


*Systematic Review*

# Prediction of Survival Outcomes in Patients with Glioma Using Magnetic Resonance Imaging (MRI): A Systematic Review and Meta-Analysis

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## Abstract

**Background:** Glioma is the most common malignancy in the central nervous system. Even with optimal therapies, glioblastoma (the most aggressive form of glioma) is incurable, with only 26.5% of patients having a 2-year survival rate. The present meta-analysis evaluated the association of magnetic resonance imaging (MRI)-derived parameters in glioma patients with progression-free survival (PFS) and overall survival. Eligible clinical articles on glioma patients included those that contained an evaluation of the association between MRI findings, PFS, and overall length of survival. **Methods:** Review of the literature included the following databases: WHO International Clinical Trials Registry Platform; Google Scholar; Web of Science; PubMed; SIGLE; NYAM; Scopus; Randomized controlled trial (RCT); Virtual Health Library (VHL); Cochrane Collaboration; EMBASE; and Clinical Trials. **Results:** The current review included 20 studies, and covered 2097 patients with gliomas. There were 1310 patients with glioblastoma and 320 with astrocytoma. There were 161 patients with grade-2 gliomas and 111 patients with grade-3. Tumour necrosis, peritumoural oedema, and multiple lesions were associated with PFS, as well as tumour necrosis and peritumoural oedema with overall survival. **Conclusions:** The present meta-analysis highlighted the ability of MRI to predict PFS and overall survival in patients with gliomas. This is crucial to identify patients at risk for poor survival outcomes and for individualising the treatment plan for such patients. **The PROSPERO Registration:** CRD42023489535, [https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=489535](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=489535).

**Keywords:** glioblastoma; glioma; MRI; survival

## 1. Introduction

Glioma is the commonest malignancy in the central nervous system (CNS) [1]. Gliomas are diffuse infiltrative tumours arising from the glial cells of the CNS. In the United States, 6 cases per 100,000 population are diagnosed with glioma yearly. There are three types of gliomas based on the phenotypic cell characteristics: astrocytoma; ependymoma; and oligodendroglioma. The most malignant type of glioma is glioblastoma, and the least malignant is pilocytic astrocytoma [2,3]. Managing gliomas necessitates adequate pre-operative imaging, surgery planning, and post-operative care. The surgical management is based mainly on tumour resection or stereotactic biopsy with the intraoperative determination of the tumour margins using accurate imaging modalities [4,5].

Glioblastoma carries a poor prognosis even after standard management. Even with the optimal therapies, glioblastoma is incurable, with only 26.5% of patients having a 2-year overall survival rate. The median survival time of glioblastoma is 14 months, and it decreases to 30 weeks at recurrence [6,7]. The presence of a glioma tumour is primarily evaluated using gadolinium-enhanced magnetic resonance imaging (MRI). However, this diagnostic modality

has a low accuracy with some treatment modalities, resulting in a pseudoresponse phenomenon. The phenomenon is associated with a rapid decline in contrast leakage of the gadolinium, thereby producing a failure to reflect tumour size or activity accurately [8]. Diffusion imaging has gained attraction recently as an effective diagnostic tool for assessing tumour response and progression. Recently, there has been a great interest in implementing multi-parametric MRI sequences in estimating tumour infiltration and determining treatment in patients with glioma [9,10]. MRI is a non-invasive tool that provides information on the physiological characteristics of the tumour. These data have been widely used to estimate the baseline risk and survival, which are essential to assigning glioma patients to the necessary treatment [11].

MRI parameters are routinely obtained from glioma patients, independent of the treatment received. These may provide crucial predictive information for prognosis and evaluation of treatment response. Feasible and accurate prognostic modalities for patients with gliomas may help to individualize treatment for each patient, in order to improve long-term outcomes. The prognosis of gliomas is unpredictable, and depends on many factors. The aggressiveness of the tumour is one of the most significant factors [12,13].



Of note, grades I and II gliomas are low-grade tumours with a reasonable prognosis, with approximately 95% of patients showing a 5-year survival rate (grade I). The survivability is less predictable and poorer with more advanced diseases, with only 7% of patients with glioblastoma surviving for 5 years after diagnosis [14]. The average survival time of glioblastoma is 12–18 months, with approximately only 25% of patients surviving for more than 12 months [15].

There was abundant literature evaluating the predictive value of MRI findings in patients with gliomas. Previously published systematic reviews investigated the accuracy of MRI in diagnosing, differentiating, and assessing treatment responses among glioma patients [16–18]. However, the literature reflected differences in MRI techniques, disease differentiation, treatment modalities, patients' characteristics, and study methods [19]. These differences highlight the need for a conclusive report to estimate the findings in different MRI modalities that may predict survival outcomes in patients with gliomas. Such knowledge is essential in order to assign patients at higher mortality risk to the necessary management plan and to decrease potential consequences of gliomas. Therefore, the present meta-analysis evaluated the association between MRI-derived parameters and progression-free survival (PFS), and overall survival, in glioma patients.

## 2. Methods

This systematic review and meta-analysis followed the recommendations offered by the Cochrane collaboration [20] and by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting systematic reviews and meta-analyses [21] (**Supplementary Materials-PRISMA\_2020\_checklist**). The protocol of the present meta-analysis was registered prospectively in the PROSPERO database (Number: CRD42023489535).

