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Laser interstitial thermal therapy for high-grade glioma: a systematic review, meta-analysis, and meta-regression

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OBJECTIVE Despite advances in the management of high-grade glioma (HGG), overall survival (OS) and progression-free survival (PFS) remain suboptimal given the aggressive nature of these tumors. Difficult-to-access tumor locations, high complication rates, and high tumor progression rates further complicate the treatment of HGG. Herein, the authors aimed to comprehensively evaluate the safety and efficacy of laser interstitial thermal therapy (LITT) for HGG.

METHODS A systematic review of the literature was conducted through four electronic databases (Web of Science, PubMed, Embase, and the Cochrane Library) to identify studies on LITT for HGG treatment. Binary and continuous outcomes were assessed using odds ratios, mean differences, and 95% confidence intervals. Meta-regression was conducted to determine the source of heterogeneity and to assess predictors of key outcomes with high heterogeneity.

RESULTS Twenty-one studies with 602 patients harboring HGG were included in this review. Mean OS following LITT was 11.74 months (95% CI 10.9–12.6 months), with 6-, 12-, and 24-month OS rates of 77.0% (95% CI 65.8%–86.6%), 48.9% (95% CI 40.5%–57.3%), and 16.1% (95% CI 10.7%–22.3%), respectively. Mean PFS was 5.3 months (95% CI 4.97–5.7 months), with 6-, 12-, and 24-month PFS rates of 37.1% (95% CI 24.3%–44.6%), 12.8% (95% CI 8.7%–17.5%), and 4.3% (95% CI 2.2%–6.9%), respectively. Postoperative permanent deficits occurred in 5.7% of patients (95% CI 0.85%–13.1%). Subgroup analysis showed that LITT for deep and unresectable HGG had a 12-month OS rate of 53.0% (95% CI 20.0%–84.7%) and 12-month PFS rate of 12.9% (95% CI 0.02%–38.3%). Additionally, newly diagnosed HGG had a significantly higher rate of permanent deficits (4.15%, 95% CI 0.4%–10.2%) than recurrent HGG (0.02%, 95% CI 0.0%–2.2%; p = 0.023). Sensitivity analysis showed significantly higher 6-month OS in newly diagnosed cases (p = 0.0069), with no differences in OS, PFS, post-LITT tumor progression, Karnofsky Performance Status change from baseline, or temporary deficits.

CONCLUSIONS LITT is an effective treatment for HGGs, with an acceptable safety profile. However, further randomized prospective studies are necessary to validate these findings and establish the procedure's long-term efficacy.

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KEYWORDS laser interstitial thermal therapy; LITT; high-grade glioma; brain tumor

High-grade gliomas (HGGs) are ranked among the most common and aggressive primary brain tumors associated with rapid growth, high progression rate, and poor outcomes.[1–3] The incidence of HGG in the United States is approximately 3.56 per 100,000 population, with glioblastoma accounting for nearly 90% of these cases.[4] Despite significant improvements in resection, radiation therapy, and chemotherapy, the management of HGG remains challenging, often requiring alternative therapeutic modalities to enhance patient outcomes and minimize complications.[3,5,6]

Laser interstitial thermal therapy (LITT) has emerged as a promising minimally invasive treatment option for patients with HGG, particularly those with recurrent or

ABBREVIATIONS HGG = high-grade glioma; KPS = Karnofsky Performance Status; LITT = laser interstitial thermal therapy; LOS = length of stay; OS = overall survival; PFS = progression-free survival; ROBINS-I = Risk of Bias in Non-randomized Studies of Interventions.

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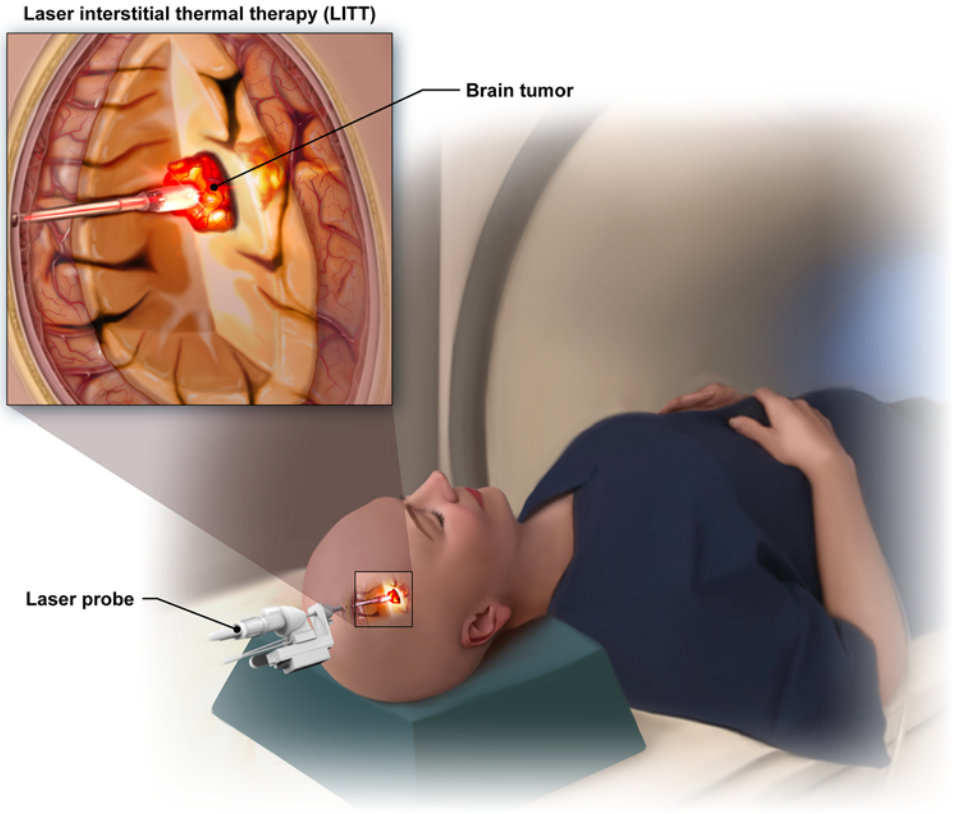

