

Research Article

Unveiling Disparities in WHO Grade II Glioma Care among Physicians in Middle East and North African (MENA) Countries: A Multidisciplinary Survey

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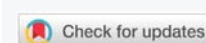
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Keywords: Low-grade glioma; IDH; Vorasidenib; Temozolomide



Abstract

Background: WHO grade II Low-grade gliomas (LGGs) need multi-disciplinary treatment from different specialties, directed by new molecular classifications and prognostic markers. Yet regional practice patterns and obstacles are not reported, especially in MENA countries.

Method: A cross-sectional survey of physicians from MENA countries (including neurosurgeons, radiation oncologists, and medical oncologists) was conducted. An electronic anonymous survey, including clinical scenarios and evidence-based treatment choices, was distributed at professional conferences. The feedback included responses regarding surgical interventions, adjuvant treatment preferences, and barriers to adoption of IDH-mutant inhibitors.

Results: 137 physicians (37.23% neurosurgery, 32.85% radiation oncology, 29.93% medical oncology). Most had 6–15 years of experience (56.21%) and worked in government (51.82%) or academic hospitals (25.55%). Maximal safe resection (MSR), if applicable, was preferred over biopsy (89.05% vs. 10.95%). For residual Astrocytoma, concurrent radiotherapy (RT) with temozolomide (TMZ) (42.34%) was the preferred adjuvant, while 44.53% prefer observation after gross total resection (GTR). For residual Oligodendroglioma, RT followed by PCV (45.99%) was preferred, with 59.85% offered observation post-GTR. Most (96.35%) agreed that resection extent impacts outcomes, while 72.99% objected to extending TMZ beyond six cycles. High-risk stratification varied: 46.72% used age ≥40 years, and 88.32% prioritized residual tumor volume. Although 64.96% supported IDH-mutant inhibitors, 58.39% cited limited availability as a barrier, followed by cost (40.88%) and insufficient long-term data (31.39%). Specialty-specific differences emerged: radiation oncologists tend more to provide adjuvant radiotherapy in the context of persistent seizure post-operatively ($\chi^2 = 20.50$, $p < 0.05$), and medical/radiation oncologists more often used age ≥40 for high-risk stratification ($\chi^2 = 10.10$, $p = 0.038$).

Conclusion: There is a wide variation in the WHO grade II LGGs management among physicians in MENA Countries. These data highlight the importance of locally derived guidelines, the increased availability of molecularly directed therapies, and ongoing collaboration between multiple disciplines to ensure optimal patient outcomes.

Key points:

- Maximal safe resection (89.05%) is the dominant surgical approach for WHO grade II LGGs, taking into consideration the location and extent of infiltration, among specialists in MENA Countries, reflecting global consensus on resection extent impacting outcomes (96.35% agreement).
- Adjuvant therapy preferences vary: concurrent RT+TMZ for astrocytomas (42.34%) and sequential RT+PCV for oligodendrogliomas (45.99%), with 59.85% observing post-GTR in oligodendrogliomas.
- IDH-mutant inhibitors (e.g., Vorasidenib) are supported by 64.96% of oncologists, but limited availability (58.39%) and cost (40.88%) hinder adoption.

Importance of the study: This multicenter survey is the first to evaluate real-world management trends and barriers for WHO grade II low-grade gliomas (LGGs) among physicians in MENA Countries. While all specialists align with international guidelines in surgical strategies (e.g., maximal safe resection), significant heterogeneity exists in adjuvant therapy choices, particularly for astrocytomas versus oligodendrogliomas. Crucially, we identify systemic barriers—such as limited access to molecular therapies (IDH inhibitors) and cost constraints—that disproportionately affect WHO grade II LGGs care in the MENA Countries. Our findings underscore the urgent need for regionally adapted guidelines and multidisciplinary collaboration to standardize practices aligned with international guidelines. By highlighting disparities in resource availability and specialty-specific decision-making (e.g., radiation oncologists prioritizing post-resection seizures, $p < 0.05$), this study provides a roadmap for optimizing WHO grade II LGGs management in resource-limited settings and advocates for the inclusion of Arab populations in global trials of novel agents like Vorasidenib.