### 2.1 Literature Search

A comprehensive review of the literature was performed from the beginning of the literature on the topic until 12th December 2023. Review of the literature included the following databases: WHO International Clinical Trials Registry Platform; Google Scholar; Web of Science; PubMed; SIGLE; NYAM; Scopus; Randomized controlled trial (RCT); Virtual Health Library (VHL); Cochrane Collaboration; EMBASE; and Clinical Trials. The search string included the following keywords: MRI; Magnetic Resonance Imaging; Magnetic Resonance Image; Glioma; Gliomas; Glioblastoma; Mortality; Death; Survival; Survivability; and Prognosis. The search strategy imposed no restrictions related to patients' demographics or to study demographics. Citation tracking and screening of the references of previous reviews was performed in addition to cross-referencing to include all potentially eligible articles.

### 2.2 Study Selection

All clinical articles that were used included (a) patients with gliomas; (b) evaluation of the association between MRI findings and PFS; and (c) overall survival data of patients with gliomas. The present study implemented the Cox regression model to calculate the hazard ratio (HR) for the time to relevant outcomes. We did not restrict the data as to glioma grade, type, differentiation, or diagnostic criteria. Furthermore, we excluded irrelevant articles, unextractable data, reviews, guidelines, case reports, cadaveric articles, studies that implemented artificial intelligence models, errata, case series, letters, comments, meeting abstracts, posters, and book chapters. The screening processes were carried out independently to determine the relevant articles that fulfil the inclusion criteria and to exclude irrelevant studies. A PRISMA flowchart was designed to document the search process, screening, and article-exclusion causes at each step of the literature review.

### 2.3 Data Extraction

The source-related data were extracted, including the title, study ID, study URL, study location, study period, and study design. Methods-related data were extracted, including the eligibility criteria, the imaging technique, the management of gliomas, study outcomes, and follow-up protocols. Baseline patients' demographic data were retrieved, including sample size, age, weight, body mass index (BMI), and comorbid disorders. The tumour-related variables were retrieved, including the type, histopathological grade, location, initial therapy, extent of resection, and post-operative radiotherapy or chemotherapy. included: contrast enhancement; tumour necro The MRI parameters examined for association with PFS, and overall survival were sis; the extent of resection; peritumoural oedema; tumour volume, diameter, and margins; apparent diffusion coefficient; and multiple lesions.

### 2.4 Quality Assessment

The quality of the eligible observational studies was evaluated using the National Institute of Health quality-assessment tool [22]. The analyzed articles were sorted into 'good', 'fair', and 'bad'.

### 2.5 Data Analysis

The summary of HR was computed by pooling the HR from all the relevant articles. A fixed-effect model was used when methodological and statistical homogeneity between the study variables was established. A random-effects model was used when the statistical heterogeneity was found. Statistical homogeneity was determined using Higgins  $I^2$  statistic, at  $>50\%$ , and the Cochrane Q ( $\chi^2$  test), at  $p \leq 0.10$  [23]. Publication bias was assumed in the presence of an asymmetrical funnel plot and based on Egger's regression test ( $p < 0.10$ ). Subgroup analysis was performed on the type of glioma. Review Manager, v. 5.4 (The

Nordic Cochrane Centre, Copenhagen, Denmark) [24], was used to analyze the data. The significant associations with PFS and overall survival were based on  $p \leq 0.05$ .

### 3. Results

A systematic review of the literature yielded 2709 studies. Of them, 713 duplicate reports were excluded, resulting in 1996 studies eligible for title and abstract screening. A further 1968 reports were removed, resulting in 128 studies that were eligible for full-text screening. Subsequently, 106 studies were excluded, resulting in 22 articles eligible for data extraction. Three reports with unextractable data were excluded, and one study was identified through citation tracking. A total of twenty articles were finally included for systematic review and meta-analysis (see Fig. 1).

#### 3.1 Demographic Characteristics and Quality Assessment of the Analyzed studies

The present meta-analysis included 20 articles, which included 2097 glioma patients [25–44]. There were four prospective studies and 15 retrospective designs. Six studies included patients from the United States, and four arti-

cles included patients from China. The age of the analyzed patients ranged from 36 to 63 years. There were 1159 males and 748 females. There were 1310 patients with glioblastoma and 320 with astrocytoma. There were 161 patients with grade-2 gliomas and 111 patients with grade-3. There were 104 patients with frontal lobe involvement, and 39 with parietal lobe involvement. The temporal lobe was affected in 89 patients and the insular region was affected in 10 patients. The follow-up period ranged from 12 to 65 months, with overall survival time ranging from 7.6 months to 18.4 months. All the analyzed articles showed good quality, with scores ranging from 66.66% to 75% (Table 1, Ref. [25–44]).

#### 3.2 Factors Associated with Progression-Free Survival (PFS)

**Contrast enhancement.** Ten articles evaluated the association between contrast enhancement of gliomas, using MRI, and PFS [25–27,29,31–33,38,39,41]. In the random-effects model ( $I^2 = 83\%$ ,  $p < 0.001$ ), there was no significant association between contrast enhancement and PFS (HR = 1.15; 95% Confidence Interval (CI): 0.84, 1.56;  $p = 0.39$ ). Subgroup analysis based on the type of glioma revealed no statistically significant association between con-

