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REVIEW

Outcome prediction in brain tumor surgery: a literature review on the influence of nonmedical factors

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Abstract
The purpose of the present study was to review the existing data on preoperative nonmedical factors that are predictive of outcome in brain tumor surgery. Our hypothesis was that also the individual characteristics (e.g., emotional state, cognitive status, social relationships) could influence the postoperative course in addition to clinical factors usually investigated in brain tumor surgery. PubMed, Embase, and Scopus were searched from 2008 to 2018 using terms relating to brain tumors, craniotomy, and predictors. All types of outcome were considered: clinical, cognitive, and psychological. Out of 6.288 records identified, 16 articles were selected for analysis and a qualitative synthesis of the prognostic factors was performed. The following nonmedical factors were found to be predictive of surgical outcomes: socio-demographic (age, marital status, type of insurance, gender, socio-economic status, type of hospital), cognitive (preoperative language and cognitive deficits, performance at TMT-B test), and psychological (preoperative depressive symptoms, personality traits, autonomy for daily activities, altered mental status). This review showed that nonmedical predictors of outcome exist in brain tumor surgery. Consequently, individual characteristics (e.g., emotional state, cognitive status, social relationships) can influence the postoperative course in addition to clinical factors.

Keywords Brain tumor · Outcome · Prediction · Craniotomy

Introduction

The prediction of surgical outcome is essential when treatment decisions have to be made and this is particularly true in brain tumor surgery, a neurosurgical specialty with high costs and risk of complications. Moreover, the outcome prediction allows to better inform the patient about the postsurgical course, including the probability to worsen the clinical status or not and the indication for adjuvant treatments. There are several studies that developed preoperative scores and models in order to predict outcome in brain tumor surgery. They usually considered clinical and surgical variables: the most used surgical outcomes are overall survival, progression-free survival, and extent of resection [18], while the predictors of outcome usually investigated are tumor characteristics, age, and patient's neurological and functional state [8, 24]. On the contrary, the evaluation of outcome in terms of postoperative psychological, environmental, and social change and the use of patient-reported outcome measures is scarce although they provide a more complete picture of the patient's functioning and a perspective of their health status different from the clinicians' one [28]. Nonmedical factors, that are all individual characteristics different from medical and surgical ones, are also rarely studied as predictors of surgical outcome. They include variables like family situation, socioeconomic status, personal characteristics, relationships, and social support. Some studies investigated the impact of variables such as anxiety, depression, cognitive status, personality traits, functional status, and the presence of new deficits on quality of life (QoL) in brain tumor patients [4, 14, 22]. Thus, it remains unclear which, if any, preoperative nonmedical factors are predictive of outcome evaluated by both the clinicians and patients themselves

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after brain tumor surgery. Nonmedical risk factors could be used together with the existing prognostic clinical information in order to plan more tailored clinical management of the postoperative course. To our knowledge, no other literature reviews exist on preoperative nonmedical predictors of outcome in brain tumor surgery and most of the previous studies focused on the prognostic value of clinical and surgical factors. The purpose of the present study was to review the existing data on preoperative nonmedical factors, specifically psychological, cognitive, and socio-demographic, that are predictive of outcome in brain tumor surgery.

Material and methods

Search strategy

PubMed, Embase, and Scopus were searched from January 2008 to December 2018 using medical subject headings and free-text terms relating to brain tumors, craniotomy, and predictors. Specific search terms used in the Web sites for this review are presented in the Online Resource.

Eligibility criteria

We included studies written in English, containing an abstract, and indexed by at least one of the websites. The selection was based on the following inclusion criteria: (1) clinical studies, (2) sample composed of patients of any age with brain tumors undergoing craniotomy, (3) surgical outcome measured by clinicians or self-reported (e.g., neurological status, mortality, QoL) with no limits in the length of postoperative outcome assessment, (4) nonmedical preoperative predictors collected by clinicians or self-reported (e.g., emotional status, cognitive functions, working situation).

Papers considering only clinical or surgical predictors of outcome or only age as socio-demographic variable, and those where the treatment performed was other than craniotomy for tumor resection were excluded.

Papers' selection and data extraction

One researcher reviewed all abstracts to determine if they met the inclusion criteria, and 20% of them were double-checked by other researchers blinded to the decision of the first one. The full texts were screened using the same procedure. All disagreements between reviewers were discussed in order to reach a joint decision.

The following data were extracted from each study: study design, characteristics of the study population, surgical outcome (clinical, cognitive, psychological), preoperative predictors (socio-demographic, cognitive, psychological), and the respective assessment scales; timing of surgical outcome assessment; relevant results of each study. Each predictor was examined for the respective related outcomes, time of outcome evaluation, methodological quality, and statistical proprieties considering significant those with $p < 0.05$. The methodological quality of all the selected studies was evaluated using criteria adapted from previous publications [1, 9] and reported in Table 1. Consistent with other literature reviews, a study was evaluated as high quality if at least 60% of the criteria were met (total score ≥ 5 out of 8). Only high-quality studies and the results from predictive statistical analysis were described. Finally, the number of studies founded for each predictor and for the three types of outcome was counted.

Results

The results of study selection are shown in Fig. 1. Out of 6,288 records, 2,410 studies were removed because they were duplicated, case studies or reviews; thus, 3,878 abstracts were screened. Full-text articles assessed for eligibility were 69, of which 16 met our inclusion criteria [2, 3, 5–7, 10, 12, 13, 16, 17, 20, 21, 25–27, 29]. Most of the articles (76%) were excluded because they reported only a description of nonmedical preoperative variables or their association with outcome without a predictive analysis, and because only clinical variables were considered as predictors. The remaining articles were excluded for the following reasons: data were not reported; the surgical outcome was not considered in the analysis; predictors were measured after surgery; the sample also involved patients who did not undergo surgery; one article was written in Spanish.