FIG. 1. Illustration of the LITT procedure in a patient with HGG. © Houston Methodist, published with permission.

otherwise inoperable tumors.[7,8] LITT utilizes laser energy to produce controlled thermal ablation of tumors while minimizing injury to surrounding healthy brain tissue (Fig. 1).[9] This modality has drawn more and more attention because of its ability to increase survival while reducing surgical morbidity.[10,11] However, the role of LITT in HGG treatment is still under investigation, and there is no consensus regarding its safety and efficacy in HGG.[12] Thus, to thoroughly assess the results of LITT in HGG management, a systematic review and meta-analysis of the existing literature are merited.

Methods

Search Strategy

This systematic review and meta-analysis adhered to PRISMA guidelines. A thorough search of the literature was performed using Web of Science, PubMed, Embase, and Cochrane Library databases, comprising research released up to February 26, 2025. The search approach was customized for every database by combining keywords and medical subject heading (MeSH) phrases associated with "high-grade glioma," "laser interstitial thermal therapy," "LITT," "progression-free survival," "overall survival," and "device brand." Studies with overlapping populations were excluded. Additionally, the reference lists of all included studies were manually reviewed to identify any relevant studies that may have been missed in the automated search.

Screening Process and Eligibility Criteria

Two independent reviewers (N.A.S. and K.M.T.) initially screened titles and abstracts using predetermined inclusion and exclusion criteria. A full-text review was conducted on studies that satisfied inclusion requirements. A third reviewer (A.M.) was consulted to settle any disagreements between the other reviewers. Studies that used LITT to treat HGG, reported at least one primary or secondary outcome, or conducted observational or comparative research pertinent to LITT outcomes were all considered eligible. Excluded studies consisted of case reports, conference abstracts, and studies with unclear methods or inadequate data.

Outcomes of Interest

The primary outcomes of interest were tumor progression posttreatment, overall survival (OS), and progression-free survival (PFS). Secondary outcomes included overall length of stay (LOS), ICU LOS, number of LITT passes, Karnofsky Performance Status (KPS) pre- and posttreatment, postoperative temporary (persisting < 6 months) and permanent neurological deficits, and mortality rate.

Data Extraction

Three authors (C.D., P.N., and A.H.) independently extracted data using a standardized data extraction form. The data included study characteristics, patient demographics,