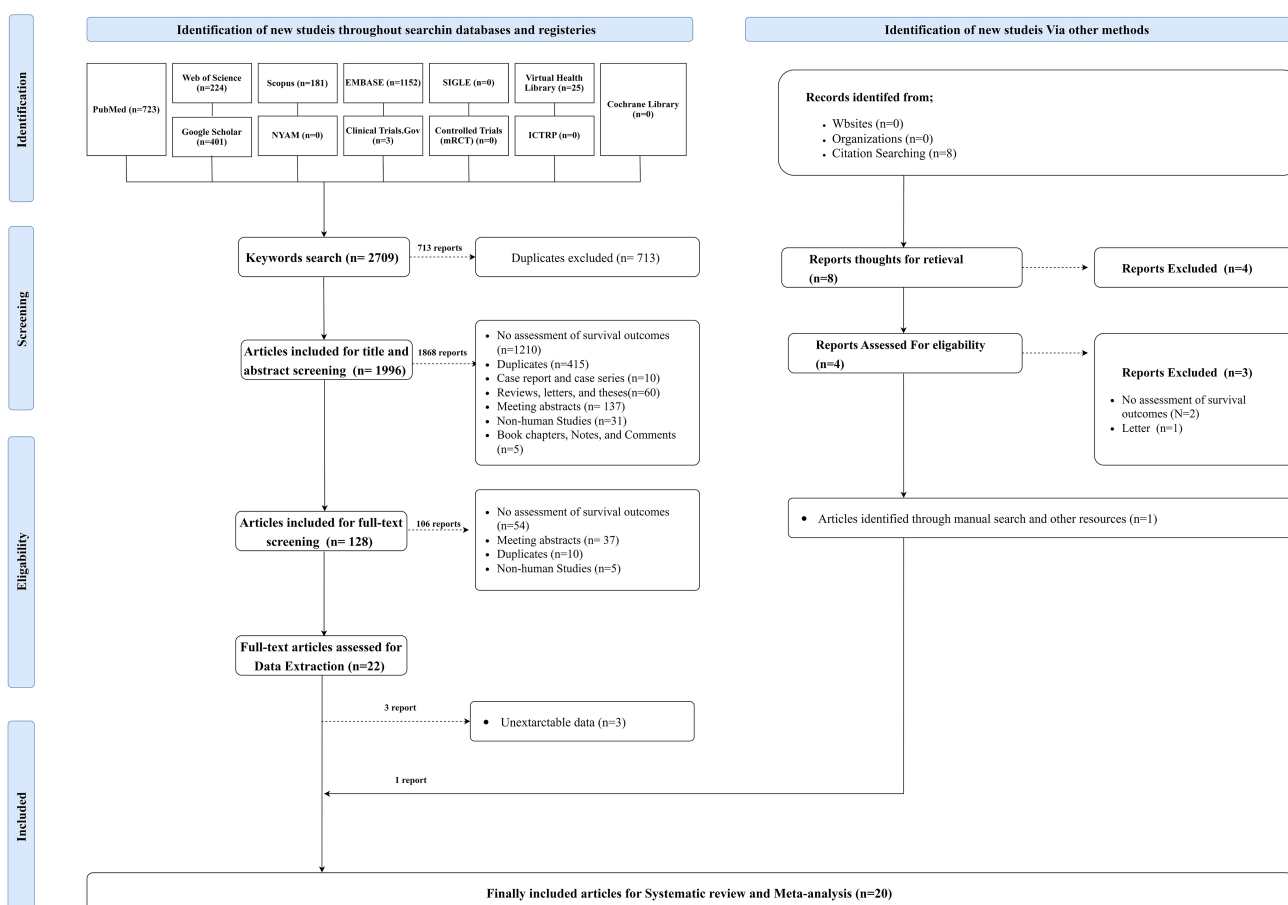


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow chart showing the selection process.

Table 1. Baseline Demographic and glioma characteristics of the analyzed studies.