The characteristics of the selected studies are reported in Table 2. The included studies involved 584,325 participants with different types of brain tumors. Nine studies were retrospective (582,868 patients), 6 were prospective (965 patients), and 1 was a combination of prospective and retrospective studies (492 patients). The timing of outcome measurement ranged from the discharge to 5 years after surgery, except for one study that evaluated also the period immediately after surgery [29].

Clinical outcomes were evaluated in 11 studies including the following measures: mortality [2, 3, 5, 6, 12, 20], adverse discharge disposition (discharge to facilities other than home/self-care) [2, 12], postoperative risk of stroke [3], myocardial infarction [3], deep surgical site infection [3], return to operating room [3], progression-free survival [5, 16], survival [5–7, 17, 20, 25, 26], length of stay [12], incidence of patient safety indicators (PSIs), and hospital-acquired conditions (HACs) [12]. Psychological outcomes were investigated in 4 studies, specifically depressive and anxiety symptoms [5], QoL [10, 27], dependency [21], and posttraumatic growth [27]. Three articles evaluated cognitive outcome: general cognitive functioning [5, 29], language [13], attention, processing speed,

Table 1 Criteria for the evaluation of the methodological quality of selected studies

Criteria		Points
Sample of patients	Consecutive sample (complete: all eligible patients included), assembled at common care pathway (e.g., first time resection or recurrent).	1
	Clinical and demographic characteristics fully described.	1
Prognostic variables	Fully defined, including details of measurement methods if relevant, precisely measured, but not reported or insufficient details (e.g., mean, range …).	1
	Measurement and reporting of potential prognostic factors with effect estimates (e.g., proportions, OR probability …).	1
Aim	Prediction or the association between preoperative variables and outcome was the primary aim of the study.	1
Outcome	Objective, fully defined including the time from the surgical procedure, appropriate, known for high proportion of patients.	1
Data analysis	Univariate technique.	1
	Multivariate technique: multivariate technique is used to adjust for other prognostic factors and the number of predictors studied was less than 1/10 of the number of patients.	1
Total score	≥ 5 = high quality	8

executive function, learning and memory, visuo-construction, and upper-extremity strength and dexterity [29]. Each study may evaluate more than one type of outcome.

Regarding nonmedical predictors, socio-demographic predictors were considered by 14 studies [2, 3, 7, 10, 12, 13, 16, 17, 20, 21, 25–27, 29], psychological variables by 6 [3, 5–7, 16, 21], and cognitive variables by 5 studies [7, 13, 16, 21, 25] (one study can focus on more than one type of predictors). Specifically, socio-demographic predictors were age [2, 3, 7, 10, 13, 16, 20, 21, 25–27, 29], gender [2, 3, 13, 16, 20, 21, 25, 27], household income [2], socio-economic status [26, 27], insurance [2, 12, 27], educational level [16, 29], marital status [20, 27], and type of hospital (private or public) [17]; psychological predictors were depressive [6, 7, 16] and anxiety symptoms [6], altered mental status [3], autonomy for daily life [3], and personality types [5]; cognitive variables were language deficits [7, 13, 21, 25], attention, executive function, psychomotor speed, global cognitive functioning, working