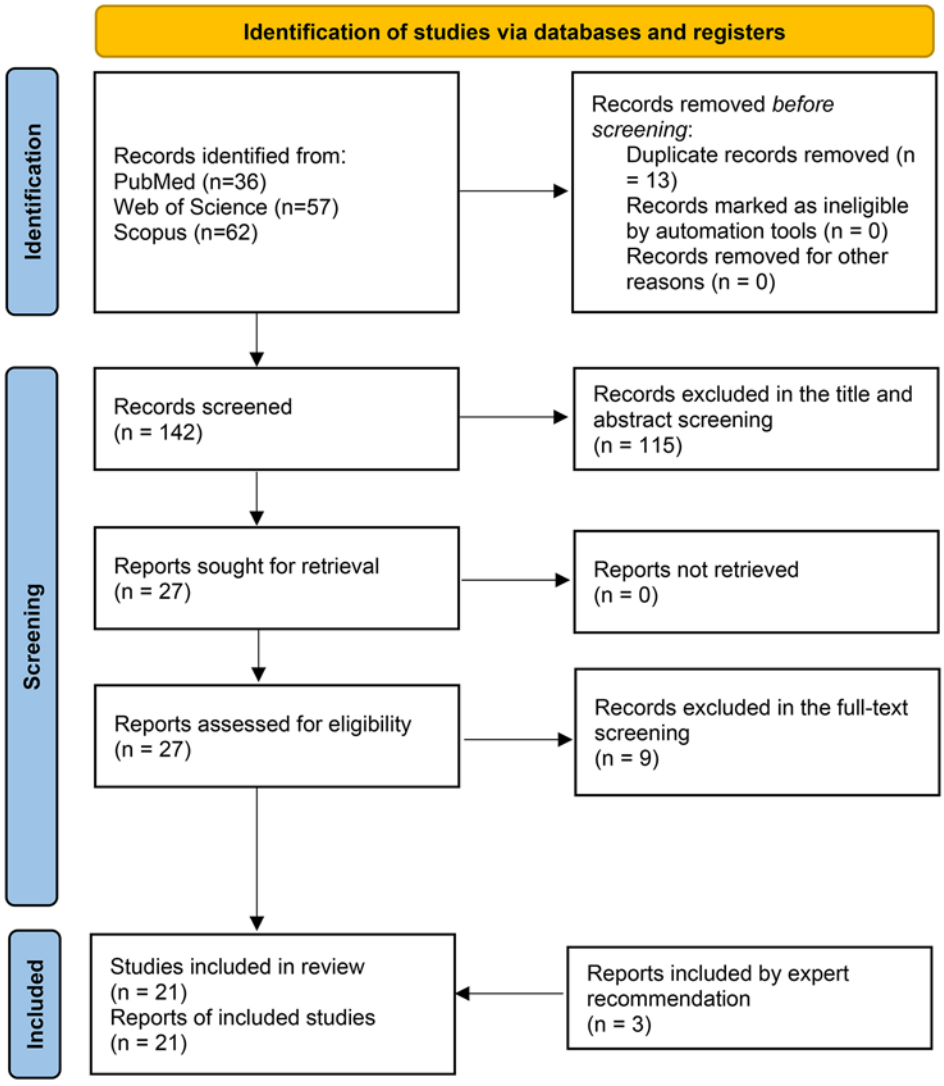

FIG. 2. PRISMA study selection flow diagram. Data added to the PRISMA template (from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71) under the terms of the Creative Commons Attribution (CC BY 4.0) License (https://creativecommons.org/licenses/by/4.0/).

tumor details, LITT device manufacturer, and outcomes of interest. A fourth author (A.A.) examined the retrieved data to verify correctness and to settle any disagreements, ensuring team consensus.

Risk of Bias Assessment

Two reviewers (B.H. and N.A.S.) independently assessed the risk of bias for each included study. The Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was utilized to evaluate potential biases across the included studies.[13]

Statistical Analysis

A random-effects meta-analysis was conducted to account for potential methodological differences among studies. We measured outcomes by calculating proportions and 95% confidence intervals (CIs). The odds ratio was calculated for binary outcomes, and mean differences were calculated for continuous outcomes, each with a corresponding 95% CI. Heterogeneity was assessed using Cochran's Q test and the I^2 statistic, with I^2 values above 50% and a significance level (α) below 0.1 indicating significant heterogeneity. Furthermore, a meta-regression was performed to find the source of heterogeneity and to assess the association between baseline characteristics and key outcomes with high heterogeneity. Publication bias was evaluated through visual inspection of contour-enhanced funnel plots, with further statistical confirmation using Egger's regression test, where a p value < 0.05 was considered indicative of significant bias. Leave-one-out sensitivity analyses were performed to ensure the robustness of findings by identifying the impact of excluding studies with high heterogeneity.

TABLE 1. Characteristics of the 21 studies on LITT in HGG included in a systematic review and meta-analysis

Authors & Year	Year Study Performed	Origin Country of Study	Study Design	Device Brand	Sample Size	Single Center or Multicenter
Beaumont et al., 2018[30]	2018	US	Retro	NeuroBlate	13	Multi
Di et al., 2021[10]	2021	US	Retro	Visualase	20	Single
Jubran et al., 2024[29]	2024	US	Retro	NeuroBlate & Visualase	31	Single
Kamath et al., 2019[28]	2019	US	Retro	NeuroBlate	54	Single
Kaisman-Elbaz et al., 2023[27]	2023	US	Retro	NeuroBlate	56	Single
Leonardi & Lumenta, 2002[26]	2002	Germany	Retro	LaserSonics	12	Single
Missios et al., 2014[24]	2014	US	Retro	NeuroBlate	11	Single
Mohammadi et al., 2014[22]	2014	US	Retro	NeuroBlate	35	Multi
Mohammadi et al., 2019[25]	2019	US	Retro	NeuroBlate	24	Multi
Muir et al., 2022[11]	2022	US	Retro	Visualase & NeuroBlate	20	Single
Murayi et al., 2020[14]	2020	US	Prosp	NeuroBlate	11	Single
Rennert et al., 2016[23]	2016	US	Retro	SmartFrame	10	Single
Viozzi et al., 2023[8]	2023	Netherlands	Retro	Visualase	10	Single
de Groot et al., 2022[7]	2022	US	Prosp	NeuroBlate	89	Multi
Butt et al., 2021[21]	2021	US	Retro	NeuroBlate	30	Single
Sun et al., 2015[20]	2015	US	Retro	Visualase	13	Single
Sloan et al., 2013[19]	2013	US	Prosp	NeuroBlate	10	Multi
Thomas et al., 2016[18]	2016	US	Retro	NeuroBlate & Visualase	21	Single
Traylor et al., 2021[17]	2021	US	Retro	NeuroBlate & Visualase	69	Single
Schwarzmaier et al., 2006[16]	2006	Germany	Retro	Dornier Medizintechnik	16	Single
Wilhelmy et al., 2024[15]	2024	US	Retro	NeuroBlate	47	Single

Multi = multicenter; prosp = prospective; retro = retrospective.