Study ID	Study region	Study design	Study period	Sample size	Age (Years)	Gender		Type of Glioma				Grade of Glioma				Tumour Location					Type of MRI	Follow-up period	Overall survival (Months)	PFS (Months)	Quality assessment		
						Males	Females	Glioblastoma	Astrocytoma	Oligodendroglioma	Other	Grade-2	Grade-3	Grade-4	Frontal lobe	Parietal lobe	Temporal lobe	Insular region	Occipital lobe	Multifocal					%	Decision	
						Number	Mean (SD)	Number	Number	Number	Number	Number	Number	Number	Number	Number	Number	Number	Number	Number					Number	Number	Number
1	Sacil-Bilmez <i>et al.</i> , 2023 [39]	Türkiye	Retrospective	September 2011 and February 2019	57	58 ± 10.47	35	22	57	0	0	0	4	8	45	19	6	12	10	8	NR	Contrast-Enhanced Perfusion	65 months	NR	NR	75%	Good
2	Burth <i>et al.</i> , 2016 [25]	Germany	Retrospective	July 2009 to August 2014	125	63 (37–71) *	75	50	125	0	0	0	NR	NR	NR	35	18	32	0	9	35	Diffusion- and Perfusion-Derived MRI	NR	10.7 (8.9–13.3) *	4.8 (4.1–6.3) *	75%	Good
3	Chen <i>et al.</i> , 2013 [26]	USA	Retrospective	2006 to 2010	191	56 (24–88) *	121	70	161	30	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Contrast-Enhanced Perfusion	12 Months	7.6 (6.7, 9.0) *	4.4 (3.5, 4.7) *	66.66%	Good	
4	Choi <i>et al.</i> , 2015 [27]	Korea	Retrospective	October 2010 through April 2014	61	63 ± 9.8	32	29	61	0	0	0	NR	NR	NR	19	15	18	0	2	0	Dynamic Contrast-Enhanced	24 to 893 days	552.6 ± 40.6 days	359.7 ± 31.2 days	75%	Good
5	Hong <i>et al.</i> , 2021 [29]	Korea	Retrospective	January 2011 and September 2016	76	47.69 (19–68) *	47	29	0	57	19	0	0	76	0	NR	NR	NR	NR	NR	NR	Conventional Dynamic Contrast Enhanced	16.3	NR	38.93 (30.42–43.88)	75%	Good
6	Hou <i>et al.</i> , 2018 [30]	USA	Retrospective	from 2009 to 2015	36	NR	22	14	36	0	0	0	NR	NR	NR	NR	NR	NR	NR	NR	NR	Diffusion- and Perfusion-Derived MRI	NR	290 ± 272	NR	66.66%	Good
7	Lasocki <i>et al.</i> , 2023 [31]	Australia	Retrospective	September 2007 and December 2013	58	36.0 years	39	19	0	36	0	0	51	7	0	NR	NR	NR	NR	NR	NR	Conventional MRI	NR	NR	NR	66.66%	Good
8	Li <i>et al.</i> , 2019 [32]	UK	Prospective	July 2010 to April 2015	112	NR	84	28	112	0	0	0	NR	NR	NR	NR	NR	NR	NR	NR	NR	Advanced Magnetic Resonance Imaging	NR	455 (52–1376 days) *	265 (25–1130 days) *	75%	Good
9	Liu <i>et al.</i> , 2017 [35]	China	Retrospective	NR	95	50 (19–76) *	59	36	95	0	0	0	NR	NR	NR	NR	NR	NR	NR	NR	NR	Conventional MRI	NR	NR	NR	75%	Good
10	Liu <i>et al.</i> , 2021 [33]	China	Retrospective	January 2010 to December 2016	90	37.7 ± 13.0	53	37	NR	NR	NR	0	90	0	NR	NR	NR	NR	NR	NR	NR	Conventional MRI	NR	NR	NR	75%	Good
11	Liu <i>et al.</i> , 2017 [34]	China	Retrospective	September 2006 and December 2011	160	NR	101	59	NR	58	NR	NR	NR	NR	24	NR	15	NR	25	NR	NR	Conventional MRI	912 days	NR	NR	66.66%	Good
12	Nakamura <i>et al.</i> , 2013 [36]	Japan	Retrospective	January 2000 and September 2009	138	NR	NR	NR	138	0	0	0	NR	NR	NR	NR	NR	NR	NR	NR	NR	Conventional MRI	24 months	13.7	4.4	75%	Good
13	Patel <i>et al.</i> , 2018 [37]	USA	Cross-sectional	2003 to 2016	45	46.4 ± 16.2	22	23	2	18	12	0	16	14	13	NR	NR	NR	NR	NR	NR	Contrast-Enhanced Perfusion	NR	NR	NR	75%	Good
14	Pérez-Beteta <i>et al.</i> , 2019 [38]	Spain	Prospective	2006–2017	311	63 (19–86) *	174	137	311	0	0	0	NR	NR	NR	NR	NR	NR	NR	NR	NR	Conventional MRI	NR	NR	NR	66.66%	Good
15	Schwarzenberg <i>et al.</i> , 2012 [40]	USA	Prospective	NR	30	NR	18	12	24	6	0	0	0	6	24	NR	NR	NR	NR	NR	NR	Conventional MRI	NR	NR	NR	66.66%	Good
16	Shin <i>et al.</i> , 2022 [41]	Korea	Retrospective	May 2001 and July 2020	56	NR	29	27	0	56	0	0	NR	NR	NR	7	0	5	0	2	NR	Conventional MRI	42.0 (20.5–107.5) *	NR	NR	75%	Good
17	Tatekawa <i>et al.</i> , 2020 [42]	USA	Retrospective	2007 and 2019	86	43.8 ± 12.6	52	34	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Contrast-Enhanced Perfusion	NR	NR	NR	75%	Good
18	Gupta <i>et al.</i> , 2018 [28]	Germany	Retrospective	NR	34	NR	NR	NR	34	0	0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Conventional MRI	18 (IQR, 13–33)	17.1	12.1	75%	Good
19	Young <i>et al.</i> , 2011 [43]	USA	Prospective	March 2003 and August 2005	39	58.4 ± 11.9	29	10	39	0	0	NR	NR	NR	NR	NR	NR	7	NR	19	4	Conventional MRI	18.2 (3.1–41.7)	15.6 (11.1–24.1) *	6.7 (5.2–7.2) *	66.66%	Good
20	Zhao <i>et al.</i> , 2022 [44]	China	Retrospective	January 2016 and December 2021	279	40.98 ± 11.84	167	112	115	89	75	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Conventional MRI	15 (3–57)	NR	NR	66.66%	Good

Abbreviations: SD, standard deviation; MRI, Magnetic Resonance Imaging; PFS, Progression free survival; NR, Non-reported; IQR, Interquartile Range. \* Median and range.

trast enhancement and PFS among patients with glioblastoma (HR = 1.25; 95% CI: 0.94, 1.68;  $p = 0.13$ ). There was no evidence of publication bias (Egger's regression test,  $p > 0.10$ ) with the symmetrical distribution of the analyzed articles within the funnel plot (Fig. 2A,B).

**Tumour necrosis.** The association between tumour necrosis of gliomas and PFS was evaluated in 6 articles [26,29,31,38,39,44]. There was no significant impact of tumour necrosis finding in MRI and PFS (HR = 1.39; 95% CI: 0.94, 2.06;  $p = 0.10$ ) in the random-effects model ( $I^2 = 32\%$ ;  $p = 0.19$ ). Subgroup analysis revealed no statistically significant association between tumour necrosis and PFS among patients with glioblastoma (HR = 1.68; 95% CI: 0.69, 4.08;  $p = 0.25$ ) (Fig. 2C).

**Peritumour edema.** Four articles evaluated the association between peritumour edema and PFS [25,28,33,41]. In the random-effects model ( $I^2 = 0\%$ ;  $p = 0.78$ ), there was a statistically significant negative relationship between peritumour edema development and PFS (HR = 2.68; 95% CI: 1.54, 4.64;  $p = 0.005$ ) (Fig. 2D).