Fig. 1 Study flow

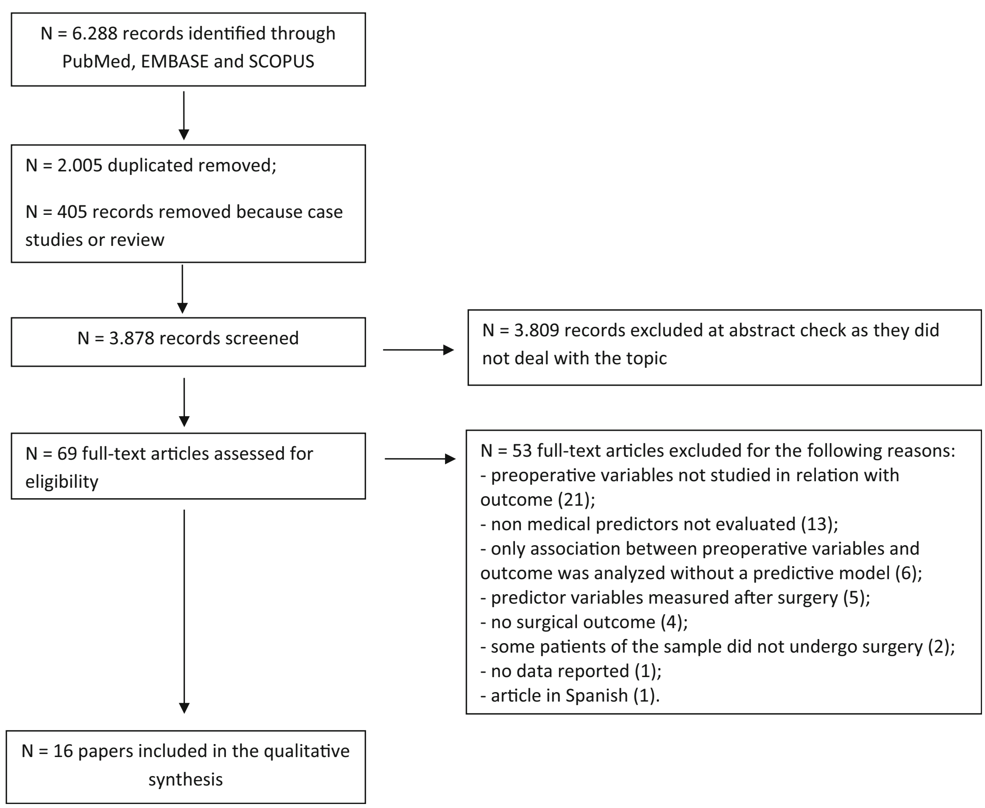

Table 2 Characteristics of the selected studies

	Study population	Study design	Outcome measures (tests)	Nonmedical preoperative predictors (tests)	Relevant results
Ambekar et al. [2]	$N = 16{,}959$ meningioma USA	Retrospective	Clinical outcome: In-patient mortality; adverse outcome at discharge	Socio-demographic: Primary payer, median household income, age, gender	Medicare insurance, increasing age, and being male were associated with higher rate of in-hospital death and adverse disposition.
Bekelis et al. [3]	$N = 1{,}834$ 25% meningioma; 75% other USA	Retrospective	Clinical outcome: Risks of stroke, myocardial infarction, death, deep surgical site infection, return to the operating room within 30 days	Psychological: Altered mental status Socio-demographic: Age, gender	Altered mental status was associated with a higher risk of death and myocardial infarction. Older age was associated with stroke.
Bunevicius, [5]	$N = 178$ 46% meningioma; 20% HGG; 15% pituitary adenoma; 12% vestibular schwannoma; 8% LGG Lithuania	Prospective	Clinical outcome: Progression-free survival; 5-year survival and mortality Psychological: Depressive and anxiety symptoms at discharge (HADS) Cognitive outcome: Cognitive functioning ad discharge (MMSE)	Psychological: personality traits (TIPI)	Emotional stability was associated with lower depressive/anxiety symptom severity at discharge, consciousness, openness and extroversion with 5 years survival in benign tumor, openness with better cognitive state at discharge.
Bunevicius et al. [6]	$N = 152$ 28% HGG 13% LGG 59% meningioma Lithuania	Prospective	Clinical outcome: Overall survival; 5-year mortality	Psychological: Depressive symptoms (HADS) Anxiety symptoms (HADS)	Greater depressive symptoms were associated with shorter survival and greater 5 year mortality risk in meningioma patients.
Chaichana et al. [7]	$N = 393$ GBM Maryland	Retrospective	Clinical outcome: Survival	Cognitive: Language deficit (any combination of receptive and/or expressive aphasia) Socio-demographic: Age Psychological: Depression (symptoms)	Language deficits, older age and depression were associated with shortened survival.
Hooten et al. [12]	$N = 548.727$ brain tumors USA	Retrospective	Clinical outcome: Clinical discharge outcome; mortality; length of stay; PSIs, HACs	Socio-demographic: Insurance type	Medicaid/self-pay patients were more likely to develop PSIs or HACs and the increase of this indexes corresponded with an increased length of stay, adverse disposition, and higher mortality rate.
Ilmberger et al. [13]	$N = 149$ 49.7% LGG 41.6% HGG Germany	Prospective	Cognitive Outcome: Language at 21 days and 1 year (AAT or clinical data)	Cognitive: Preoperative aphasic disturbances (AAT or clinical data) Socio-demographic: Age, gender	Aphasia was a risk factor for early and persistent language deficits. Increased age was associated with persistent language deficits.

Table 2 (continued)

	Study population	Study design	Outcome measures (tests)	Nonmedical preoperative predictors (tests)	Relevant results
Lee et al. [16]	$N = 50$ GBM South Korea	Retrospective	Clinical outcome: Progression free survival at 6 months	Cognitive: Cognitive function (MMSE, digit span forward, digit span backsard, COWA, TMT, Stroop test) Psychological: Depressive symptoms (Geriatric Depression Scale) Socio-demographic: Age, education, gender	Patients with PFS-6 had more total years of education and more good performance in TMT-A and TMT-B tests. TMT-B predicted PFS-6.
Lynch et al. [17]	$N = 66$ GBM Brazil	Retrospective	Clinical outcome: Survival	Socio-demographic: Type of hospital[a]	There was a superior survival rate among the patients operated at private hospitals.
Pan et al. [20]	$N = 14.675$ GBM USA	Retrospective	Clinical outcome: Mortality at 12 months minimum	Socio-demographic: Marital status, age, gender	Those who never married, those who were married at the time of diagnosis, female and younger patients had a lower risk for mortality.
Pirracchio et al. [21]	$N = 90$ meningioma, HGG, metastasis, neurinoma, adenoma, others France	Prospective	Psychological: Dependency for daily life activities at 1 year	Psychological: patient's autonomy (ADL) Cognitive: Language Socio-demographic: age, gender	Preoperative patients' autonomy for daily activities was predictive of the functional status at 1 year.
Stark et al. [25]	$N = 492$ GBM Germany	Retrospective and prospective	Clinical outcome: Survival	Cognitive: Aphasia and neuropsychological deficits (clinical examination) Socio-demographic: Age, gender	Aphasia, neuropsychological deficits and older age was associated with a better survival.
Trikalinos et al. [26]	$N = 131$ GBM Maryland	Retrospective	Clinical outcome: Overall survival	Socio-demographic: socioeconomic status (census tract poverty level); age	Patients with age > 70 had a higher hazard of death than age < 52.
Wang et al. [27]	$N = 260$ LGG China	Prospective	Psychological: Quality of life (FACT-B) and posttraumatic growth (PTGI) at 1 month and 1 year	Socio-demographic: Gender, age, marital status, social insurance, SES	Better financial conditions and social insurance positively predicted quality of life.
Wu et al. [29]	$N = 33$ Insular glioma Texas	Retrospective	Cognitive outcome: Attention (SPAN); processing speed (SYMB, TMT-A); executive function (TMT-B, SIM, COWA); learning and memory (HVLT-R); language (NAME, TOKEN); visuoconstraction (BD);	Socio-demographic: Education, age	Age and educational level were not associated with postoperative change in neurocognitive performance.

