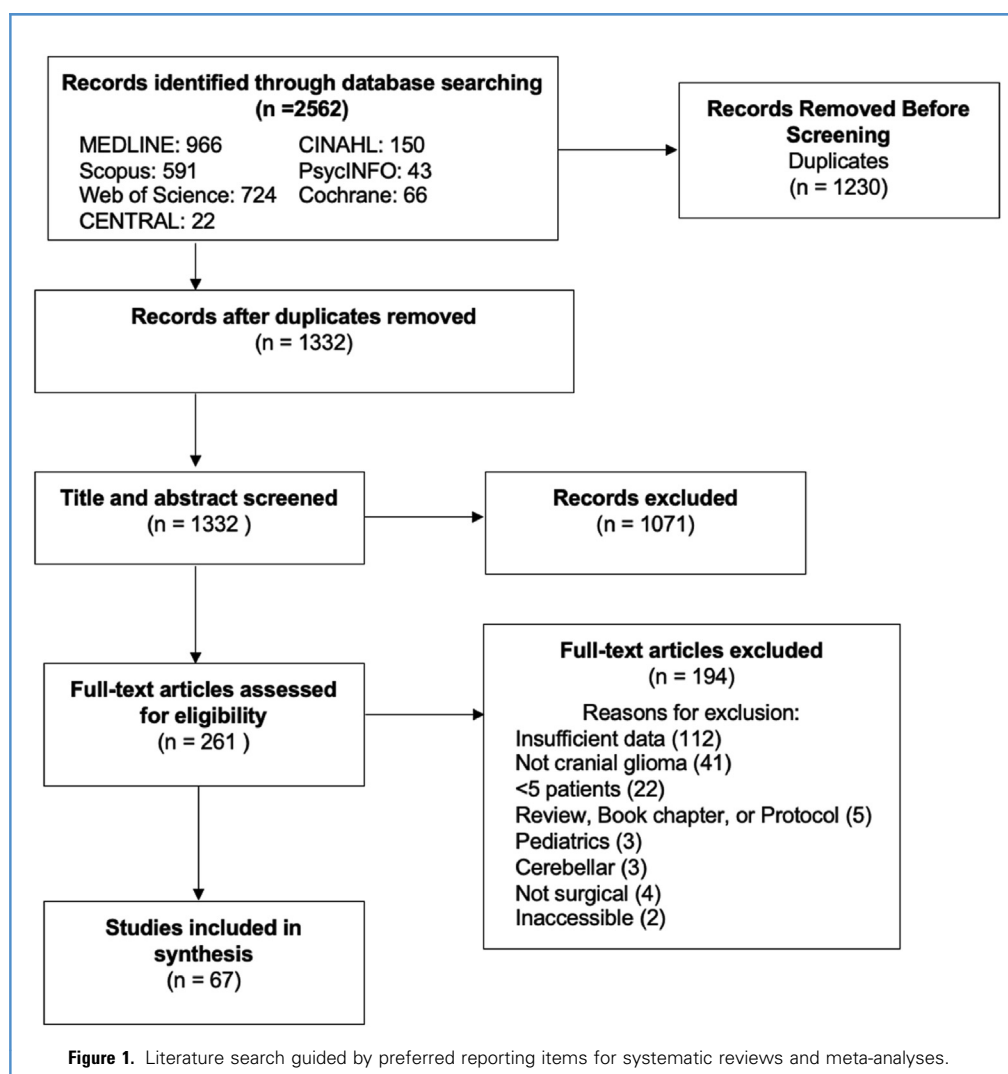
Tumor histological grade was classified as either high (III or IV) or low (I or II), and cell type as astrocytoma or other (oligodendroglioma, ependymoma, neuroepithelial, ganglioglioma, other). Tumor location was noted as either left or right hemisphere and either frontal lobe or other. When available, the presence or absence of preoperative motor or sensory deficit was recorded. The presence or absence of any sort of intraoperative monitoring was recorded. Possible modalities of intraoperative monitoring included awake monitoring, use of MEP or SEP, or subjective monitoring of muscle contraction while the patient was under general anesthesia. Craniotomy type was classified as either awake or asleep (i.e., under general anesthesia). Extent of resection was documented as gross total ($\geq 95\%$ pathological enhancement) or subtotal.