**Tumour volume.** The association between tumour volume and PFS was assessed in four articles [25,34,35,38]. There was no statistically significant association between tumour volume and PFS (HR = 1.09; 95% CI: 0.99, 1.21;  $p = 0.07$ ) in the random-effects model ( $I^2 = 0\%$ ;  $p = 0.44$ ) (Fig. 2E).

**Tumour diameter.** Three studies evaluated the impact of tumour diameter on PFS among patients with gliomas [38,40,44]. In the random-effects model ( $I^2 = 81\%$ ;  $p = 0.005$ ), there was no statistical association between tumour diameter and PFS (HR = 1.37; 95% CI: 0.68, 2.73;  $p = 0.38$ ) (Fig. 3A).

**Apparent diffusion coefficient.** The impact of the apparent diffusion coefficient on PFS among patients with gliomas was reported in two studies [29,32]. There was no statistically significant association between the apparent diffusion coefficient and PFS (HR = 0.69; 95% CI: 0.05, 9.06;  $p = 0.77$ ) in the random-effects model ( $I^2 = 82\%$ ;  $p = 0.02$ ) (Fig. 3B).

**Multiple lesions.** Three articles evaluated the association between multiple lesions, seen on MRI, and PFS [32,43,44]. In the random-effects model ( $I^2 = 12\%$ ;  $p = 0.32$ ), there was no significant association between multiple lesions and PFS (HR = 1.57; 95% CI: 0.92, 2.69;  $p = 0.10$ ) (Fig. 3C).

### 3.3 Factors Associated with Overall Survival

**Contrast enhancement.** Eight articles evaluated the impact of contrast enhancement on overall survival in patients with glioma [25–27,32,33,37,39,41]. No significant association was observed between contrast enhancement and overall survival (HR = 1.12; 95% CI: 0.87, 1.44;  $p = 0.38$ ) in the random-effects model ( $I^2 = 69\%$ ;  $p = 0.002$ ). Subgroup analysis revealed no significant association between contrast enhancement and overall survival (HR =

1.37; 95% CI: 0.78, 2.40;  $p = 0.48$ ) (Fig. 3D).

**Tumour necrosis.** The impact of tumour necrosis on the overall survival in patients with gliomas was evaluated in three studies [26,39,44]. There was a statistically significant negative association between tumour necrosis and overall length of survival (HR = 1.74; 95% CI: 1.04, 2.90;  $p = 0.03$ ) (Fig. 3E).

**Peritumour edema.** Four studies showed an association between peritumour edema and overall survival in glioma patients [25,28,32,41]. Pooling the effect sizes in the random-effects model ( $I^2 = 0\%$ ;  $p = 0.40$ ) revealed a statistically significant negative association between peritumour edema development and overall survival time (HR = 2.43; 95% CI: 1.42, 4.17;  $p = 0.001$ ) (Fig. 3F).

**Tumour volume.** The impact of the tumour volume on the overall survival in patients with gliomas was reported in three articles [25,34,35]. In the random-effects model ( $I^2 = 96\%$ ;  $p < 0.001$ ), there was no significant association between tumour volume and overall survival (HR = 1.34; 95% CI: 0.83, 2.16;  $p = 0.24$ ) (Fig. 4A).

**Tumour diameter.** Three articles reported the association between tumour diameter and overall survival in patients with gliomas [33,40,44]. There was no significant association between tumour diameter and overall survival (HR = 1.71; 95% CI: 0.21, 13.98;  $p = 0.62$ ) in the random-effects model ( $I^2 = 81\%$ ;  $p = 0.005$ ) (Fig. 4B).

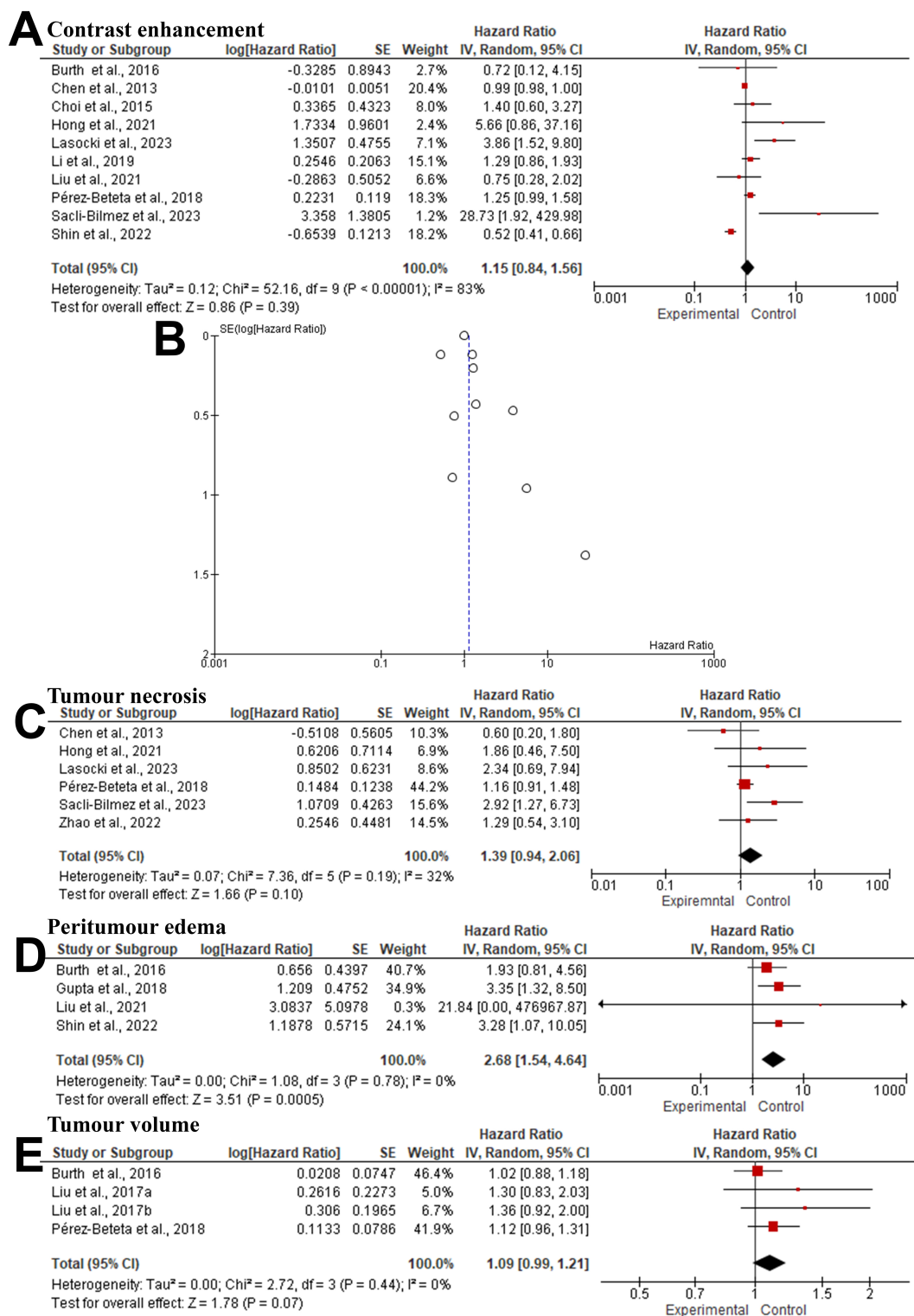
**Apparent diffusion coefficient.** The association between the apparent diffusion coefficient and overall survival in patients with gliomas was evaluated in three articles [30,36,42]. There was no statistically significant association between apparent diffusion coefficient and overall survival (HR = 1.06; 95% CI: 0.50, 2.25;  $p = 0.88$ ) in the random-effects model ( $I^2 = 88\%$ ;  $p = 0.0002$ ) (Fig. 4C).