Table 2 (continued)

	Study population	Study design	Outcome measures (tests)	Nonmedical preoperative predictors (tests)	Relevant results
			motor (GRIP, PEG) early and at 3 month		
Drewes et al. [10]	$N = 136$ 71% HGG, 29% LGG Norway	Prospective	Psychological: Quality of life (EQ-5D 3 L) at 1 and 6 months	Socio-demographic: Age	Age was not a predictor for negative development of quality of life

[a] This is an environmental factor that could influence the survival due to the different characteristics of people accessing to private or public hospital. Specifically, patients from public hospital had low level of education, low family income, and worse KPS and radiotherapy performance compared with those from private hospital

AAT, Aachener Aphasie Test; *ADL*, activities of daily life; *BD*, block design; *BDI*, Beck Depression inventory; *COWA*, Controlled Oral Word Association; *EQ-5D*, EuroQol-5 dimensions; *FACT-B*, Functional Assessment of Cancer Therapy–Brain; *GBM*, glioblastoma multiforme; *HACs*, hospital-acquired conditions; *HADS*, Hospital Anxiety and Depression Scale; *HGG*, high-grade glioma; *HVLT-R*, Hopkins Verbal Learning Test-Revised; *KPS*, Karnofsky Performance Status; *LGG*, low-grade glioma; *MMSE*, Mini Mental State Examination; *NAME*, naming; *PASS-20*, Pain Anxiety Symptom Scale; *PEG*, Pegboars; *PFS-6*, 6-month progression-free survival; *PSIs*, Patient Safety Indicators; *PTGI*, Posttraumatic Growth Inventory; *SES*, socioeconomic status; *TMT*, Trail Making Test;; *SIM*, similarities; *SRR*, skin resistance response; *STAI-Y*, State-Trait Anxiety Inventory form y; *SYMB*, symbol; *TIPI*, Ten Item Personality Inventory

memory [16], and neuropsychological deficits [25]. Tables 3 and 4 show the details for each predictor: the respective studies with quality scores, associated outcomes, timing of outcome evaluation, and statistical characteristics. All selected studies were high-quality articles on the basis of the criteria and cut-off described in Table 1.

Socio-demographic predictors

Most of the studies considering socio-demographic predictors focused on clinical outcome. In this literature review, we found seven socio-demographic factors that significantly predict surgical outcome.

In patients with glioblastoma (GBM), older age was found to be a predictor of shorter survival [7, 20, 25, 26] and language deficits at 1 year [13], female patients had a lower risk of mortality and adverse discharge disposition [20], being married or never married at time of diagnosis was related to a lower risk for mortality [20]. In a study on the prognosis of GBM, private hospitals reported a superior survival rate [17]. In low-grade glioma (LGG), older age was found to be a predictor of language deficits at 1 year [13], while better financial conditions and social insurance were determinants of QoL [24].

Age, gender, and insurance were significant predictors also in meningioma patients: older age predicted hospital death [2], adverse discharge disposition [2], and stroke within 30 days [3]; female and patients with private insurance had a lower risk of mortality and adverse discharge disposition [2].

Finally, in a mixed sample of brain tumors, patients with private insurance had a lower incidence of PSIs and HACs, shorter length of stay, and lower mortality rate compared with Medicaid/self-pay [12].

Preoperative psychological predictors

Depressive symptoms, altered mental status, personality traits, and autonomy for daily activity were found to be significant psychological predictors. Most of them were analyzed in relation to clinical outcome, specifically survival, complications, and functional status.

In patients with meningioma, depressive symptoms were predictors of shorter survival [6], altered mental status at admission was predictive of mortality and myocardial infarction within 30 days, but a definition of altered mental status was not given [3], lower autonomy for daily activity was a predictor of an increase probability to be nondependent at 1 year [21], greater consciousness and openness scores were associated with reduced mortality risk, greater emotional stability with lower depressive and anxiety symptoms at discharge, and openness with better cognitive state at discharge [5].

Depressive symptoms were found to be predictors of shorter survival also in a study on GBM [7], while autonomy