Results

Study Selection

A systematic literature search initially identified 155 records. After the removal of duplicate studies and subsequent title/abstract and full-text screenings, 21 studies on LITT in HGG were included in our analysis.[7,8,10,11,14–30] The study selection process demonstrated substantial reliability, with Cohen's κ values of 0.88 for title/abstract screening and 0.96 for full-text screening.[31] The PRISMA study selection flowchart is presented in Fig. 2.

Study Characteristics and Baseline Demographics

A detailed assessment of the characteristics of each study is provided in Table 1. A total of 602 patients with HGG who underwent LITT were included in our analysis.[7,8,10,11,14–30] The majority of patients were males (60.6%, 95% CI 57.1%–64.0%), and 55.8% of tumors (95% CI 30.3%–80%) were deep seated. Most tumors were in the corpus callosum and frontal lobe. The mean post-LITT follow-up was 19.48 ± 32.6 months (95% CI 15.9–23.1 months). Other baseline demographics and characteristics are reported in Table 2.

Outcomes of Patients With HGG

OS and PFS

The mean OS after LITT was 11.74 months (95% CI 10.9–12.6 months). The 6-, 12-, and 24-month OS rates were 77.0% (95% CI 65.8%–86.6%), 48.9% (95% CI 40.5%–57.3%), and 16.1% (95% CI 10.7%–22.3%), respectively (Table 3). The mean PFS was 5.3 months (95% CI 4.97–5.7 months), with 6-, 12-, and 24-month PFS rates of 37.1% (95% CI 24.3%–44.6%), 12.8% (95% CI 8.7%–17.5%), and 4.3% (95% CI 2.2%–6.9%), respectively. Tumor progression after LITT was observed in approximately 80.0% of patients (95% CI 61.9%–93.8%), and the overall mortality rate was 67.7% (95% CI 47.5%–85.2%).

Procedural Outcomes

The mean operation time was 246.8 ± 150.5 minutes (95% CI 224.5–269.1 minutes). Overall LOS and ICU stay were 5.9 days (95% CI 1.4–10.5 days) and 1.8 days (95% CI 1.1–2.5 days), respectively. Weakness and hemiparesis were the most common complications with a rate of 19.2% (95% CI 0.0%–54.8%) and 13.6% (95% CI 1.7%–31.9%), respectively. Postoperative temporary deficits were reported in 17.2% of patients (95% CI 7.2%–29.8%), whereas permanent deficits occurred in 5.7% of patients (95% CI 0.85%–13.1%; Table 3).

Newly Diagnosed Versus Recurrent HGG

There was a significantly higher rate of permanent deficits in patients with newly diagnosed HGG (4.15%, 95% CI 0.4%–10.2%) than in those with recurrent HGG (0.02%, 95% CI 0.0%–2.2%; $p = 0.023$) without any heterogeneity ($I^2 = 0.00\%$). And although there was no signif-

TABLE 2. Baseline characteristics and demographics of patients with HGG treated with LITT

Characteristic	Value	Weighted Proportion (95% CI)
Male	343/581 (59.0)	60.6% (57.1%–64.0%)
Age in yrs	57.4 ± 12.4	(56.3–58.4)
Baseline tumor vol in cm^3	16.03 ± 17.4	(14.4–17.6)
Deep-seated tumor	150/290 (51.7)	55.8% (30.3%–80%)
Baseline KPS	80.3 ± 76.4	(72.1–88.5)
Laterality of lesion		
Rt	83/198 (41.9)	41.3% (32.3%–50.5%)
Lt	102/198 (51.5)	51.7% (42.3%–62.1%)
Bilat	13/85 (15.3)	14.9% (3%–32%)
Midline	17/80 (21.3)	18.6% (0.0%–100%)
Lesion location		
Corpus callosum	33/137 (24.1)	30% (2.5%–68.4%)
Thalamus	13/92 (14.1)	12.8% (0.3%–34.8%)
Insula	10/91 (11.0)	10.4% (2.1%–22.6%)
Temporal	56/213 (26.3)	23.8% (14.5%–34.3%)
Frontal	75/198 (37.9)	35.8% (25.7%–46.5%)
Parietal	39/176 (22.2)	21.6% (11.7%–33.2%)
Basal ganglia	2/67 (3.0)	2.6% (0.0%–45.0%)
Occipital	5/86 (5.8)	4.9% (0.8%–11.0%)
Genetic marker		
MGMT methylation	112/332 (33.7)	34.1% (25.7%–43%)
IDH mutation	23/256 (9.0)	7.8% (2%–16.1%)
IDH wildtype mutation	281/338 (83.1)	82.04% (52.1%–99.6%)
Tumor vol in cm^3		
≤10	126/250 (50.4)	56.9% (36.3%–76.3%)
>10	131/250 (52.4)	51.4% (37.7%–65.1%)
FU in mos	19.48 ± 32.6	(15.9–23.1)
Prior treatment		
Resection	244/382 (63.9)	56.6% (28.6%–82.7%)
Radiation	163/289 (56.4)	48.05% (18.7%–78.1%)
Chemo	185/389 (47.6)	37.8% (14.8%–63.8%)
Post-LITT treatment		
RT	48/187 (25.7)	27.9% (4.9%–59.5%)
Chemo	247/289 (85.5)	87.8% (72.2%–98%)
Temozolomide	79/190 (41.6)	45.5% (21.5%–70.6%)
Bevacizumab	51/177 (28.8)	21.9% (1.7%–52.7%)
Lomustine	25/166 (15.1)	13.9% (2.1%–32.0%)
Chemo + RT	58/99 (58.6)	72.4% (21.4%–100%)
Temozolomide + RT	23/45 (51.1)	54% (7.9%–96.3%)
Received steroids at time of LITT	100/230 (43.5)	61.3% (17.7%–96.4%)