**Multiple lesions.** Three studies evaluated the association between multiple lesions observed in MRI and overall survival among patients with gliomas [33,43,44]. Meta-analysis revealed no statistically significant association between multiple lesions and overall survival (HR = 1.42; 95% CI: 0.92, 2.19;  $p = 0.11$ ) in the random-effects model ( $I^2 = 0\%$ ;  $p = 0.38$ ) (Fig. 4D).

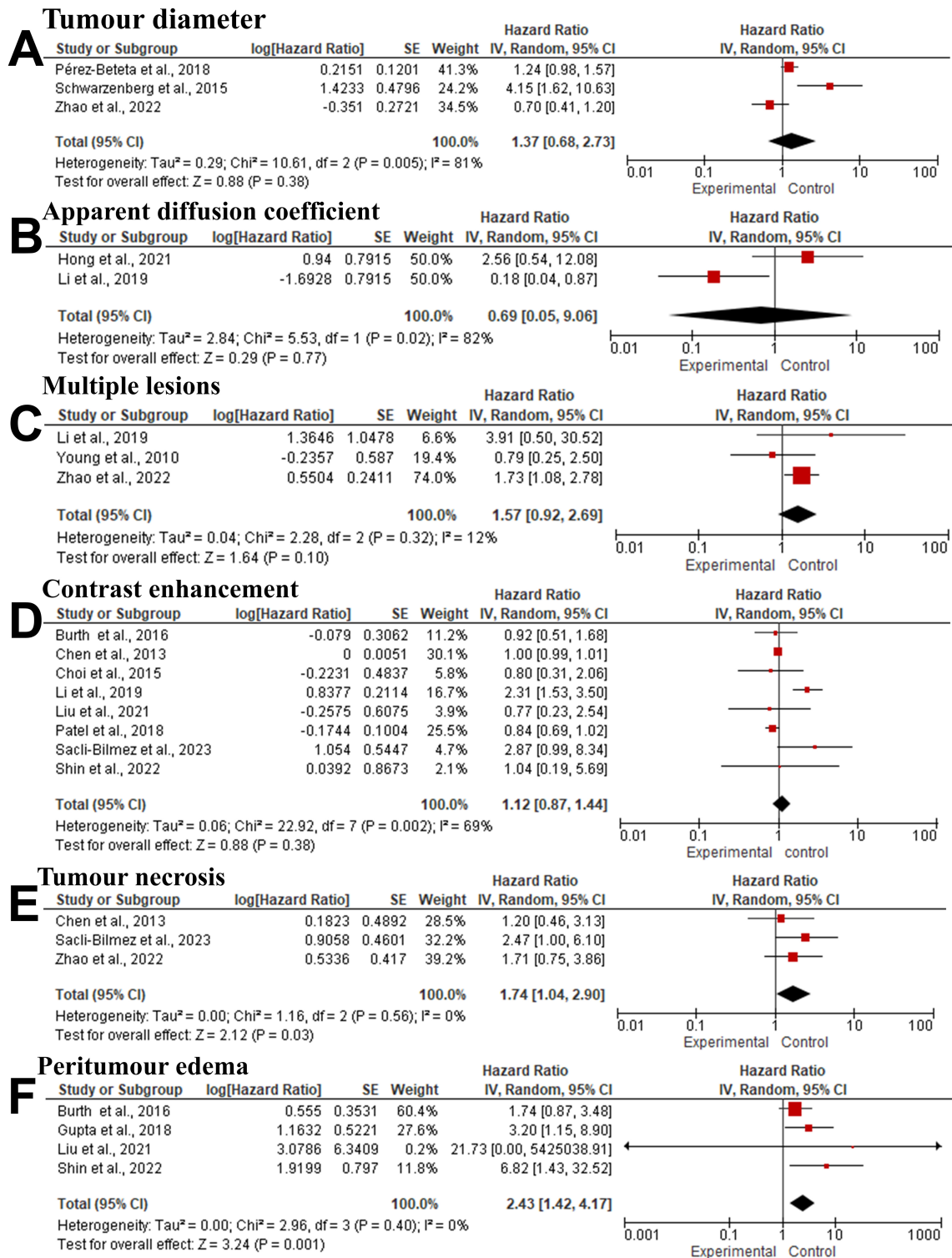
**Tumour margins.** The impact of tumour margins evaluated by MRI on the overall survival in patients with gliomas was reported in two articles [31,41]. In the random-effects model ( $I^2 = 93\%$ ;  $p = 0.0002$ ), there was no statistically significant association between tumour margins and overall survival (HR = 2.16; 95% CI: 0.05, 86.13;  $p = 0.68$ ) (Fig. 4E).