Table 3 Socio-demographic predictors

Predictor	Outcome	Outcome time	Statistical analysis	P value	OR[a] (95% CI)	Definition variable	Study	Quality score
Age	Mortality	Hospitalization	Univariate	$p < 0.001$*	4.88 (3.5–6.7)	≥ 80 years vs < 80 years	Ambekar et al.,[2]	7
		Within 30 days	Multivariate	$p = 0.104$	1.021 (0.996–1.047)	Older age	Bekelis et al. [3]	5
	Adverse disposition	Discharge	Univariate	$p < 0.001$*	7.5 (6.47–8.76)	≥ 80 years vs < 80 years	Ambekar et al. [2]	7
	Survival	≥ 12 months	Univariate	$p < 0.0001$*	NA		Pan et al. [20]	8
		≥ 12 months	Multivariate	$p < 0.0001$*	5.46 (4.80–6.22)	≥ 75 years vs 19–34 years	Pan et al.,[20]	8
		NA	Multivariate	$p < 0.001$*	1.512–2.357	< 61 years	Stark et al. [25]	6
		NA	Multivariate	$p < 0.05$*	3.95 (1.8–5.0)	> 70 years vs age < 52	Trikalinos et al. [26]	5
	Shortened survival		Univariate	$p < 0.05$*	NA	Older age	Chaichana et al [7]	7
		\	Multivariate	$p < 0.001$*	1.020 (1.011–1.029)	Older age	Chaichana et al. [7]	7
	Stroke	Within 30 days	Multivariate	$p = 0.015$*	1.031 (1.006–1.057)	Older age	Bekelis et al. [3]	5
	Deep surgical site infection	Within 30 days	Multivariate	$p = 0.324$	1.013 (0.987–1.040)	Older age	[3]	5
	Return to operating room	Within 30 days	Multivariate	$p = 0.406$	1.007 (0.991–1.022)	Older age	Bekelis et al. [3]	5
	Myocardial infarction	Within 30 days	Multivariate	$p = 0.061$	1.044 (0.998–1.091)	Older age	Bekelis et al. [3]	5
	Language disturbance	21 days	Multivariate	$p > 0.05$	NA	> 40 years of age	Ilmberger et al. [13]	5
		1 year	Multivariate	$p < 0.02$*	NA	\	Ilmberger et al. [13]	5
	Cognitive performance	Immediate; 3 months	Multivariate	$p > 0.05$	NA	\	Wu et al. [29]	5
		6 months	Multivariate	$p = 0.915$	1.15 (0.095–13.77)	Age < 50 years	Lee et al. [16]	7
	To be nondependent	1 year	Univariate	$p = 0.41$	0.95 (0.85–1.07)		Pirracchio et al. [21]	7
		1 and 6 months	Univariate	$p = 0.003$*	1.04 (1.01–1.07)		Drewes et al. [10]	7
		1 and 6 months	Multivariate	$p = 0.562$	1.01 (0.98–1.05)		Drewes et al. [10]	7
Gender	Mortality	Hospitalization	Univariate	$p < 0.001$*	0.49 (0.38–0.65)	Female	Ambekar et al. [2]	7
		Within 30 days	Multivariate	$p = 0.223$	0.675 (0.358–1.271)	Male	Bekelis et al. [3]	5
		≥ 12 months	Multivariate	$p < 0.0001$*	0.92 (0.88–0.95)	Female	Pan et al. [20]	8
	Adverse disposition	Discharge	Univariate	$p < 0.001$*	0.83 (0.77–0.89)	Female	Ambekar et al. [2]	7
	Survival	≥ 12 months	Univariate	$p = 0.822$	NA	\	Pan et al. [20]	8
	Stroke	Within 30 days	Multivariate	$p = 0.754$	0.908 (0.496–1.662)	Male	Bekelis et al. [3]	5
	Deep surgical site infection	Within 30 days	Multivariate	$p = 0.782$	1.097 (0.571–2.107)	Male	Bekelis et al. [3]	5
	Return to operating room	Within 30 days	Multivariate	$p = 0.178$	0.766 (0.519–1.130)	Male	Bekelis et al. [3]	5
	Myocardial infarction	Within 30 days	Multivariate	$p = 0.904$	1.061 (0.407–2.765)	Male	Bekelis et al. [3]	5
	Language disturbance	21 days	Multivariate	$p > 0.05$	NA	\	Ilmberger et al. [13]	5
		1 year	Multivariate	$p > 0.05$	NA	\	Ilmberger et al. [13]	5
	To be nondependent	1 year	Univariate	$p = 0.66$	0.83 (0.35–1.94)		Pirracchio et al. [21]	7
Household income	Mortality	Hospitalization	Univariate	$p = 0.28$	1.25 (0.83–1.9)	1st quartile vs 4th quartile	Ambekar et al. [2]	7
	Adverse disposition	Discharge	Univariate	$p = 0.2$	1.1 (0.95–1.25)	1st quartile vs 4th quartile	Ambekar et al. [2]	7
Socio-economic status	Overall survival	1 month; 1 year	Multivariate	$p > 0.05$	NA	Absolute poverty category	Trikalinos et al. [26]	5

Table 3 (continued)

Predictor	Outcome	Outcome time	Statistical analysis	*P* value	OR[a] (95% CI)	Definition variable	Study	Quality score
	Quality of life		Multivariate	$p=0.00$*	$t=4.61$; $\beta=0.38$	Good	Wang et al. [27]	6
			Multivariate	$p=0.00$*	$t=4.52$; $\beta=0.37$	Good	Wang et al. [27]	6
Insurance	Mortality	Hospitalization	Univariate	$p<0.001$*	2.79 (2.13–3.66)	Medicare vs others	Ambekar et al. [2]	7
			Univariate	$p<0.001$*	0.36 (0.27–0.49)	Private vs others	Ambekar et al. [2]	7
			Multivariate	$p=0.217$	0.907–1.02	Medicaid/self-pay vs private	Hooten et al. [12]	5
	Adverse disposition	Discharge	Univariate	$p<0.001$*	4.1 (3.8–4.37)	Medicare vs others	Ambekar et al. [2]	7
			Univariate	$p<0.001$*	0.54 (0.5–0.57)	Private vs others	Ambekar et al. [2]	7
		Database	Multivariate	$p<0.001$*	1.2 (1.15–1.25)	Medicaid/self-pay vs private	Hooten et al. [12]	5
	Quality of life	1 month; 1 year	Multivariate	$p=0.03$*	$t=2.25$; $\beta=3.32$	Social insurance	Wang et al. [27]	6
			Multivariate	$p=0.02$*	$t=2.33$; $\beta=3.411$	Social insurance	Wang et al. [27]	
	Length of stay	Database	Multivariate	$p<0.001$*	0.7 (0.580–0.849)	Medicaid/self-pay vs private	Hooten et al. [12]	5
	PSIs	Database	Multivariate	$p=0.067$	0.02–6.53%	Medicaid/self-pay vs private	Hooten et al. [12]	5
	HACs	database	Multivariate	$p=0.185$	2.83–16.0	Medicaid/self-pay vs private	Hooten et al. [12]	5
Educational level	PFS-6	6 months	Multivariate	$p=0.986$	1.02 (0.149–6.94)	> 12 years	Lee et al. [16]	7
	Cognitive performance	Immediate;3 months	Multivariate	$p>0.05$	NA	\	Wu et al. [29]	5
Marital status	Survival	≥ 12 months	Univariate	$p<0.0001$*	NA	\	Pan et al. [20]	8
	Mortality		Multivariate	$p<0.0001$*	0.86 (0.82–0.90)	Married vs separated, divorced, widowed	Pan et al. [20]	8
Hospital	Survival		Univariate	$p=0.007$*	2.59 (1.29–5.18)	Public vs private	Lynch et al. [17]	6
			Multivariate	$p=0.313$	1.54 (0.67–3.56)	Public vs private	Lynch et al. [17]	6

[a] Odds ratio, risk ratio, hazard ratio, or values of the statistical tests used