Statistical Analysis

As preliminary analysis, univariate analysis was performed to compare postoperative motor deficit outcomes as they pertained to each variable of interest. Pearson's χ^2 test was performed on categorical variables and Wilcoxon signed-rank test was performed on continuous variables to compare permanent motor deficit versus no permanent deficit and to compare temporary motor deficit versus no motor deficit. Missing data were excluded from preliminary analysis. Significance was defined as $P < 0.05$. Using a stepwise variable selection approach, generalized estimating equations (GEEs) models with the logit link function were used to identify an optimal set of predictors for both permanent and temporary motor deficits. Missing data were included as factors in the GEEs models. Goodness-of-fit was determined by the model with quasi-likelihood information criterion while optimizing the inclusion of appropriate predictors. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to construct Forest plots. All statistical analysis was performed in R (2025).

Results

Data from 607 patients across 67 studies were analyzed (**Table 1**). No randomized or controlled trials were identified. Permanent deficits occurred in 14% of all patients included while temporary



deficit occurred in 18%, and 68% of patients had no postoperative motor deficit. Variables found to be potentially associated with permanent motor deficit in patients undergoing resection of gliomas on preliminary analysis included: high grade tumors ($P = 0.04$), preoperative motor deficit ($P < 0.0001$), intraoperative MEP changes ($P < 0.0001$). Use of intraoperative monitoring was associated with decreased rate of permanent motor deficits ($P = 0.085$) (Table 2). Variables that were associated with temporary motor deficit in patients undergoing resection of gliomas on preliminary analysis included: low grade tumors ($P = 0.009$), frontal lobe tumor location ($P = 0.001$), intraoperative MEP changes ($P < 0.0001$), awake craniotomy ($P < 0.0001$), and supra-total resection ($P = 0.03$) (Table 3).

GEEs were applied to determine predictors of permanent and temporary postoperative motor deficit by adding appropriate variables in a stepwise progression to achieve a low QIC (Figures 2 and 3). Higher odds of permanent postoperative motor deficit following resection of glioma were identified in patients with a

preoperative deficit over no deficit (OR 6.40, CI 2.82–14.5, $P < 0.0001$), and this was the most commonly reported factor among our variables of interest.^{13,14,16,18,19,21–24,28,30–37,39–41,43,46–48,50,53,57,62,63,66,75–77,79} The next greatest predictor of permanent postoperative motor deficit was intraoperative MEP changes (OR 5.18, CI 1.99–13.5, $P = 0.00075$). A greater preoperative KPS (OR 0.98, CI 0.97–0.99, $P < 0.0001$) and subcortical rather than superficial tumor location (OR 0.14, CI 0.030–0.62, $P = 0.001$) had a lower odds of permanent postoperative motor deficit. Other nonsignificant variables included in the model were right hemisphere compared to left (OR 1.29, CI 0.73–2.28), frontal lobe tumors compared to other locations (OR 1.20, CI 0.68–2.10), astrocytoma compared to other tumor cell types (OR 1.32, CI 0.65–2.68), awake versus asleep craniotomy (OR 1.44, CI 0.74–2.80), and use of any intraoperative monitoring (OR 0.86, CI 0.30–2.45). Missing data were not significant for any of the predictors included in the model.