Chemo = chemotherapy; RT = radiotherapy.
Values are expressed as number/total (percentage), mean ± standard deviation, or weighted proportion (95% CI).

icant difference between newly diagnosed and recurrent HGG in terms of OS, PFS, post-LITT tumor progression, KPS change from baseline, or temporary deficits, leave-one-out sensitivity analysis after resolving heterogeneity for 6-month PFS showed a significant higher survival rate in patients with newly diagnosed HGG than in those with recurrent HGG (p = 0.0069; Table 4).

Subgroup Analysis

Deep and Unresectable Tumors

Five studies[8,10,11,22,27] exclusively evaluated deep and unresectable HGGs among 141 patients, reporting a 12-month OS rate of 53.0% (95% CI 20.0%–84.7%) and a 24-month rate of 12.9% (95% CI 0.0%–86.1%). The 12- and 24-month PFS rates were 12.9% (95% CI 0.02%–

TABLE 3. Survival and safety outcomes for patients with HGG following LITT treatment

Outcome	Value	Effect Size	95% CI
KPS change from baseline*	NA	−12.7	−20.5 to −4.95
OS			
Mean in mos	11.74 ± 9.9	NA	10.9–12.6
At 6 mos	200/260 (76.9)	77%	65.8%–86.6%
At 12 mos	226/440 (51.4)	48.9%	40.5%–57.3%
At 24 mos	76/405 (18.8)	16.1%	10.7%–22.3%
PFS			
Mean in mos	5.3 ± 3.8	NA	4.97–5.7
At 6 mos	147/406 (36.2)	37.1%	24.3%–44.6%
At 12 mos	56/406 (13.8)	12.8%	8.7%–17.5%
At 24 mos	20/394 (5.1)	4.3%	2.2%–6.9%
Progression after LITT	105/143 (73.4)	79.95%	61.9%–93.8%
Op time in mins	246.8 ± 150.5	NA	224.5–269.1
LOS in days			
Overall	5.9 ± 7.4	NA	1.4–10.5
ICU	1.8 ± 2.7	NA	1.1–2.5
Postop deficit			
Temporary	59/356 (16.6)	17.2%	7.2%–29.8%
Permanent	36/403 (8.9)	5.7%	0.85%–13.1%
Complication			
Edema	11/166 (6.6)	5.9%	0%–21.1%
Hemiparesis	8/55 (14.5)	13.6%	1.7%–31.9%
Weakness	14/64 (21.9)	19.2%	0.0%–54.8%
Seizures	19/299 (6.4)	8.0%	0.24%–21.9%
Hydrocephalus	4/78 (5.1)	5.6%	0.0%–38.3%
Visual field defect	3/43 (7.0)	6.6%	0.62%–16.2%
DVT	6/144 (4.2)	5.7%	0.0%–29.6%
Infection	9/186 (4.8)	3.75%	0.3%–9.4%
No. of trajectories	1.42 ± 0.6	NA	1.35–1.5
Death	240/399 (60.2)	67.7%	47.5%–85.2%

DVT = deep vein thrombosis; NA = not applicable.
Values are expressed as mean ± standard deviation and number/total (percentage) unless indicated otherwise.
* Analysis was done using the mean difference and 95% CI of KPS at admission and the last follow-up (I^2 = 0.00%, p = 0.014).

38.3%) and 1.43% (95% CI 0.0%–5.5%), respectively. Post-treatment disease progression was observed in 87.9% of cases (95% CI 0.0%–100%), with a mortality rate of 47.3% (95% CI 0.0%–100%) following LITT. Further comparative analysis between the 5 studies evaluating only deep and unresectable HGGs and the other 16 studies demonstrated a significantly lower 24-month PFS rate in the deep and unresectable HGG cohort (1.43% vs 5.6%, p = 0.008, I^2 = 0.0%). At the same time, no significant differences were found in other outcomes. Leave-one-out sensitivity analysis effectively resolved any significant heterogeneity, confirming the robustness and consistency of the findings.