*$p<0.05$

NA, not available

Table 4 Psychological and cognitive predictors

Predictor	Outcome	Outcome time	Statistical analysis	p value	OR[a] (95% CI)	Definition variable	Study	Quality score
Depressive symptoms	Shortened survival	NA	Univariate	$p < 0.05$*	NA		Chaichana et al. [7]	7
			Multivariate	$p > 0.05$	NA	\	Chaichana et al. [7]	7
	Mortality	5 years	Univariate	$p = 0.025$*	3.708 (1.178–11.673) (M)	Severe vs mild/moderate	Bunevicius et al. [6]	6
			Multivariate	$p = 0.006$*	7.083 (1.755–28.588) (M)	Severe vs mild/moderate	Bunevicius et al. [6]	6
			Multivariate	$p = 0.971$	NA (LGG)	Severe vs mild/moderate	Bunevicius et al. [6]	6
			Multivariate	$p = 0.386$	NA (HGG)	Severe vs mild/moderate	Bunevicius et al. [6]	6
Anxiety symptoms	Mortality	5 years	Multivariate	$p = 0.779$	NA (M)		Bunevicius et al. [6]	6
			Multivariate	$p = 0.941$	NA (LGG)	\	Bunevicius et al. [6]	6
			Multivariate	$p = 0.809$	NA (HGG)	\	Bunevicius et al. [6]	6
Extroversion personality trait	Depressive symptoms	Discharge	Univariate	$p = 0.393$	$\beta = -0.072$	\	Bunevicius [5]	6
	Anxiety symptoms	Discharge	Univariate	$p = 0.453$	$\beta = -0.063$	\	Bunevicius [5]	6
	Cognitive status	Discharge	Univariate	$p = 0.239$	$\beta = -0.098$	\	Bunevicius [5]	6
	Survival	5 years	Univariate	$p > 0.05$	NA (HGG, LGG)	\	Bunevicius [5]	6
	Mortality	5 years	Univariate	$p > 0.05$	NA (benign)	\	Bunevicius [5]	6
	PFS	5 years	Univariate	$p > 0.05$	NA (LGG, HGG)	\	Bunevicius [5]	6
Agreeableness personality trait	Depressive symptoms	Discharge	Univariate	$p = 0.184$	$\beta = -0.112$	\	Bunevicius [5]	6
	Anxiety symptoms	Discharge	Univariate	$p = 0.879$	$\beta = -0.013$	\	Bunevicius [5]	6
	Cognitive status	Discharge	Univariate	$p = 0.977$	$\beta = -0.002$	\	Bunevicius [5]	6
	Survival	5 years	Univariate	$p > 0.05$	NA (HGG, LGG)	\	Bunevicius [5]	6
	Mortality	5 years	Univariate	$p > 0.05$	NA (benign brain tumor)		Bunevicius [5]	6
	PFS	5 years	Univariate	$p > 0.05$	NA (LGG, HGG)	\	Bunevicius [5]	6
Consciousness personality trait	Depressive symptoms	Discharge	Univariate	$p = 0.524$	$\beta = -0.054$	\	Bunevicius [5]	6
	Anxiety symptoms	Discharge	Univariate	$p = 0.284$	$\beta = 0.090$	\	Bunevicius [5]	6
	Cognitive status	Discharge	Univariate	$p = 0.064$	$\beta = -0.154$	\	Bunevicius [5]	6
	Survival	5 years	Univariate	$p > 0.05$	NA (HGG, LGG)	\	Bunevicius [5]	6
	Mortality	5 years	Univariate	$p = 0.001$*	0.641 (0.493–0.834) (benign)		Bunevicius [5]	6
			Multivariate	$p = 0.06$	NA (benign)	\	Bunevicius [5]	6
	PFS	5 years	Univariate	$p > 0.05$	NA (LGG, HGG)	\	Bunevicius [5]	6
Emotional stability personality trait	Depressive symptoms	Discharge	Univariate	$p < 0.001$*	$\beta = -0.359$	\	Bunevicius [5]	6
			Multivariate	$p < 0.001$*	$\beta = -0.404$	\	Bunevicius [5]	6
	Anxiety symptoms	Discharge	Univariate	$p < 0.001$*	$\beta = -0.317$	\	Bunevicius [5]	6
			Multivariate	$p < 0.001$*	$\beta = -0.319$	\	Bunevicius [5]	6
	Cognitive status	Discharge	Univariate	$p = 0.822$	$\beta = 0.019$	\	Bunevicius [5]	6
	Survival	5 years	Univariate	$p > 0.05$	NA (HGG, LGG)	\	Bunevicius [5]	6
	Mortality	5 years	Univariate	$p > 0.05$	NA (benign)	\	Bunevicius [5]	6
	PFS	5 years	Univariate	$p > 0.05$	NA (LGG, HGG)	\	Bunevicius [5]	6
Openness personality trait	Depressive symptoms	Discharge	Univariate	$p = 0.158$	$\beta = -0.119$	\	Bunevicius [5]	6
	Anxiety symptoms	Discharge	Univariate	$p = 0.642$	$\beta = -0.039$	\	Bunevicius [5]	6
	Cognitive status	Discharge	Univariate	$p = 0.008$*	$\beta = 0.220$		Bunevicius [5]	6
			Multivariate	$p = 0.127$	$\beta = 0.127$	\	Bunevicius [5]	6
	Survival	5 years	Univariate	$p > 0.05$	NA (HGG, LGG)	\	Bunevicius [5]	6
	Mortality	5 years	Univariate	$p = 0.004$*	0.612 (0.438–0.857) (benign)		Bunevicius [5]	6
			Multivariate	$p = 0.003$*	0.554 (0.376–0.814)		Bunevicius [5]	6

Table 4 (continued)