Introduction

Low-grade gliomas (LGGs; WHO grade II) are invasive intra-axial brain tumors, which mainly affect young adults [1]. The 2021 WHO CNS tumor classification underlines molecular markers, in particular IDH mutations and 1p/19q codeletion, as integral diagnosis requirements that also strongly impact the prognostic and predictive value for therapeutic approaches to patients. However, the best current management for an individual patient remains somewhat uncertain, based on symptom burden and risk factors [2]. Several prognostic models for risk stratification have historically been introduced, including the Pignatti criteria and RTOG 9802 trial [3,4], which weighted clinical and histological factors such as age, tumor size, and subtotal resection (STR). However, there is accumulating evidence that molecular characteristics and tumor load could override these classic paradigms in the therapeutic approach [5,6]. Although international guidelines (ASCO-SNO, EANO) provide extensive recommendations for the management of WHO grade II LGGs, the use of these guidelines across various health settings remains unknown [7].

Traditionally, radiotherapy (RT) is recommended for patients with residual tumors or those at higher risk of progression. Nonetheless, concerns about potential long-term neurocognitive side effects, especially in younger individuals, significantly influence oncologists’ choices regarding timing and dosing [8]. Chemotherapy (e.g., temozolomide (TMZ), procarbazine, lomustine, and vincristine (PCV) regimen) has been shown to improve outcomes in WHO grade II LGGs patients, with guidelines suggesting adjuvant RT and sequential PCV while considering TMZ as a reasonable alternative for patients who may not tolerate PCV, given the lack of strong evidence supporting upfront TMZ in this context [7].

The current literature regarding the management of contemporary WHO grade II LGGs in MENA countries is limited. It was evident that there is considerable variation in the mortality-to-incidence ratio (MIR) of brain tumors compared to other tumors and between the Arab countries [9,10]. We aimed at investigating how physicians make real-world decisions, and apply the new guidelines, and to identify the obstacles towards integrating novel targeted therapies such as IDH-mutant inhibitors [11].

We report management trends for WHO grade II LGGs in MENA institutions. We take a structured approach in comparing practice to guidelines among neurosurgeons, radiation oncologists, and medical oncologists. Our work seeks to define consensus-based treatment pathways by characterizing the differences in management. The available knowledge will allow the most effective multidisciplinary management of this patient group.

Therefore, this study aimed to explore real-world practice

patterns in the management of WHO grade II LGGs across MENA countries, with particular emphasis on multidisciplinary decision-making, adherence to contemporary guidelines, and barriers to implementing molecularly driven therapies.

Methods

A cross-sectional electronic survey was conducted through professional networks of oncology and neurosurgery, email lists, and regional medical meetings between January and March 2025. Participating neurosurgeons, radiation oncologists, and medical oncologists are based in MENA countries, irrespective of current practice in the care of WHO grade II LGGs. The questionnaire had five sections: (1) respondents’ demographics, (2) clinical vignettes for WHO grade II LGGs treatment decisions, (3) questions on the preference for adjuvant therapy, (4) criteria for high-risk stratification, and (5) perceived barriers to implementing IDH-targeted therapies. The questionnaire contained both single-choice, case study, and true/false statements. Ethical approval was obtained from the Ethics Committee at King Fahad Specialist Hospital, Dammam, Saudi Arabia. All responses were confidential, and informed consent was acquired online. While the primary focus of the analysis was descriptive, chi-square tests were used in an exploratory manner to assess associations between physician specialty and selected clinical decision-making variables (Table 1).

Table 1: Biographical Data.