Table 1. Studies Included in Analysis

First Author	Year	No Deficit	Temporary Deficit	Permanent Deficit
		1780 (68)	465 (18)	371 (14)
Abdoul-Enein	2015	5 (100)	0 (0)	0 (0)
Akiyama	2017	7 (100)	0 (0)	0 (0)
Bai	2011	58 (59)	38 (38)	3 (3)
Barz	2018	11 (61)	0 (0)	7 (39)
Berger	2022	172 (72)	0 (0)	67 (28)
Burks	2016	44 (79)	0 (0)	12 (21)
Carraba	2007	84 (60)	55 (40)	0 (0)
Chen	2018	63 (100)	0 (0)	0 (0)
Clavreul	2021	41 (89)	0 (0)	5 (11)
D'elia	2022	2 (7)	23 (79)	4 (14)
Fandino	1999	4 (57)	1 (14)	2 (29)
Firsching	2002	3 (30)	0 (0)	7 (70)
Fukaya	2003	10 (53)	5 (26)	4 (21)
Gempt	2013	47 (67)	13 (19)	10 (14)
Gong	2022	86 (91)	0 (0)	9 (9)
Gulati	2009	18 (72)	0 (0)	7 (28)
Ille	2021	59 (82)	3 (4)	10 (4)
Iyer	2018	10 (100)	0 (0)	0 (0)
Kombos	2009	12 (80)	3 (20)	0 (0)
Krainik	2004	0 (0)	10 (83)	2 (17)
Krieg	2012	77 (69)	21 (19)	14 (12)
Lang	2001	15 (75)	1 (5)	4 (20)
Lang	2017	9 (100)	0 (0)	0 (0)
Leote	2020	13 (68)	0 (0)	6 (32)
Lutz	2023	7 (58)	5 (42)	0 (0)
Mikuni	2007	6 (67)	3 (33)	0 (0)
Morshed	2024	154 (96)	0 (0)	6 (4)
Moser	2017	28 (65)	6 (14)	9 (21)
Muir	2022	35 (83)	0 (0)	7 (17)
Nakjima	2015	0 (0)	7 (88)	1 (13)
Nakajima	2020	21 (78)	0 (0)	6 (22)
Nakajima	2021	20 (63)	11 (34)	1 (3)
Neuloh	2007	51 (70)	13 (18)	9 (12)
Noell	2015	17 (68)	4 (16)	4 (16)
Ohue	2015	1 (3)	19 (63)	10 (33)
Ojemann	1996	13 (93)	0 (0)	1 (7)
Politicchio	2020	6 (32)	9 (47)	4 (21)
Continues				

Table 1. Continued

First Author	Year	No Deficit	Temporary Deficit	Permanent Deficit
Quinones-Hinojosa	2017	23 (100)	0 (0)	0 (0)
Raffa	2017	20 (65)	1 (3)	10 (32)
Rech	2017	2 (16)	5 (42)	5 (42)
Reithmeier	2003	32 (100)	0 (0)	0 (0)
Rosenberg	2010	20 (100)	0 (0)	0 (0)
Rosenstock	2017	17 (57)	5 (16)	8 (27)
Rosenstock	2021	50 (82)	2 (3)	9 (15)
Rosenstock	2022	129 (78)	16 (10)	20 (12)
Saito	2017	5 (100)	0 (0)	0 (0)
Saito	2021	20 (56)	12 (33)	4 (11)
Sakurada	2012	23 (77)	2 (7)	5 (16)
Sarmiento	2015	0 (0)	12 (80)	3 (20)
Schucht	2013	0 (0)	0 (0)	5 (100)
Schucht	2014	47 (70)	17 (25)	3 (5)
Seidel	2019	0 (0)	4 (33)	8 (67)
Takakura	2017	2 (14)	4 (29)	8 (57)
Tamura	2022	2 (20)	2 (20)	6 (60)
Tate	2011	0 (0)	19 (86)	3 (14)
Vassal	2013	0 (0)	7 (100)	0 (0)
Vassal	2017	0 (0)	6 (100)	0 (0)
Voets	2020	17 (61)	9 (32)	2 (7)
Weiss Lucas	2020	24 (67)	7 (19)	5 (4)
Weiss Lucas	2022	30 (49)	26 (43)	5 (8)
Wu	2014	0 (0)	17 (77)	5 (23)
Yamamoto	2004	19 (51)	12 (32)	6 (16)
Yang	2024	30 (71)	7 (17)	5 (12)
Yu	2021	11 (100)	0 (0)	0 (0)
Yuanzheng	2014	25 (64)	12 (31)	2 (5)
Zhou	2021	23 (72)	4 (13)	5 (16)
Zhu	2012	0 (0)	7 (47)	8 (53)

Higher odds of temporary postoperative motor deficits following resection of glioma were identified in patients with intraoperative MEP changes temporary motor deficit was intraoperative MEP changes (OR 9.44, CI 2.78–32.0, $P = 0.0003$). Other nonsignificant variables included in the model were intraoperative MEP monitoring (OR 92.3, CI 0.60–1.14 $\times 10^4$), subcortical rather than superficial tumor location (OR 4.75, CI 0.27–85.1), frontal lobe tumor location versus other lobes (OR 0.99, CI 0.38–2.57), awake compared to asleep craniotomy (OR 3.79 CI 0.95–15.0), astrocytoma compared to other cell types (OR