Predictor	Outcome	Outcome time	Statistical analysis	p value	OR[a] (95% CI)	Definition variable	Study	Quality score
	PFS	5 years	Univariate	$p > 0.05$	NA (LGG, HGG)	\	Bunevicius [5]	6
Altered mental status	Mortality	Within 30 days	Multivariate	$p < 0.0001$*	4.330 (2.199–8.527)	Presence of AMS	Bekelis et al. [3]	5
	Myocardial infarction	Within 30 days	Multivariate	$p = 0.003$*	4.933 (1.751–13.893)	Presence of AMS	Bekelis et al. [3]	5
	Stroke	Within 30 days	Multivariate	$p = 0.680$	0.802 (0.280–2.294)	Presence of AMS	Bekelis et al. [3]	5
	Deep surgical site infection	Within 30 days	Multivariate	$p = 0.102$	1.969 (0.875–4.433)	Presence of AMS	Bekelis et al. [3]	5
	Return to operating room	Within 30 days	Multivariate	$p = 0.058$	1.668 (0.982–2.833)	Presence of AMS	Bekelis et al. [3]	5
Autonomy for daily activity	To be nondependent	1 year	Univariate	$p = 0.01$*	1.64 (1.12–2.40)	Greater ADL score	Pirracchio et al. [21]	7
			Multivariate	$p = 0.02$*	1.67 (1.10–2.54)	Greater ADL score	Pirracchio et al. [21]	7
Language	Shortened survival		Univariate	$p < 0.05$*	NA	Language deficits	Chaichana et al. [7]	7
			Multivariate	$p = 0.001$*	1.585 (1.204–2.065)	Language deficits	Chaichana et al. [7]	7
	Survival		Univariate	$p = 0.014$*	NA	Absence of aphasia	Stark et al. [25]	6
			Multivariate	$p > 0.05$	NA	Aphasia	Stark et al. [25]	6
	Language	21 days	Multivariate	$p < 0.0002$*	NA	Aphasia	Ilmberger et al. [13]	5
		1 year	Multivariate	$p < 0.001$*	NA	Aphasia	Ilmberger et al. [13]	5
	To be nondependent	1 year	Univariate	$p = 0.14$	0.39 (0.11–1.35)	Aphasia evaluated clinically	Pirracchio et al. [21]	7
Attention, executive function, psychomotor speed	PFS-6	6 months	Multivariate	$p = 0.016$*	37.15 (1.98–696.16)	Good performer (TMT-B)	Lee et al. [16]	7
			Multivariate	$p = 0.280$	0.22 (0.015–3.37)	Good performer (TMT–A)	Lee et al. [16]	7
Cognitive deficits	Survival		Univariate	$p < 0.01$*	NA	No cognitive deficits	Stark et al. [25]	6
			Multivariate	$p > 0.05$	NA	Cognitive changes	Stark et al. [25]	6

[a] Odds ratio, risk ratio, hazard ratio, or values of the statistical tests used

*$p < 0.05$

AC, awake craniotomy; *AMS*, altered mental status; *GA*, general anesthesia; *M*, meningioma for daily activity was a predictor of independence at 1 year in high-grade glioma (HGG) [21].

Finally, anxiety did not predict survival both in meningioma and glioma patients [6], and no personality traits were related to survival in glioma patients [5].

Preoperative cognitive predictors

Cognitive predictors were mostly investigated in relation to clinical outcome [7, 16, 21, 25] and only in one study to the postoperative language function [13]. Significant results were found for patients with glioma. Specifically, in patients with GBM, preoperative language deficits predicted poorer survival [7, 25] and the Trail Making Test part B (TMT-B) measuring attention, executive functions, and psychomotor speed was predictive of 6-month progression-free survival [16]; in HGG and LGG, preoperative language deficits were predictors of persistent aphasic disturbance [13].

Discussion

Most of the nonmedical factors analyzed in the selected articles were found to be significant predictors of the postoperative outcome. Specifically, age, marital status, type of insurance, gender, socio-economic status, type of hospital, preoperative language disturbance, cognitive deficits, performance at TMT-B test, depressive symptoms, personality traits, autonomy for daily activities, and altered mental status were significant predictors of outcome in brain tumor surgery.

Considering the survival outcome, the following factors had a negative predictive value: older age, not being married, male gender, not having private insurance, surgery in public hospital, language and cognitive deficits, poor performance at TMT-B cognitive test, depressive symptoms, and altered mental status and some types of personality. Older age was also associated with increase adverse discharge disposition rate and stroke within 30 days, male gender with increase adverse discharge disposition, altered mental status with higher risk of myocardial infarction at 30 days, and not having private insurance with increase adverse discharge disposition, length of stay, PSIs, and HACs.

Considering cognitive outcomes, older age and preoperative aphasia were risk factors for postoperative language deficits, while openness personality predicted a better cognitive status at discharge. Finally, considering psychological outcomes, preoperative autonomy for daily activity was predictive of a good autonomy at 1 year, high socioeconomic status and social insurance were determinants of QoL at 1 month and 1 year, and low emotional stability negatively predicted depressive and anxiety symptoms at discharge.

Some observations on the predictors identified in this review are necessary. The predictive value of socio-demographic factors shows the negative impact of some social conditions on surgical outcome and survival: older age and being single were found to be risk factors of a worse outcome. The influence of patient age on outcome in brain tumor surgery has been widely reported in literature [11, 15, 19, 23] and it seems to be related to medical issues (e.g., comorbidities, less favorable genetic profile in GBM, less aggressive treatment, less adjuvant therapy), while marital status may influence the way of dealing with the disease and treatments (e.g., compliance with adjuvant treatments, low family income) with a consequent impact on outcome. These last characteristics are usually common among people going to public hospital and this could indirectly clarify the better surgical outcome that was found in private hospitals [17]. Regarding socioeconomic status and the type of insurance, their impact on outcome measures could be related to the specific health system of countries where the studies were conducted.

Some cognitive dysfunctions showed a prognostic value in relation to the survival. In particular, preoperative language deficits and poor performance at TMT-B were found to be negative prognostic factors for survival in GBM patients. Both studies concluded that these cognitive deficits are likely indicative of a more infiltrative tumor and consequently their evaluation should be integrated preoperatively in the prognostic process. Among psychological factors, preoperative depressive symptoms were found to be predictors of shortened survival in meningioma, while conflicting results exist regarding their impact in glioma patients. Some personality traits were found to be predictive of survival, postoperative cognitive status, and depressive and anxiety symptoms at discharge in benign tumor, but further studies are needed to confirm their role in influencing surgical outcome.