Category	Percentage	Count
Neurosurgery	37.23%	51
Radiation Oncology	32.85%	45
Medical Oncology	29.93%	41
Years of Experience		
0-5 years	16.06%	22
6-10 years	24.82%	34
11-15 years	31.39%	43
16-20 years	13.14%	18
More than 20 years	14.6%	20
Treating Adult Neuro-Oncological Tumors		
Yes	89.05%	122
No	10.95%	15
Country Distribution		
Saudi Arabia	51.09%	70
UAE	5.84%	8
Bahrain	2.19%	3
Oman	1.46%	2
Qatar	0%	0
Kuwait	3.65%	5
Egypt	18.98%	26
Jordan	5.11%	7
Other	11.68%	16
Institution Type		
Government/Ministry of Health hospital	51.82%	71
University/academic hospital	25.55%	35
Private hospital	11.68%	16
Military hospital	9.49%	13
Other	1.46%	2



Results

The survey results are presented according to respondent characteristics, followed by surgical preferences, adjuvant treatment decisions, risk stratification criteria, and perceived barriers to implementing IDH-targeted therapies.

The study included 137 participants, primarily from Neurosurgery (37.23%), Radiation Oncology (32.85%), and Medical Oncology (29.93%). Most had 6-15 years of experience (56.21%), and 89.05% treated adult neuro-oncological tumors (10.95% were non-neuro-oncologists). Geographically, 51.09% were from Saudi Arabia, followed by Egypt (18.98%) and other Gulf countries. Institutionally, 51.82% worked in Government/Ministry of Health hospitals, while 25.55% were in academic hospitals.

As shown in Table 2, most participants (89.05%) preferred Maximum Safe Resection (MSR), if applicable, over biopsy (10.95%).

Table 2: Surgical and adjuvant treatment decision-making for WHO grade II LGGs according to tumor subtype and extent of resection.

Scenario	Management Option	Percentage	Count
Preferred Resection Type	Biopsy	10.95%	15
	Maximum Safe Resection (MSR)	89.05%	122
Astrocytoma - Adjuvant Management (Residual Tumor)	RT alone	5.84%	8
	RT followed by PCV chemotherapy	24.82%	34
	RT followed by TMZ chemotherapy	22.63%	31
	RT with concurrent TMZ followed by adjuvant TMZ	42.34%	58
	Observation until progression	4.38%	6
Astrocytoma - Adjuvant Management (Gross total Resection GTR)	RT alone	19.71%	27
	RT followed by PCV chemotherapy	8.03%	11
	RT followed by TMZ chemotherapy	11.68%	16
	RT with concurrent TMZ followed by adjuvant TMZ	16.06%	22
	Observation until progression	44.53%	61
Oligodendroglioma - Adjuvant Management (Residual Tumor)	RT alone	12.41%	17
	RT followed by PCV chemotherapy	45.99%	63
	RT followed by TMZ chemotherapy	10.95%	15
	RT with concurrent TMZ followed by adjuvant TMZ	24.82%	34
	Observation until progression	5.84%	8
Oligodendroglioma - Adjuvant Management (GTR)	RT alone	13.87%	19
	RT followed by PCV chemotherapy	11.68%	16
	RT followed by TMZ chemotherapy	5.11%	7
	RT with concurrent TMZ followed by adjuvant TMZ	9.49%	13
	Observation until progression	59.85%	82

For residual astrocytoma tumors, the most common adjuvant approach was RT with concurrent TMZ, followed by adjuvant TMZ (42.34%), while sequential RT followed by PCV (24.82%) or RT followed by TMZ (22.63%) were also considered. In complete resection cases, 44.53% favored observation, with the rest opting for RT alone (19.71%), RT with concurrent TMZ (16.06%), RT with sequential TMZ (11.68%), or RT with sequential PCV (8.03%). On the other hand, for residual oligodendroglioma, RT with sequential PCV (45.99%) was the most chosen option, followed by RT with concurrent TMZ (24.82%), RT alone (12.41%), and RT with sequential TMZ (10.95%), while 5.84% preferred observation. For complete resection, 59.85% favored observation, with fewer participants selecting RT alone (13.87%), RT with sequential PCV (11.68%), RT with concurrent TMZ (9.49%), and RT followed by TMZ (5.11%).