## 4. Discussion

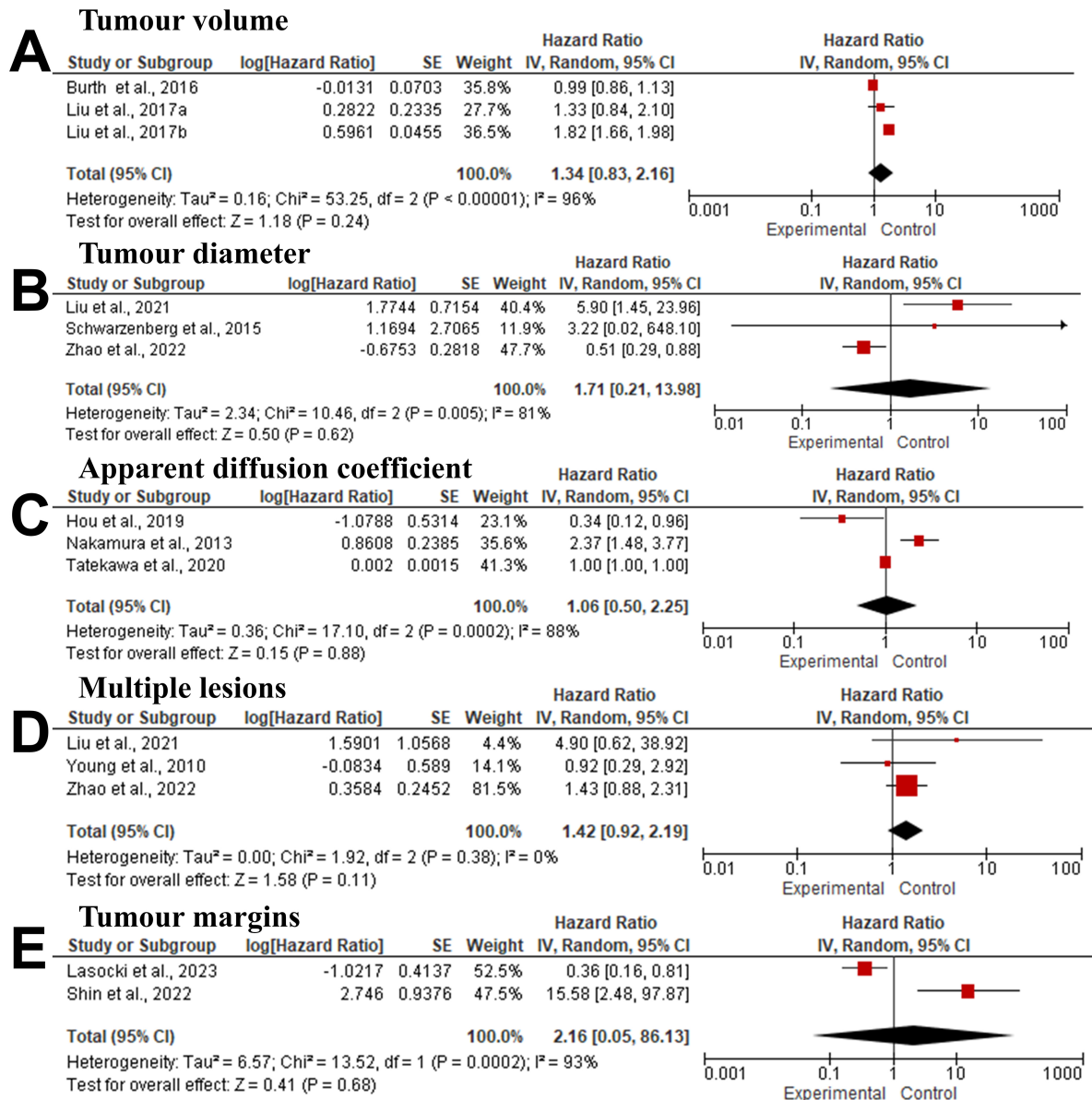
MRI technology has evolved as a non-invasive tool for diagnosing, evaluating, and predicting treatment responses in patients with gliomas. It overcomes the drawbacks of molecular biomarkers that can only be obtained by invasive procedures such as resection or biopsy. Post-operative MRI has a significant role for symptomatic patients, particularly



**Fig. 2. Factors Associated with Progression-Free Survival.** Forest plot of pooled analysis of the (A) HR and 95% CI of the association between contrast enhancement, using MRI, and PFS. (B) Funnel plots showing no evidence of publication bias of the association between contrast enhancement, using MRI, and PFS. (C) HR and 95% CI of the association between tumour necrosis using MRI and PFS. (D) HR and 95% CI of the association between peritumour edema using MRI and PFS. (E) HR and 95% CI of the association between tumour volume, using MRI and PFS. MRI, magnetic resonance imaging; PFS, progression-free survival; HR, hazard ratio; CI, Confidence Interval; IV, inverse variance; SE, standard error.



