Clinical Interventions in Aging

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

The Shifting Prognostic Value of Performance Status in Aging Glioblastoma Patients: A Retrospective Cohort Study

Qiushi Zhang[1,*], Lei Zhang[1,*], Haiying Liu[1], Lize Chen[2], Shiduo Li[1], Xiaoyan Gao[1], Jason H Huang[3,4], Erxi Wu[3–6], Jing Tong[1]

[1]Department of Neurosurgery, the Fourth Hospital of Hebei Medical University, Shijiazhuang, Hebei, People's Republic of China; [2]Department of Neurosurgery, Northwest University First Hospital, Xian, Shaanxi, People's Republic of China; [3]Department of Neurosurgery, Baylor Scott & White Health, Temple, TX, USA; [4]Department of Neurosurgery, Baylor College of Medicine, School of Medicine, Temple, TX, USA; [5]Naresh K. Vashisht College of Medicine and Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, TX, USA; [6]Cancer Research Center and Department of Internal Medicine, Dell Medical School, the University of Texas at Austin, Austin, TX, USA

*These authors contributed equally to this work

Correspondence: Jing Tong, Department of Neurosurgery, The Fourth Hospital of Hebei Medical University, No. 12 Jiankang Road, Shijiazhuang, Hebei, 050011, People's Republic of China, Tel +86- 13833389738, Email jing_tong@hebmu.edu.cn; Erxi Wu, Department of Neurosurgery, Baylor Scott & White Health, 2401 S 31st Street, Temple, TX, 76508, USA, Email Erxi.Wu@BSWHealth.org

Purpose: To evaluate how advancing age affects the prognostic value of preoperative versus postoperative Karnofsky Performance Status (KPS) for guiding clinical interventions in glioblastoma (GBM) patients aged 60 and older.

Patients and Methods: This retrospective cohort study included 89 patients (≥60 years) with newly diagnosed GBM treated between 2017 and 2021. We analyzed demographic, clinical, and treatment data, identifying prognostic factors for overall survival (OS) via Cox proportional hazards models. The utility of preoperative and postoperative KPS was assessed in age-stratified subgroups (60–64, 65–69, and ≥70 years) using Kaplan-Meier analysis.

Results: Multivariable analysis confirmed greater extent of resection (P<0.001), higher postoperative KPS (HR: 0.981, P=0.006), and chemoradiation (P<0.001) as independent predictors of improved OS. Age-stratified analysis revealed that preoperative KPS was prognostic only in the "young-elderly" group (60–64 years, P=0.003), losing its predictive power in patients aged ≥65. In contrast, postoperative KPS remained a robust and consistent prognostic indicator across all elderly age groups (P≤0.001 for all).

Conclusion: The prognostic utility of preoperative KPS diminishes significantly after age 65, suggesting its use as a standalone determinant for aggressive interventions should be reconsidered in the older-elderly. Postoperative KPS, however, is a powerful predictor across the aging spectrum. These clinical-only findings underscore that interventions preserving functional status are critical to improving outcomes in this aging population.

Keywords: geriatric oncology, glioblastoma, functional status, karnofsky performance scale, prognosis, clinical decision-making

Introduction

Glioblastoma (GBM) is the most common and aggressive primary malignant brain tumor in adults, with an incidence that rises sharply with age.[1] Patients aged 65 and older account for a substantial proportion of new diagnoses, yet their prognosis remains exceptionally poor, with a median overall survival (OS) of less than one year and a 5-year survival rate of only 5.3%.[2] The management of this vulnerable population is complicated by factors such as increased comorbidities, diminished physiological reserve, and heightened risk of treatment-related toxicity, creating a pressing need for refined prognostic tools to guide individualized therapeutic strategies.[3,4] Recent studies continue to emphasize that individualized treatment, guided by both clinical and molecular parameters, is essential for optimizing outcomes in this heterogeneous patient group.[5,6] While the 2021 WHO classification integrates molecular markers like IDH mutation and

https://doi.org/10.2147/CIA.S574787
Received: 16 October 2025
Accepted: 13 February 2026
Published: 5 March 2026

MGMT promoter methylation as central prognostic factors, clinical predictors remain indispensable, particularly when molecular testing is unavailable or inconclusive in real-world settings.