Table 2. Pearson's χ^2 Test was Performed to Compare Categorical Variables

Independent Variable	No Permanent Motor Deficit (%)	Permanent Motor Deficit (%)	P Value
Total	2245 (86)	371 (14)	
Patient and tumor characteristics			
Sex			
Female	156 (73)	57 (27)	0.06
Male	254 (49)	61 (51)	
Missing	1835	253	
Age (SD), n	47.5 (15.1), 422	50.7 (16.8), 118	0.09
Missing	1823	253	
Size (SD), n	45.3 (37.6), 74	51.6 (32), 25	0.198
Missing	2171	346	
Histological grade			
Low grade	263 (83)	53 (17)	0.04
High grade	511 (77)	150 (23)	
Missing	1471	168	
Astrocytoma			
Other	88 (81)	20 (19)	0.271
Astrocytoma	582 (76)	182 (24)	
Missing	1704	165	
Hemisphere			
Left	171 (78)	47 (22)	0.198
Right	154 (73)	58 (27)	
Missing	1920	266	
Tumor lobe location			
Other	267 (80)	66 (20)	0.426
Frontal	274 (77)	80 (23)	
Missing	1704	225	
Tumor depth			
Superficial	73 (79)	19 (21)	0.072
Subcortical	41 (93)	3 (7)	
Missing	2131	349	
Preoperative condition			
KPS (SD), n	73.5 (15.8), 48	68.6 (13.5), 14	0.358
Missing	2197	357	
Preoperative motor deficit			
No deficit	485 (87)	70 (13)	<0.0001
Motor deficit	83 (56)	65 (44)	
Missing	1677	236	
Continues			

Table 2. Continued

Independent Variable	No Permanent Motor Deficit (%)	Permanent Motor Deficit (%)	P Value
Preoperative sensory deficit			
No deficit	154 (82)	33 (18)	1
Sensory deficit	2 (100)	0 (0)	
Missing	2089	338	
Procedure variables			
Intraoperative MEP changes			
No change	195 (92)	18 (8)	<0.0001
Yes change	100 (70)	42 (30)	
Missing	1950	311	
Intraoperative SEP monitoring			
No SEP	126 (86)	20 (14)	0.885
Yes SEP	120 (88)	17 (12)	
Missing	1999	334	
Intraoperative MEP Monitoring			
No MEP	14 (100)	0 (0)	0.26
Yes MEP	1227 (86)	199 (14)	
Missing	1004	172	
Any intraoperative monitoring			
No monitoring	35 (69)	16 (31)	0.0085
Yes Monitoring	1434 (84)	281 (16)	
Missing	776	74	
Craniotomy type			
Asleep	644 (88)	92 (12)	0.111
Awake	511 (84)	95 (16)	
Missing	1090	184	
Extent of resection			
Subtotal	121 (73)	44 (27)	0.309
Gross total	116 (79)	31 (21)	
Missing	2008	296	
Supratotal resection			
Gross or subtotal	325 (80)	79 (20)	1
Supratotal	4 (80)	1 (20)	
Missing	1916	291	
Wilcoxon-signed-rank test was performed to compare continuous variables. Patients for which the variable of interest was not reported in the included study were reported as "Missing" but were not included in the analysis.			
Bolded P values indicate statistical significance (P < 0.05).			
KPS, Karnofsky Performance Scale; MEP, motor-evoked potential; SD, standard deviation; SEP, somatosensory-evoked potential.			

Table 3. Similar to the Permanent Motor Deficit Preliminary Analysis, χ^2 and Wilcoxon Signed-Rank Tests Were Performed

Independent Variable	No Motor Deficit (%)	Temporary Motor Deficit (%)	P Value
Total	1780 (80)	465 (20)	
Patient and tumor characteristics			
Sex			
Female	106 (68)	50 (32)	1
Male	172 (68)	82 (32)	
Missing	1502	333	
Age (SD), n	47.5 (15.1), 285	47.8 (15.3), 137	0.885
Missing	1495	328	
Size (SD), n	41.9 (38.8), 45	50.5 (35.7), 29	0.06
Missing	1735	436	
Histological grade			
Low grade	189 (72)	74 (28)	0.009
High grade	411 (80)	100 (20)	
Missing	1180	291	
Astrocytoma			
Other	64 (73)	24 (27)	0.20
Astrocytoma	462 (78)	120 (22)	
Missing	1254	321	
Hemisphere			
Left	99 (58)	72 (42)	0.90
Right	91 (59)	63 (41)	
Missing	1590	330	
Tumor lobe location			
Other	191 (72)	76 (28)	0.001
Frontal	159 (58)	115 (42)	
Missing	1430	274	
Tumor depth			
Superficial	48 (66)	25 (34)	0.30
Subcortical	22 (54)	19 (46)	
Missing	1710	421	
Preoperative condition			
KPS (SD), n	72.4 (14.8), 25	74.8 (17), 23	0.50
Missing	1755	442	
Preoperative motor deficit			
No deficit	323 (67)	162 (33)	0.0
Motor deficit	53 (64)	30 (36)	
Missing	1404	273	
Continues			