IDH-Wildtype Mutation

Three studies[7,27,30] comprising 158 patients with *IDH*-wildtype HGG were included in the analysis. Among these cases, 75.7% of tumors (95% CI 0.7%–100%) were in deep-seated regions. The 12- and 24-month OS rates were 53.9% (95% CI 24.1%–82.3%) and 18.0% (95% CI 0.0%–60.6%), respectively. The 6- and 12-month PFS rates were 26.6% (95% CI 1.9%–63.5%) and 8.6% (95% CI 1.0%–21.0%), respectively. At the last follow-up, the overall mortality rate was 63.5% (95% CI 0.0%–100%).

Meta-Regression

Meta-regression was conducted to evaluate the heterogeneity observed in 6-month OS and PFS analyses, death, and permanent deficit. The heterogeneity observed in 6-month OS was explained by the baseline KPS, baseline tumor volume, tumor locations in frontal and parietal lobes, and tumor size (≤ or > 10 cm^3; Table 5). At the time of LITT, a higher baseline KPS (p = 0.015) and smaller

TABLE 4. Comparative analysis of newly diagnosed versus recurrent HGG

Variable	Newly Diagnosed HGG	Recurrent HGG	p Value	I^2 (%)	τ^2	H-Statistic	Leave-One-Out Analysis
KPS change from baseline	−13.5 (−15.15 to −11.8)	−7.75 (−22.6 to 7.1)	0.32	42.0	28.45	1.31	NS
Postop deficit							
Temporary	19.8% (0.0%–60%)	5.3% (0.2%–14.4%)	0.23	80.9	0.06	2.29	NS
Permanent	4.15% (0.4%–10.2%)	0.02% (0.0%–2.2%)	**0.023**	0.00	0.00	1.00	NS
Tumor progression after LITT	95.4% (69%–100%)	77.4% (0.0%–100%)	0.37	75.3	0.05	2.01	NS
OS							
Mean in mos	13.3 (11.3–15.3)	10.0 (9.1–11)	0.39	88.7	7.34	8.18	NS
At 6 mos	72.3% (28.5%–100%)	79.1% (58.3%–94.7%)	0.56	64.7	0.03	1.68	NS
At 12 mos	34.3% (21.2%–48.5%)	51.5% (28.7%–74%)	0.12	79.3	0.03	2.20	NS
At 24 mos	7.2% (2.3%–13.7%)	9.6% (6.1%–37.1%)	0.08	68.9	0.02	1.79	NS
PFS							
Mean in mos	4.3 (3.7–4.8)	4.9 (4.2–5.6)	0.17	83.0	1.1	5.89	NS
At 6 mos	33.8% (25.3%–42.7%)	32.1% (11.5%–56.7%)	0.88	58.4	0.01	1.55	Sig
At 12 mos	9.02% (3.9%–15.5%)	10.5% (4.2%–18.6%)	0.55	0.00	0.00	1.00	NS
At 24 mos	6.8% (5%–8.8%)	2.05% (0.0%–11.2%)	0.09	0.00	0.00	1.00	NS

NS = not significant; Sig = significant.
Values are expressed as percentages unless indicated otherwise. Boldface type indicates statistical significance.

tumor size (p = 0.002) were associated with significantly higher rates of OS at 6 months. For 6-month PFS, baseline tumor volume, tumor location in the frontal lobe, and tumor size (≤ or > 10 cm^3) were the sources of heterogeneity. Additionally, a higher number of tumors ≤ 10 cm^3 (p = 0.028) was associated with a higher PFS rate at 180 days.

Findings of the meta-regression for death showed that a temporal lobe tumor location, an *IDH*-wildtype mutation, and operation time were sources of heterogeneity. A higher percentage of *IDH*-wildtype mutations (p = 0.026) and temporal tumor locations (p = 0.037) were associated with a higher mortality rate (Table 5). Furthermore, analysis of postoperative permanent deficits demonstrated that age, admission tumor volume, as well as frontal and parietal tumor locations were the sources of heterogeneity. Moreover, a larger admission tumor size was associated with higher permanent deficits (p = 0.049).

Quality Assessment

Risk of bias assessment using the ROBINS-I tool revealed a low risk of bias in 13 studies, moderate risk in 7 studies, and serious risk in 1 study. Contour-enhanced funnel plots showed no significant evidence of publication bias for OS, PFS, or mortality.

Discussion

Summary of Findings

This meta-analysis included 21 studies comprising 602 patients with HGGs treated via LITT. By consolidating patient survival and procedural outcomes, we provide a statistically robust evaluation of the efficacy of LITT and increase understanding of the procedure's effectiveness and associated risks. The mean OS after LITT was 11.74 months (95% CI 10.9–12.6 months), with 6-, 12-, and 24-month OS rates of 77.0%, 48.9%, and 16.1%, respectively. The mean PFS was 5.3 months (95% CI 4.97–5.7 months), with corresponding 6-, 12-, and 24-month rates of 37.1%, 12.8%, and 4.3%, respectively. In approximately 80% of patients (95% CI 61.9%–93.8%), tumor progression occurred following LITT, and overall mortality was 67.7% (95% CI 47.5%–85.2%). Procedure outcome analysis revealed a mean operating time of 246.8 minutes (95% CI 224.5–269.1 minutes), an overall hospital stay of 5.9 days (95% CI 1.4–10.5 days), and an ICU stay of 1.8 days (95% CI 1.1–2.5 days). Common LITT-related complications included hemiparesis (13.6%, 95% CI 1.7%–31.9%) and weakness (19.2%%, 95% CI 0.0%–54.8%), with temporary deficits in 17.2% of patients (95% CI 7.2%–29.8%) and permanent deficits in 5.7% (95% CI 0.85%–13.1%).