A patient's functional status, commonly quantified by the Karnofsky Performance Status (KPS) score, is a cornerstone in clinical decision-making for GBM. It is widely used to determine eligibility for aggressive treatments, including extensive surgery and standard chemoradiation (the Stupp protocol).[7] However, the prognostic utility of preoperative KPS in the elderly remains a subject of debate. While some studies support its predictive value,[7] others have found no significant association between preoperative KPS and survival outcomes.[8–10] This inconsistency suggests that the impact of performance status may be modified by other factors, such as chronological age itself.

The distinction between the "young-elderly" (eg, 60–70 years) and the "older-elderly" (eg, >70 years) is increasingly recognized in oncology, as treatment tolerance and outcomes can differ significantly.[6,11] Geriatric oncology guidelines suggest that physiological decline accelerates non-linearly, necessitating finer age stratification.[12,13] It remains unclear whether preoperative Karnofsky Performance Status (KPS) retains its prognostic power across this entire spectrum, particularly given that age and functional status interact in complex ways and may not be exhaustive predictors on their own.[6] Furthermore, the significance of postoperative KPS, reflecting the immediate impact of surgical intervention, may offer distinct prognostic information, as studies suggest that postoperative KPS $\geq$ 80 is a stronger predictor of survival than preoperative KPS in elderly glioblastoma patients.[14] Therefore, this study was designed to dissect the prognostic role of both preoperative and postoperative KPS within specific age strata of elderly GBM patients, aiming to provide a more nuanced understanding to guide surgical and adjuvant therapy decisions in this challenging demographic.

Materials and Methods

Study Design and Patient Population

This single-center, retrospective cohort study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[15] We retrospectively identified all consecutive patients aged 60 years or older with newly diagnosed, histopathologically confirmed primary GBM (WHO Grade IV) at the Fourth Hospital of Hebei Medical University between January 1, 2017, and December 31, 2021. Patients with recurrent GBM or those who did not undergo any surgical procedure (biopsy or resection) were excluded. A final cohort of 89 eligible patients was included for analysis. A post-hoc power calculation indicated that with a sample size of 89 and the observed effect sizes, the study had >80% power to detect significant hazard ratios for the primary variable of postoperative KPS (alpha=0.05).

Ethical Considerations

The study protocol received full approval from the Institutional Committee on Human Research of the Fourth Hospital of Hebei Medical University (No. 2024KS147). The committee granted a waiver of the requirement for individual patient informed consent due to the retrospective nature of the research, the use of de-identified data, and the confirmation that the study posed no more than minimal risk to subjects. The study was conducted in accordance with the Declaration of Helsinki.

Data Collection and Variables

A comprehensive dataset was extracted from electronic medical records. Demographic data included age at diagnosis and gender. Clinical variables included tumor characteristics (laterality, location, number of lesions), presence of systemic comorbidities, and preoperative KPS score. Preoperative KPS was assessed by a consensus of two senior neurosurgeons upon admission to minimize inter-observer variability. Treatment-related variables included the extent of resection (EOR), postoperative KPS score, and details of adjuvant therapies. Postoperative KPS was assessed prior to discharge (median postoperative day 12, range 7–21) to reflect the immediate functional outcome of surgery. EOR was determined based on postoperative MRI scans within 72 hours of surgery and categorized as gross total resection (GTR, >95% resection), subtotal resection (STR, <95% resection), or biopsy only. In the absence of routine volumetric software, EOR was determined via comparison of pre- and post-operative contrast-enhanced T1-weighted images by a neuroradiologist and the operating surgeon. Adjuvant treatments were categorized as: early chemotherapy, concurrent chemoradiation

(CCRT), and adjuvant chemotherapy. Standard CCRT followed the Stupp protocol: Radiotherapy consisted of a total dose of 60 Gy delivered in 30 fractions over 6 weeks. Concurrent chemotherapy consisted of temozolomide (75 mg/m^2 daily). All patients were followed until death or the study census date of June 30, 2022.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics, Version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize patient characteristics. Continuous variables were presented as means with ranges, and categorical variables as frequencies and percentages. The primary survival analysis was conducted using the Kaplan-Meier method, and differences between survival curves were assessed using the Log rank test. To enhance visual interpretation, number-at-risk tables were generated and displayed below the survival curves. To evaluate the age-dependent effect of KPS, patients were stratified into three groups: 60–64 years, 65–69 years, and ≥70 years. This stratification was chosen a priori to distinguish between "young-elderly," "intermediate-elderly," and "older-elderly" subgroups, consistent with geriatric oncology frameworks that identify age 65 and 70 as critical inflection points for frailty.[16] Univariable Cox proportional hazards regression was performed to identify potential prognostic factors for OS. Covariates with a P-value <0.20 in the univariable analysis were subsequently included in a multivariable Cox proportional hazards model using a forward stepwise method to identify independent prognostic factors. Hazard ratios (HR) and their 95% confidence intervals (CI) were calculated. A two-sided P-value <0.05 was considered statistically significant for all analyses.