Most participants (96.35%) agreed that the extent of resection impacts patient outcomes, taking into consideration the location and extent of infiltration (Table 3). While 67.88% stated that post-resection persistent seizures do not affect adjuvant management, 32.12% considered them a significant criterion of management selection. As shown in Table 3, 72.99% opposed extending adjuvant TMZ beyond six cycles, while 27.01% supported it.

Age was a key factor in stratifying high-risk WHO grade II LGGs, with 46.72% using ≥ 40 years as a cutoff, while 8.76% set it at ≥ 45 years. However, 44.53% did not consider age alone as a high-risk factor. As shown in Table 4, the primary influence on treatment decisions was significant residual tumor volume (88.32%), whereas initial tumor size >6 cm was considered important by only 11.68% as shown in Table 4.

As shown in Table 5, while 64.96% of participants supported using IDH-mutant inhibitors (Vorasidenib), 35.04% opposed it. The main barriers included lack of availability (58.39%),

Table 3: General Questions.

Question	Percentage	Count
Extent of Resection Effect on Outcome		
Yes	96.35%	132
No	3.65%	5
Seizures Post-Resection Affecting Adjuvant Management		
Yes	32.12%	44
No	67.88%	93
Increasing Adjuvant TMZ Duration >6 Cycles		
Yes	27.01%	37
No	72.99%	100

Table 4: Treatment Decision Factors in Management of WHO grade II LGGs.

Factor	Percentage	Count
High-Risk LGGs Age Cutoff		
40-years-old and more	46.72%	64
45-years-old and more	8.76%	12
I don't consider age alone as high-risk	44.53%	61
Primary Factor Influencing Treatment Decision		
Significant Residual Volume	88.32%	121
Initial Tumor Size > 6 cm	11.68%	16



Table 5: Barriers in Management of WHO grade II LGGs with IDH Mutant Inhibitors.

Barrier	Percentage	Count
Would Recommend IDH Mutant Inhibitors (Vorasidenib)?		
Yes	64.96%	89
No	35.04%	48
Reasons Preventing Use of Vorasidenib		
Poor Design of the Trial	15.33%	21
High Treatment Costs	40.88%	56
Lack of Long-Term Follow-Up	31.39%	43
Lack of Availability in My Country	58.39%	80

as follows: - high treatment costs (40.88%), insufficient long-term follow-up data (31.39%), and concerns over trial design (15.33%).

Discussion

This survey provides significant insights into the management of WHO grade II LGGs across oncology centers in MENA countries. While many participants generally adhere to international guidelines, notable deviations exist. Aligning with global evidence, taking into consideration the location and extent of infiltration, maximal safe resection (MSR) continues to be the favored initial surgical intervention for WHO grade II LGGs, reflecting its established benefits in enhancing progression-free survival (PFS) and overall survival (OS) in LGG patients [2,12,13]. In case of feasible GTR, observation was the preferred option irrespective of LGG histological subtypes.

However, notable heterogeneity remains in adjuvant therapies preferences. These preferences varied by tumor type and extent of resection (EOR). For residual astrocytoma tumors, the most common adjuvant approach was RT with concurrent TMZ, followed by adjuvant TMZ for six cycles. Given the lack of robust data to extend adjuvant TMZ beyond six cycles [14]. In a cohort of 103 adult patients with astrocytoma treated with TMZ-based chemoradiation, a median follow-up of 9.0 years, revealing median PFS and OS of 9 years (95% CI, 6.6–10.3) and 11.8 years (95% CI, 9.3–13.4), respectively. Median PFS was notably higher in the early RT group compared to the delayed RT group (10.6 years vs. 6 years; hazard ratio (HR) 0.30; 95% CI 0.16–0.59; $p = 0.0005$). However, OS did not significantly differ between the two groups (12.8 vs. 10.4 years; HR 0.64; 95% CI 0.33–1.25; $p = 0.23$).