Continues

Table 3. Continued

Independent Variable	No Motor Deficit (%)	Temporary Motor Deficit (%)	P Value
Preoperative sensory deficit			
No deficit	125 (81)	29 (19)	1
Sensory deficit	2 (100)	0 (0)	
Missing	1653	436	
Procedure variables			
Intraoperative MEP changes			
No change	173 (89)	22 (11)	<0.0001
Yes change	53 (53)	47 (47)	
Missing	1554	396	
Intraoperative SEP monitoring			
No SEP	93 (74)	33 (26)	0.06
Yes SEP	74 (81)	46 (19)	
Missing	1613	386	
Intraoperative MEP monitoring			
No MEP	13 (93)	1 (7)	0.20
Yes MEP	932 (76)	295 (24)	
Missing	835	169	
Any intraoperative monitoring			
No monitoring	25 (71)	10 (29)	0.40
Yes monitoring	1134 (79)	300 (21)	
Missing	621	155	
Craniotomy type			
Awake	358 (70)	153 (30)	<0.0001
Asleep	542 (84)	102 (16)	
Missing	880	210	
Extent of resection			
Subtotal	63 (52)	58 (48)	0.60
Gross total	55 (47)	61 (53)	
Missing	1662	346	
Supratotal			
Gross or subtotal	215 (66)	110 (34)	0.03
Supratotal	0 (0)	4 (100)	
Missing	1565	351	
Missing data reported, but not included in the analysis.			
Bolded P values indicate statistical significance (P < 0.05).			
KPS, Karnofsky Performance Scale; MEP, motor-evoked potential; SD, standard deviation; SEP, somatosensory-evoked potential.			

Missing data reported, but not included in the analysis.

Bolded P values indicate statistical significance ($P < 0.05$).

KPS, Karnofsky Performance Scale; MEP, motor-evoked potential; SD, standard deviation; SEP, somatosensory-evoked potential.

1.46, CI 0.73–2.91), SEP monitoring (OR 1.62, CI 0.168–15.5), gross total compared to subtotal resection (OR 1.45, CI 0.54–3.88), preoperative KPS (OR 1.02, CI 0.97–1.07), tumor size (OR 1.01, CI 0.99–1.02), preoperative motor deficit (OR 1.00, CI 0.31–3.27), male sex (OR 0.98, CI 0.55–1.74), high grade compared to low grade tumors (OR 0.74, CI 0.29–1.90), right compared to left hemisphere (OR 0.59, CI 0.34–1.03), and use of intraoperative monitoring (OR 0.15 CI 9.6×10^{-3} –2.32).