Results

Patient Demographics and Treatment Characteristics

A total of 89 patients met the inclusion criteria. The cohort had a nearly balanced gender distribution (49.4% male) and a mean age at diagnosis of 66.4 years. The cohort was stratified into three age groups: 35 patients (39.3%) were 60–64 years old, 33 (37.1%) were 65–69, and 21 (23.6%) were 70 years or older. All patients underwent a surgical procedure: GTR was achieved in 64 patients (71.9%), STR in 18 (20.2%), and biopsy in 7 (7.9%). Following surgery, 74 patients (83.1%) received CCRT, and 68 (76.4%) proceeded to adjuvant chemotherapy. Molecular marker status (IDH mutation, MGMT methylation) was unavailable for the majority of patients (87.6%) due to the historical nature of the cohort (Supplementary Table S1). The detailed clinicopathological characteristics are presented in Table 1.

Overall Survival Outcomes

As of the final follow-up, the mean OS for the entire cohort was 14.8 months. A trend of decreasing survival with increasing age was observed: the mean OS was 17.2 months for the 60–64 age group, 14.3 months for the 65–69 group, and 9.8 months for the ≥70 group. However, this trend did not reach statistical significance in regression analysis (Table 2).

Prognostic Factor Analysis for Overall Survival

Univariable Cox regression analysis identified several factors significantly associated with OS (Table 2). Male gender (HR=2.223, P=0.002) and bilateral tumor growth (HR=4.003, P=0.001) were associated with worse outcomes. In contrast, GTR (vs biopsy, HR=0.210, P=0.001), higher postoperative KPS (HR=0.984, P=0.008), receiving CCRT (HR=0.199, P<0.001), and receiving adjuvant chemotherapy (HR=0.348, P<0.001) were protective. Notably, preoperative KPS as a continuous variable was not significantly associated with OS in the overall cohort (P=0.871).

In the subsequent multivariable analysis (Table 3), four factors remained independent predictors of OS. Male gender was confirmed as an independent risk factor for mortality (HR=3.787, 95% CI: 2.111–6.794, P<0.001). GTR (vs biopsy, HR=0.187, 95% CI: 0.074–0.470, P<0.001), higher postoperative KPS score (HR=0.981, 95% CI: 0.967–0.994, P=0.006), and receipt of CCRT (HR=0.200, 95% CI: 0.099–0.404, P<0.001) were independently associated with prolonged survival.

https://doi.org/10.2147/CIA.S574787

Table 1 Patient and Treatment Characteristics (N=89)

Covariate	Category	N (%)	Mean OS (Months, Range)
Gender	Male	44 (49.4)	11.4 (0.8–47.8)
	Female	45 (50.6)	18.2 (1.3–64.9)
Age Group (years)	60-64	35 (39.3)	17.2 (0.8–64.9)
	65-69	33 (37.1)	14.3 (4.0–42.1)
	≥70	21 (23.6)	9.8 (1.2–47.8)
Lesion Laterality	Unilateral	82 (92.1)	15.5 (0.8–64.9)
	Bilateral	7 (7.9)	6.2 (1.3–14.8)
Tumor Location	Supratentorial superficial	42 (47.2)	17.0 (1.2–42.1)
	Supratentorial deep	47 (52.8)	12.9 (0.8–64.9)
Number of Tumors	Single	71 (79.8)	15.6 (0.8–64.9)
	Multiple	18 (20.2)	11.6 (1.4–42.1)
Extent of Resection	Biopsy	7 (7.9)	5.9 (1.9–11.3)
	Subtotal resection	18 (20.2)	9.6 (0.8–37.9)
	Total resection	64 (71.9)	17.2 (1.6–64.9)
Systemic Disease	Yes	47 (52.8)	14.8 (0.8–64.9)
	No	42 (47.2)	14.7 (1.2–42.1)
Early Chemotherapy	Yes	32 (36.0)	12.9 (0.8–39.2)
	No	57 (64.0)	15.8 (1.2–64.9)
Concurrent Chemoradiation	Yes	74 (83.1)	16.7 (1.3–64.9)
	No	15 (16.9)	5.3 (0.8–18.2)
Adjuvant Chemotherapy	Yes	68 (76.4)	17.0 (1.3–64.9)
	No	21 (23.6)	7.5 (0.8–23.9)