This study indicated that factors such as EOR, Karnofsky Performance Score (KPS), and small residual disease were associated with OS, with postoperative tumor volume ≤ 1 cc emerging as a crucial independent predictor (HR: 0.27; 95% CI 0.08–0.87; $p = 0.01$). Thus, TMZ-based chemoradiation demonstrates a survival benefit for patients with astrocytoma, suggesting that treatment can be deferred until progression in younger patients undergoing extensive resection, while early intervention is advisable for high-risk patients [4,15].

For residual oligodendroglioma, RT followed by PCV is preferred among MENA physicians. However, this approach is

less practiced than TMZ, with ongoing discussions regarding optimal timing and patient selection, particularly for younger patients under 40 years old [14,16]. Notably, our physicians, especially neurosurgeons, assign less importance to age alone as an independent high-risk factor, with the majority prioritizing residual tumor volume over initial tumor size > 6 cm. This is consistent with emerging data suggesting that tumor burden may better predict outcomes in contemporary treatment paradigms [6,17].

Mutations in the IDH1/2 gene are frequently observed in adult LGGs. Mutated IDH1 contributes to the production of 2-hydroxyglutarate, which significantly affects gliogenesis by regulating cell death, the epigenome, and metabolism within the tumors. The efficacy of various IDH1/IDH2 inhibitors has shown promise in preclinical models [18].

The recent INDIGO trial was the first to evaluate the effectiveness of Vorasidenib among patients with residual and recurrent LGGs who had not received prior adjuvant treatment. The study demonstrated a significant PFS benefit with Vorasidenib in WHO grade II LGGs, reinforcing the potential role of targeted agents in delaying the need for conventional RT or chemotherapy [16].

One of the primary findings of our study is the considerable support from the majority of oncologists for IDH-mutant inhibitors, despite numerous challenges hindering their use, including limited availability, high costs, and insufficient long-term data. And the widespread adoption of these therapies will necessitate addressing issues related to affordability, regulatory approvals, and availability across MENA countries.

Notably, differences in management strategies emerged across specialties. Radiation oncologists were more likely to favor adjuvant radiotherapy in the presence of persistent postoperative seizures, whereas neurosurgeons placed greater emphasis on the extent of resection and residual tumor volume. Medical and radiation oncologists more frequently utilized age ≥ 40 years as a high-risk criterion compared to neurosurgeons. These findings highlight how specialty-specific training and clinical priorities contribute to heterogeneity in WHO grade II LGG management, even within the same institutional settings.

These results emphasize the urgent need for regionally customized guidelines that integrate molecular stratification, manage neurotoxicity risks, and account for resource constraints. Enhanced multinational collaboration, increased healthcare investment, and the inclusion of MENA countries in clinical trials could assist in bridging these disparities.

The primary limitation of this study is its relatively small sample size, which may affect the generalizability of the findings. Self-reporting survey data is also open to bias. However, this is one of the rare studies on exploring the situation of WHO grade II LGGs management in the MENA region.



Conclusion

These findings have important implications for regional policy development, emphasizing the need for MENA-adapted clinical guidelines that integrate molecular stratification, resource availability, and multidisciplinary decision-making. Improving access to molecular diagnostics and IDH-targeted therapies, alongside fostering multinational collaboration and inclusion of MENA populations in prospective clinical trials, represents a critical avenue for future research aimed at optimizing WHO grade II LGG outcomes in MENA countries.

Ethics and confidentiality

The Ethics Committee of King Fahad Specialist Hospital in Dammam approved the study. Approval No. ONC0423. Participation was voluntary and anonymous.

Authorship statement

Conceptualization and design of the study: I.A., S.A., L.C.

Data collection and analysis: F.K., R.H., S.O., R.S.

Drafting of the manuscript: F.K., L.M.H., S.S., R.H., S.O., R.S.

Critical review and final approval of the manuscript: F.K., L.M.H., S.S., I.A., S.A., L.C.

Data availability statement

Upon Request: The data is available from the corresponding author upon reasonable request.

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