Comparative and Subgroup Analyses

Our comparative analyses revealed no significant difference between newly diagnosed and recurrent HGG in terms of OS, PFS, post-LITT tumor progression, KPS change from baseline, and temporary deficits; however, resolving for heterogeneity for 6-month PFS via leave-one-out sensitivity analysis showed a significant higher survival rate in newly diagnosed HGG cases than in recurrent cases (p = 0.0069). This survival advantage may be attributable to the aggressive nature of recurrent HGGs due to acquired treatment resistance and potential increased spread.[32] Interestingly, previous studies have historically reported a greater association with permanent postoperative deficits in cases of recurrent HGG than in newly diagnosed HGG treated with LITT;[32,33] however, our comparative analysis revealed the opposite, with a significantly higher number of permanent postoperative deficits associated with LITT procedures targeting newly diagnosed HGG versus recurrent HGG (4.15% vs 0.02%, p = 0.023). The observed discrepancy in our results pushes us to examine surgery- and recovery-related challenges associated with treating newly

TABLE 5. Univariate meta-regression of association between variables and key outcomes with high heterogeneity

Covariate	No. of Studies	Coefficient	p Value	R^2
6-month OS				
Sample size	10	0.002	0.48	0.0
Year of publication	10	−0.006	0.74	0.0
Age	9	−0.012	0.59	0.0
Sex (male)	10	0.003	0.44	0.0
Baseline KPS	7	0.034	**0.015**	84.1
Baseline tumor vol in cm^3	9	−0.013	**0.002**	100
Tumor size in cm^3				
>10	6	0.0033	0.33	99.9
≤10	6	0.0036	0.32	98.5
MGMT methylation	5	0.015	0.36	0.5
IDH-wildtype mutation	8	0.0018	0.69	0.0
Overall LOS	8	0.017	0.2	22.9
Tumor location				
Corpus callosum	3	−0.01	0.36	0.0
Thalamus	3	−0.016	0.71	0.0
Temporal	6	−0.005	0.79	0.0
Frontal	5	−0.0235	0.17	43.2
Parietal	4	0.0435	0.21	100
Op time	3	−0.0007	0.17	0.0
No. of passes	4	−0.016	0.95	0.0
Deep-seated tumor	4	0.004	0.34	0.0
6-month PFS				
Sample size	10	0.0017	0.41	0.0
Year of publication	10	−0.011	0.47	0.0
Age	9	−0.009	0.54	0.0
Sex (male)	10	0.004	0.25	3.7
Baseline KPS	7	0.0002	0.98	0.0
Baseline tumor vol in cm^3	8	−0.012	0.06	71.2
Tumor size in cm^3				
>10	5	0.01	0.052	100
≤10	5	0.0105	**0.028**	100
MGMT methylation	7	0.0065	0.43	0.0
IDH-wildtype mutation	7	−0.0007	0.79	0.0
Overall LOS	8	0.0103	0.51	0.0
Tumor location				
Thalamus	3	−0.0115	0.66	0.0
Temporal	4	−0.0064	0.65	0.0
Frontal	3	−0.0164	0.29	100
Op time	3	−0.0015	0.52	0.0
No. of passes	4	−0.0405	0.93	0.0
Deep-seated tumor	5	0.0054	0.43	0.0
Death				
Sample size	14	−0.0038	0.35	0.1
Year of publication	14	0.0046	0.82	0.0
Age	12	−0.0121	0.72	0.0
Sex (male)	14	−0.0048	0.5	0.0
Baseline KPS	10	−0.003	0.93	0.0

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TABLE 5. Univariate meta-regression of association between variables and key outcomes with high heterogeneity

Covariate	No. of Studies	Coefficient	p Value	R^2
Death (*continued*)				
Baseline tumor vol in cm^3	12	0.013	0.22	7.2
Tumor size in cm^3				
>10	8	0.0094	0.48	0.0
≤10	8	−0.0015	0.93	0.0
MGMT methylation	7	−0.02	0.22	13.8
IDH-wildtype mutation	7	0.01	**0.026**	64.7
Overall LOS	9	0.0018	0.97	0.0
Tumor location				
Corpus callosum	4	0.0418	0.45	0.0
Temporal	5	0.0338	**0.037**	100
Frontal	7	0.024	0.3	7.1
Parietal	5	−0.0692	0.66	0.0
Op time	5	0.0041	0.18	33.8
No. of passes	8	0.031	0.95	0.0
Deep-seated tumor	6	−0.0007	0.96	0.0
Permanent deficit				
Sample size	14	−0.0001	0.96	0.0
Year of publication	14	0.0007	0.94	0.0
Age	13	−0.021	0.11	29.3
Sex (male)	12	0.0007	0.86	0.0
Baseline KPS	10	−0.011	0.58	0.0
Baseline tumor vol in cm^3	12	0.0111	**0.049**	46.3
Tumor size in cm^3				
>10	8	0.0001	0.98	0.0
≤10	8	0.0063	0.45	0.0
MGMT methylation	6	0.003	0.81	0.0
IDH-wildtype mutation	7	−0.0005	0.89	0.0
Overall LOS	9	0.018	0.4	1.7
Tumor location				
Corpus callosum	4	−0.0038	0.83	0.0
Temporal	5	−0.02	0.1	0.0
Frontal	6	−0.0092	0.28	100
Parietal	4	0.0904	0.31	100
Op time	3	−0.0003	0.79	0.0
No. of passes	6	−0.454	0.47	0.0
Deep-seated tumor	5	−0.0013	0.84	0.0