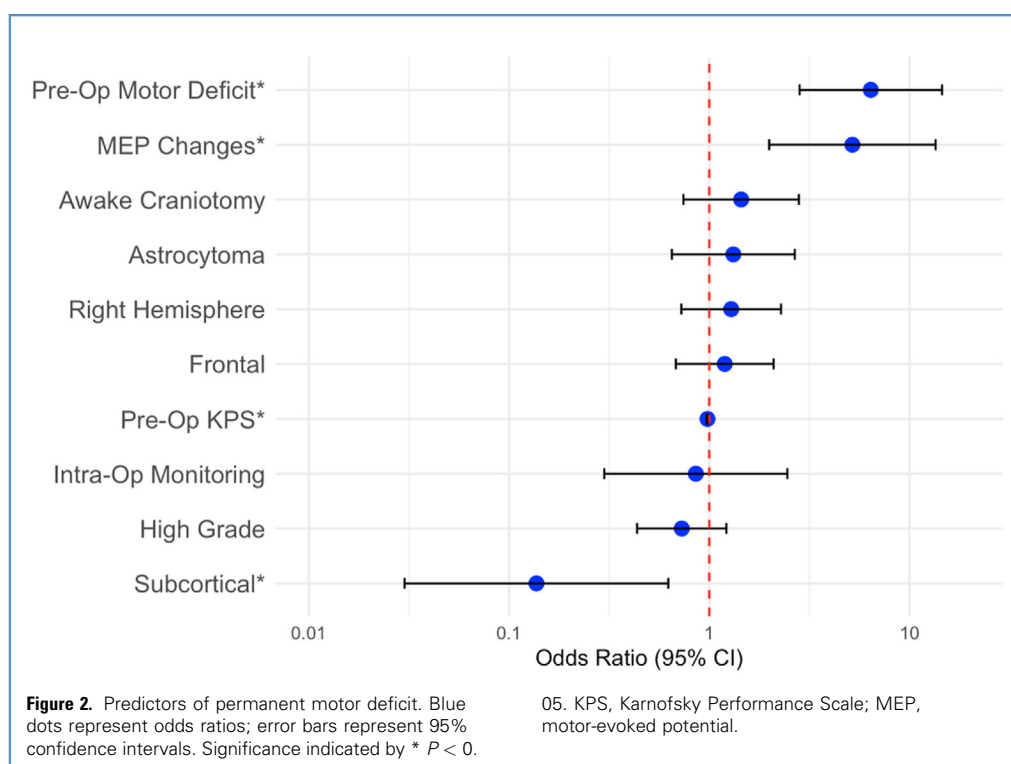
Discussion

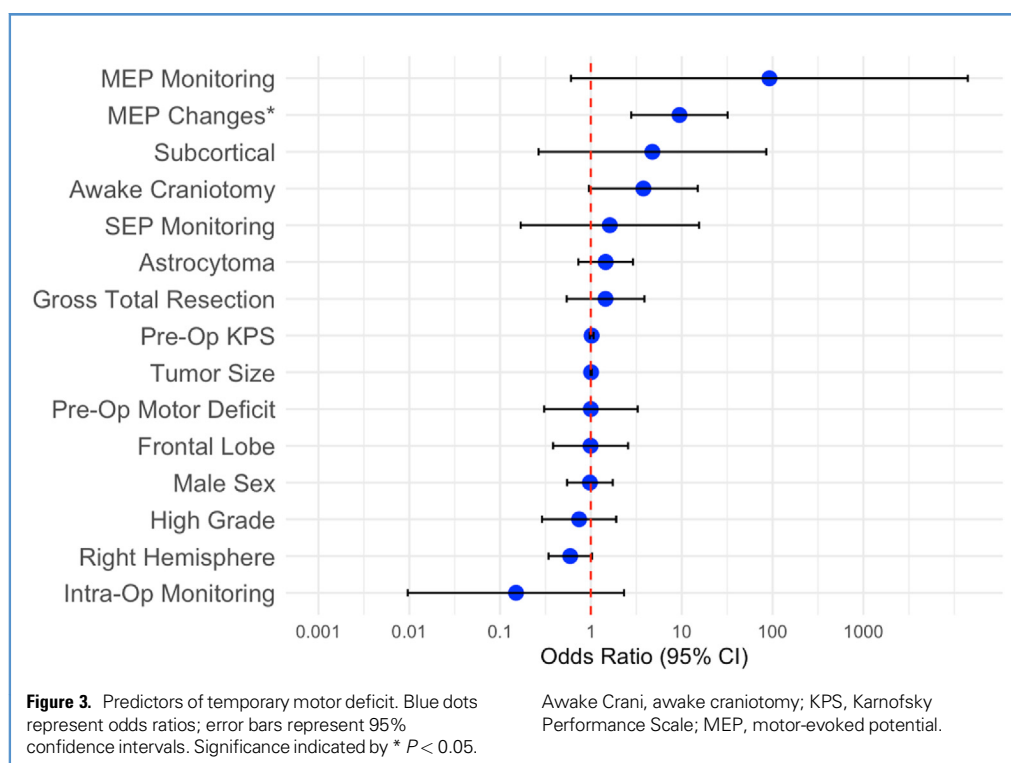
Due to the incurable nature of diffuse gliomas, balancing the oncological goals of aggressive resection with optimizing quality of life by preservation of function can be difficult and patient-specific.^{2,81} Knowledge of evidence-based functional outcomes may help neurosurgeons anticipate otherwise unforeseen trends and counsel patients preoperatively. However, such data are currently limited to case series and retrospective reviews with variable findings, likely due to small sample sizes and heterogeneity of the cases.⁸² Therefore, here we analyzed data from 2616 patients across 67 studies to provide the first meta-analysis of motor deficits following glioma resections. Of the patients analyzed, 465 (18%) experienced a temporary motor deficit, 371 (14%) had a permanent motor deficit, and the remaining 1780 (68%) had no deficit. Ultimately, we show that, when considered in aggregate, a preoperative motor deficit was the strongest factor associated with permanent postoperative motor deficit. Intraoperative MEP changes were associated with both permanent and temporary motor deficits. Additionally, high preoperative KPS and