Some differences and similarities can be found in significant predictors between patients with meningioma and glioma. Our review showed that age, gender, type of insurance, and depressive symptoms and autonomy for daily living are outcome predictors among both diagnoses. It is plausible that older age had a common influence due to the usually associated worse medical conditions independently from the type of tumor, while the influence of depressive symptoms could be similar because of the impact of the behavioral consequences of depression on the health status. Regarding uncommon predictors, language deficits, TMT-B scores, type of hospital, socio-economic situation, and marital status were found significant in glioma patients, while personality types and altered mental status in meningioma. More studies would be necessary to clarify these differences; however, it is plausible that cognitive deficits were more evaluated in glioma patients due to their implication in this disease, and that the presence of partner is more important in glioma patients as support and help to follow the treatments usually requested for this brain tumor.

Our study has some limitations mainly related to the variety of the selected studies and to the review process. A formal meta-analysis was not possible due to the wide variety in the outcome measures, statistical analyses, and factors considered as potential predictors. Thus, only a qualitative synthesis of the prognostic factors was performed, considering each study mostly individually. In fact, the studies' results were difficult to compare due to the heterogeneity of outcomes and predictors that were used. Most of the studies had a retrospective design using data from clinical reports and notes, without performing standard evaluations or employing specific scales. Some studies did not specify how the variables were measured, e.g., the altered mental status [3] and language deficits [7, 21, 25]. The comparison of the studies' results was difficult due to the heterogeneity between articles with respect to outcomes and predictors investigated, patients' population (only meningioma, glioma or people with various diagnosis of brain tumor), statistical analyses used, and time of outcome assessment. Moreover, some studies reported only the unadjusted effect estimates, while others performed also multivariable analyses that, however, were adjusted using different variables so that a comparison was not possible. The focus on the predictors that can be evaluated preoperatively probably reduced the number of articles selected in this review, but our aim was to find factors that can be investigated before surgery and included in the prognostic process. Finally, the applicability of this review may be affected by limited data for each individual predictor and by the fact that outcome and predictor assessments were performed differently.

The major strength of our study is that it represents the first attempt to summarize data on the predictive value of nonmedical factors in relation to the outcome in brain tumor surgery. The hypothesis was that also the individual characteristics (e.g., emotional state, cognitive status, social relationships) could influence the postoperative course in addition to clinical factors. Consequently, the results of this review could be taken into account by researchers when investigating predictors of surgical outcome and by clinicians for a more comprehensive preoperative evaluation of risk factors with the aim to plan additional treatments for modifiable predictors (e.g., occupational therapy, cognitive rehabilitation, psychological support). In particular, we suggested to consider the following factors as the most important outcome predictors during the prognostic process: preoperative language deficits and TMT-B test scores with glioma patients, and depressive symptoms and independence in daily living with both meningioma and glioma patients. Additionally, more attention should be paid to elderly and in general disadvantaged patients, such as people with poor social support or low socioeconomic status, in order to help them to better understand and follow care plans.

Future research is needed to confirm the predictive value of most of the described variables in relation to the postoperative outcome. This is particularly important for psychological and cognitive factors because they could be modified by tailored interventions with a consequent positive impact on postoperative course and in general on patients' life. For example, if the effect of depressive symptoms on survival is evident, they could be treated maybe working on the compliance with the postoperative treatments and therapies that could be low in patients with mood disorders. The impact of socio-demographic variables on surgical outcome should be also further investigated. Even if they are not modifiable factors, specific interventions can be planned to help patients with difficulties related to their status, e.g., additional social support for single patients with GBM and educational interventions for elderly people or those with low educational level. Such interventions could improve the compliance during the postoperative course and consequently the surgical outcome. There is also a need to further explore whether the depressive symptoms and personality types influence the surgical outcome differently in glioma patients and in those with benign tumor, and to confirm which cognitive tests have a prognostic value and can be used before surgery. Furthermore, future research should also investigate the preoperative predictors of return to work and work ability, two types of outcome that were not found in this review but that are fundamental for patients with brain tumor who usually are adult working age population. Finally, future studies on prognostic factors in brain tumor surgery should be done using prospective designs, standardized and validated measures, populations of patients with specific diagnoses, and controlling factors that could influence the surgical outcome.

Conclusion

This literature review summarizes the existing data on the predictive value of preoperative nonmedical factors in relation to the outcome in brain tumor surgery. Only a qualitative synthesis of the prognostic factors was performed due to the wide variety in the outcome measures, statistical analyses, and potential predictors. Socio-demographic (age, marital status, type of insurance, gender, socio-economic status, type of hospital), cognitive (preoperative language and cognitive deficits, performance at TMT-B test), and psychological factors (preoperative depressive symptoms, personality traits, autonomy for daily activities, altered mental status) were found to be predictors of surgical outcomes considering both clinical outcome and cognitive, psychological, and social ones. Future research should be done to confirm the predictive value of these factors and to explore further potential nonmedical predictors in order to take into account also these variables in the prognostic process before brain tumor surgery.

Code availability Not applicable.

Authors' contributions Silvia Schiavolin had the idea for this article, performed the literature review and data analysis, and drafted the work. Alberto Raggi, Chiara Scaratti, Claudia Toppo, Fabiola Silvaggi, and

Davide Sattin performed literature review and critically revised the work. Morgan Broggi, Paolo Ferroli, and Matilde Leonardi critically revised the work.

Data availability Not applicable.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval No ethical approval was required, as this is a literature review.

Informed consent This article, being a literature review, does not contain any studies with human participants performed by any of the authors, and is based solely on the analysis of previously published literature.

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