Boldface type indicates statistical significance.

diagnosed HGGs that may not have been considered in the past. For example, previous surgeries and treatments for recurrent HGG can cause localized scarring, facilitating a more precise delineation of tumor versus healthy tissue in subsequent operations and comparatively increasing the potential for damage of surrounding neurologically important regions when treating HGG not surrounded by scar tissue.[34] Additionally, it is plausible that while patients with recurrent HGG may have adapted to specific deficits caused by previous treatment targeting the glioma, those with newly diagnosed HGG present with an arguably steeper learning curve postsurgery that may be perceived as a more significant deficit.

In subgroup analyses, it was revealed that deep-seated and unresectable HGGs were associated with a lower 24-month PFS compared to controls (1.43% vs 5.6%, p = 0.008). This finding corroborates the notion that, while LITT remains one of the best treatment options for tumors

in surgically inaccessible areas of the brain, the limitations of treating such tumors are not erased by the use of LITT.[35] Meta-regression further identified prognostic factors like a higher baseline KPS ($p = 0.015$), smaller tumor size ($p = 0.002$), and higher number of tumors ≤ 10 cm^3 ($p = 0.028$) to be associated with better survival outcomes. Contrastingly, tumors with *IDH*-wildtype mutations ($p = 0.026$), a temporal lobe location ($p = 0.037$), or larger size on admission ($p = 0.049$) were associated with increased mortality. Previous studies align with these findings and assert that *IDH*-wildtype gliomas exhibit a more aggressive behavior, temporal tumors often present closer to eloquent brain regions, and larger tumors are inherently more challenging to treat because of their greater degree of infiltration.[36–39]

Limitations and Future Directions

While our meta-analysis is comprehensive, limitations must be addressed. First, because of the limited number of randomized controlled trials evaluating the effectiveness of LITT for the treatment of HGG, there is difficulty in determining whether observed differences are attributable to the intervention itself or to inherent differences in patient populations. Because some of the included studies are observational, they exhibit variety in their patient selections and treatment protocols. This inadvertently contributes to our inability to establish causality between any assessed variables despite meta-regression and sensitivity analyses. Further research should address these limitations through well-designed prospective studies and randomized controlled trials that standardize patient selection and treatment protocols. This would be especially beneficial when assessing OS and PFS at specific times, as the heterogeneity in follow-up durations posed a significant challenge when selecting studies and pooling results. To address this limitation, we reported OS and PFS rates at defined time points as well as overall mean survival, ensuring consistency in follow-up time and reducing the impact of heterogeneity in results. Studies should also involve greater efforts to identify particular variables in their patient populations like race, *MGMT* methylation, tumor size and location characteristics, and comorbidities that may impact the effectiveness of LITT, as many did not often report such values. Despite these limitations, our study provides a robust analysis of LITT outcomes for HGG and offers insights into the association of specific factors with the procedure's efficacy and safety.

Conclusions

The present meta-analysis showed that LITT is an effective therapeutic modality for HGG, exhibiting a low rate of postoperative deficits. Subgroup analyses further substantiated the feasibility and safety of LITT in challenging cases, including deep-seated, unresectable tumors and tumors with *IDH*-wildtype mutations. Prospective, multicenter, randomized studies are warranted to confirm these results.

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Conception and design: Faraji, Mortezaei, Taghlabi, Dib, Abdelsalam. Acquisition of data: Mortezaei, Al-Saidi, Hajikarimloo, Dib, Nemer, Sheehan. Analysis and interpretation of data: Faraji, Mortezaei, Al-Saidi, Nemer, Sheehan. Drafting the article: Faraji, Mortezaei, Al-Saidi, Taghlabi, Dib, Hussein. Critically revising the article: Faraji, Mortezaei, Al-Saidi, Taghlabi, Abdelsalam, Shepard, Sheehan. Reviewed submitted version of manuscript: Faraji, Al-Saidi, Taghlabi, Hajikarimloo, Abdelsalam, Nemer, Shepard, Sheehan. Approved the final version of the manuscript on behalf of all authors: Faraji. Statistical analysis: Mortezaei. Administrative/technical/material support: Faraji, Taghlabi, Abdelsalam, Shepard, Sheehan. Study supervision: Faraji, Taghlabi, Abdelsalam, Shepard, Sheehan.

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