subcortical tumor location had a lower odds of permanent motor deficit.

Predictors of Permanent Motor Deficit. While multiple variables were significantly associated with permanent neurological deficits on preliminary analysis, only preoperative motor deficits and intraoperative MEP changes were significant predictors on meta-analysis while high preoperative KPS and subcortical tumor location had a lower odds of permanent deficit. It is important to note that postoperative motor deficit was defined as any sort of motor deficit present three months postoperatively, not necessarily a new deficit. Therefore, our results suggest the most significant factor associated with permanent motor dysfunction following glioma resection is an existing motor deficit prior to the actual surgery. Additionally, our findings regarding preoperative KPS corroborate these findings as intact motor function and ability to perform activities of daily living suggests a lower likelihood of experiencing a postoperative motor deficit.

Counterintuitively, subcortical tumor location was found to have lower odds of permanent postoperative motor deficits. Data were extracted on 136 patients from nine published manuscripts on tumor depth classified as either “superficial” or “subcortical” based on descriptions of tumor location relative to superficial gyri. Of the 44 patients with subcortical tumors, only three (7%) were reported to have a permanent motor deficit, whereas 19 (21%) of the 92 patients with superficial tumors were reported to have a permanent motor deficit.^{13,14,24,30,32,33,43,65,73} All three patients with subcortical tumors were from a study by Tate et al. on the morbidity associated with cingulate gyrus gliomas.⁶⁵ Many of





the patients experienced a supplementary motor area (SMA) syndrome immediately following surgery, but 6 months after, two patients experienced persistence of SMA syndrome symptoms (although improved from their immediate postoperative state), and 1 patient had continued hemiparesis.⁶⁵ On further review of patients with a subcortical tumor, many had tumors located away from the primary motor cortices or that were near (but not infiltrating) white matter motor tracts.^{13,14,30} While subcortical tumors are typically considered more disruptive given their ability to infiltrate white matter tracts with less potential for neuroplastic recovery, our results are likely a reflection of selection bias that included tumors far away from motor tracts.^{30,33,83}

Intraoperative MEP Changes

When analyzed in aggregate, we found intraoperative MEP changes were significantly associated with both permanent and temporary motor deficits. A total of 9 studies^{13,14,26,44,62,63,72,78,79} reported whether patients experienced intraoperative MEP changes. In the study by Gempt et al., they include 70 patients who underwent glioma resection.²⁶ A total of 10 of their patients experienced a permanent decline in motor function and 13 had transient deficits.²⁶ All 10 patients with permanent postoperative deficits experienced intraoperative MEP changes. Whereas only seven of the patients with transient deficits had intraoperative MEP changes. Overall 16 of the patients with deficits had new ischemic lesions on diffusion-weighted imaging MRI.²⁶ Given these findings, the authors indicate ischemic events were the

major reason for motor deficits rather than direct mechanical injury, especially in patients with permanent deficits.²⁶ Regardless, the data suggest intraoperative MEP changes are a harbinger for poor motor outcomes.²⁶

Due to limited studies reporting reversible versus irreversible MEP changes, the association of each with temporary or permanent motor deficit was not investigated in the present meta-analysis. However, individual studies suggest irreversible MEP changes may be associated with permanent motor deficits while reversible MEP changes may be associated with temporary motor deficits.^{14,26,44,63,79}