**Fig. 3. Factors Associated with Overall Survival** a. Forest plot of summary analysis of the (A) HR and 95% CI of the association between tumour diameter, using MRI. and PFS. (B) HR and 95% CI of the association between apparent diffusion coefficient using MRI and PFS. (C) HR and 95% CI of the association between multiple lesions using MRI and PFS. (D) HR and 95% CI of the association between contrast enhancement using MRI and overall survival. (E) HR and 95% CI of the association between tumour necrosis using MRI and overall survival. (F) HR and 95% CI of the association between peritumour edema, using MRI, and overall survival.



**Fig. 4. Factors Associated with Overall Survival b.** Forest plot of summary analysis of the (A) HR and 95% CI of the association between tumour volume using MRI and overall survival. (B) HR and 95% CI of the association between tumour diameter using MRI and overall survival. (C) HR and 95% CI of the association between apparent diffusion coefficient using MRI and overall survival. (D) HR and 95% CI of the association between multiple lesions using MRI and overall survival. (E) HR and 95% CI of the association between tumour margins using MRI and overall survival.

in determining recurrence and pseudoresponse. MRI may change the treatment strategy and help clinical decision-making for glioma patients [45,46]. However, conflicting results were reported regarding the value of different MRI findings in predicting PFS and overall survival in patients with gliomas [47,48]. The present meta-analysis evaluated the association between MRI-derived parameters and PFS, and overall survival time among patients with gliomas. In particular, tumour necrosis visualized with MRI was associated with 1.39 times shorter PFS, and tumour volume was

associated with 1.37 times shorter PFS. Peritumour oedema was associated with more than twofold shorter PFS, and multiple lesions revealed 1.57 times shorter PFS. In this respect, peritumoural oedema showed 2.43 times shorter overall survival. Tumour volume and tumour diameter showed a significant association with overall survival, with an HR of 1.4 and 1.37, respectively. The presence of multiple lesions showed shorter overall survival with an HR of 1.42, and tumour margins showed more than twofold shorter overall survival.

The present meta-analysis showed the predictive ability of MRI to diagnose patients with poor survival outcomes. This knowledge helps to stratify patients and potentially provide targets for individualized treatment guidelines. Consistent with these findings, Brancato *et al.* [49] reported that MRI metrics provided useful information to predict the survival of patients with glioblastoma, particularly if combined with multi-modality imaging properties and clinical factors. Oltra-Sastre *et al.* [50] reported on the importance of MRI in predicting clinical outcomes in patients with gliomas. Zhou *et al.* [51] showed the ability of non-invasive imaging modalities to predict treatment response and prognosis in patients with high-grade gliomas before surgery. Tumour necrosis was associated with shorter PFS and overall survival. The presence of tumour necrosis reflects the aggressiveness of the gliomas, and which carry poor prognosis. This necrosis is due to activation of the hypoxia-mediated coagulation system, which results in endothelial proliferation, intravascular thrombosis, and necrosis [52]. Peritumoural oedema was associated with worse survival outcomes, with approximately two times shorter PFS and overall survival than patients without oedema [53]. Contrary to this finding, Liu *et al.* [54] reported inconclusive results regarding the association between pre-operative peritumoural oedema and overall survival outcomes in patients with gliomas. The discrepancy between their findings and this meta-analysis may be attributable to the number of analyzed articles included in both systematic reviews. Tumour size and diameter were associated with poor survival outcomes, worsening the PFS, and shortening of overall survival by approximately 40%. Tumour necrosis, peritumoural oedema, and tumour size were easy to determine with routine MRI evaluations and could provide instructive information for clinical practice [55]. Another factor that may be associated with survival outcomes, but was not examined in the present review, is glioma-associated macrophages. These have a vital role in the recurrence of glioblastoma microenvironment. Macrophages reflect tumour aggressiveness and overall survival in patients with glioblastoma [56].

The present study quantified the ability of MRI to predict PFS and overall survival in patients with gliomas. However, the results of this study should be cautiously interpreted in the context of some limitations. The main limitation is that MRI technology needs more standardization with different technical modalities and diagnostic approaches for patients with gliomas. This limitation and the difference in study designs, and in type, grade, location, and differentiation of glioma, may result in significant heterogeneity among the analyzed predictors. The majority of the analyzed articles were retrospective designs, conveying a higher risk of information selection and reporting biases. As mentioned, there are other factors that may be associated with survival outcomes in patients with gliomas, but these factors have not been studied sufficiently to subject them to

meta-analysis. Prospective-cohort studies with strict methods are necessary to mitigate the limitations of the present meta-analysis.

## 5. Conclusions

The present meta-analysis highlighted the ability of MRI to predict PFS and overall survival in patients with gliomas. Tumour necrosis, peritumoural oedema, or multiple lesions seen in MRI were associated with shorter PFS. There was an association between overall survival and peritumoural oedema, tumour volume, diameter, or multiple lesions. Subgrouping based on the type of glioma revealed no significant association between contrast enhancement, tumour necrosis, and survival outcomes. Identifying such evidence is critical for identifying patients at higher risk of survival outcomes and individualising the treatment plan for the patients.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Author Contributions

MFH, ZYL and JS designed the research study. MFH, ZYL and JS performed the literature searches and analyzed the data. JGL provided help and advice on data analysis. MFH and ZYL wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

Not applicable.

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## Conflict of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/JIN23389>.

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