Extent of Resection

Prior studies have focused on determining the impact of gross total versus subtotal resection on postoperative morbidity in patients with glioma. While gross total resection has demonstrated enhanced survival compared to subtotal resection,^{5,8} the association with postoperative deficits must be considered due to the impact on quality of life upon achieving a favorable survival outcome. Prior studies also suggest that motor deficits from surgery negate any survival benefit that may have been achieved through more aggressive resection due to the impact on quality of life.⁷ Interestingly, recent data also indicate subtotal resections are associated with worse long term functional outcomes even when a deficit is not induced during surgery, as this may mean functional areas were found within the tumor itself which leads to immediate or delayed deficits as the disease progresses.⁸⁴ Here, there was no significant impact

of gross total versus subtotal resection on the development of either permanent or temporary postoperative motor deficits.^{7,26,79}

Surgical Technique

Studies investigating differences in motor outcomes between awake versus asleep craniotomies tend to be small case series due to the limited feasibility of controlled trials for these complex surgical patients.^{57,82,85} Analysis of our large, aggregate sample with data available on whether patients underwent asleep versus awake craniotomies^{15,20,21,23-26,28,31,33,35,37,41,43,44,46-48,50-53,57,60,62,63,66-68,72,74,77-79,86} did not identify a significant impact on the development of permanent or temporary motor deficits. A recent systematic review and meta-analysis by Suarez-Meade et al. had similar findings.⁸⁷ We note that retrospective comparisons between awake and asleep craniotomies such as our analysis are subject to selection bias, as the need for awake or asleep motor mapping depends on proximity to both motor and language systems. Therefore, the authors note that this data does not support the equivalence of the approaches for any given case, and that the appropriate monitoring technique must be chosen based on the anatomy of each individual case.

Limitations

While our study extracted data from 2616 patients with gliomas from 67 studies, it is limited by the retrospective nature of most included studies, as well as potential selection and publication biases.⁸² Our comprehensive search of multiple databases yielded no randomized clinical trials—not uncommon in neurosurgical systematic reviews and meta-analyses^{9,87,88} given the complex and individualized nature of patients' surgical care and overall lower prevalence of gliomas compared to other chronic diseases. Additionally, there was inherent variability between the studies which could not be controlled, such as surgical technique, preoperative/postoperative chemotherapy, and radiation. Furthermore, not all studies specifically focused on postoperative motor deficits as a primary outcome, but rather reported it as a secondary outcome to supplement a different objective. Therefore, faithful attempts at our best interpretation of each studies' data were required. Interpretation error was mitigated by having two independent reviewers extract and unanimously agree on the data, as is consistent with other similar meta-analyses.⁸⁸ Many included studies investigated the impact of various treatments not widely accepted as the standard of care, such as use of diffusion tensor imaging for surgical planning⁵⁴ or transcranial magnetic stimulation to

investigate the plasticity of tumor-infiltrated areas,¹⁶ which could have influenced postoperative outcomes as well.

Another limitation is the under-reporting of different variables of interest. For example, subcortical tumor location data was extracted as subcortical or superficial and only coded as such when sufficient terminology was provided, such as “superficial”, “cortical”, or “subcortical”, “deep”, or “periventricular”.^{13,30,65} When the tumor depth was ambiguous, these studies were not included in the analysis of that variable. More detailed reporting of tumor depth may have altered the significance of the results. Despite these limitations, this study represents by far the largest pooled analysis of motor outcomes in glioma surgery to date, and, in the absence of a large, prospective, randomized controlled trial, represents the best evidence we have to offer to date regarding predictors of motor outcomes following glioma surgery.

CONCLUSIONS

Here we provide the first quantitative meta-analysis of predictors or permanent and temporary postoperative motor deficits in patients undergoing glioma surgery. Permanent motor deficits (present at three months or later) were observed in 14% of patients while temporary deficits were seen in 18% of patients. The presence of a preoperative motor deficit was the strongest predictors of a permanent postoperative deficit, followed by intraoperative MEP changes. Higher preoperative KPS and subcortical tumor location had a lower odds of permanent postoperative motor deficits. Intraoperative MEP changes were significantly associated with temporary postoperative motor deficits. It is our hope that these comprehensive meta-analysis results can guide future clinical practice and inform future studies to enhance the survival and quality of life for patients with gliomas.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Brian J. Conway: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Visualization, Writing — original draft, Writing — review & editing. **Stephanie A. Armstrong:** Data curation, Methodology, Project administration, Resources, Writing — review & editing. **Nada Botros:** Data curation, Writing — review & editing. **Sergey Tarima:** Formal analysis, Investigation, Methodology, Supervision, Visualization, Writing — review & editing. **Max O. Krucoff:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Writing — review & editing.

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