Table 2 Univariable Cox Regression Analysis for Overall Survival

Covariate	Level	P-value (Sig.)	Hazard Ratio (Exp(B))	95% Confidence Interval
Gender	Male vs Female	0.002*	2.223	1.354–3.649
Age	65-69 vs 60–64	0.495	1.213	0.696–2.116
	≥70 vs 60–64	0.307	1.398	0.735–2.660
Lesion Laterality	Bilateral vs Unilateral	0.001*	4.003	1.773–9.039
Tumor Location	Deep vs Superficial	0.072	1.568	0.961–2.557
Number of tumors	Multiple vs Single	0.122	1.585	0.885–2.838
Extent of resection	Subtotal resection vs Biopsy	0.063	0.386	0.141–1.053
	Total resection vs Biopsy	0.001*	0.210	0.085–0.520
Preoperative KPS	Continuous	0.871	0.999	0.984–1.014
Systemic disease	Yes vs No	0.875	1.040	0.641–1.688
Postoperative KPS	Continuous	0.008*	0.984	0.972–0.996
Early chemotherapy	Yes vs No	0.723	1.098	0.656–1.836
Concurrent chemoradiation	Yes vs No	<0.001*	0.199	0.107–0.372
Adjuvant Chemotherapy	Yes vs No	<0.001*	0.348	0.199–0.608

Note: *P < 0.05 indicates statistical significance.

Age-Stratified Prognostic Value of KPS

Given the non-significant finding for preoperative KPS in the overall cohort, we performed a planned age-stratified survival analysis to explore its nuanced role (patient distribution across subgroups is detailed in Supplementary Table S2). This analysis revealed a striking divergence. In the "young-elderly" group (60–64 years), preoperative KPS was a strong and significant predictor of OS, with higher scores correlating with better survival (log-rank P=0.003; Table 4 and Figure 1A). However, this association was lost in patients aged 65–69 years (log-rank P=0.798; Figure 1B) and those aged ≥70 years (log-rank P=0.354; Figure 1C).

 https://doi.org/10.2147/CIA.S574787

Table 3 Multivariable Cox Regression Analysis for Overall Survival

Covariate	Level	P-value (Sig.)	Hazard Ratio (Exp(B))	95% Confidence Interval
Gender	Male vs Female	<0.001*	3.787	2.111–6.794
Extent of resection	Subtotal resection vs Biopsy	0.020*	0.274	0.092–0.818
	Total resection vs Biopsy	<0.001*	0.187	0.074–0.470
Postoperative KPS	Continuous	0.006*	0.981	0.967–0.994
Concurrent chemoradiation	Yes vs No	<0.001*	0.200	0.099–0.404

Note: *P < 0.05 indicates statistical significance.

Table 4 Log Rank Test for Equality of Survival Distributions by Preoperative KPS

Age Group (years)	Test	Chi-Square	df	P-value (Sig.)
60-64	Log Rank (Mantel-Cox)	15.940	4	0.003*
	Breslow (Generalized Wilcoxon)	14.637	4	0.006*
	Tarone-Ware	15.187	4	0.004*
65-69	Log Rank (Mantel-Cox)	1.661	4	0.798
	Breslow (Generalized Wilcoxon)	1.134	4	0.889
	Tarone-Ware	1.297	4	0.862
≥**70**	Log Rank (Mantel-Cox)	5.535	5	0.354
	Breslow (Generalized Wilcoxon)	4.015	5	0.547
	Tarone-Ware	4.712	5	0.452

Note: *P < 0.05 indicates statistical significance.

In stark contrast, postoperative KPS demonstrated robust and consistent prognostic power across all age strata (Table 5). A higher postoperative KPS was significantly associated with superior OS in the 60–64 age group (log-rank P<0.001; Figure 2A), the 65–69 age group (log-rank P=0.001; Figure 2B), and the ≥70 age group (log-rank P<0.001; Figure 2C).

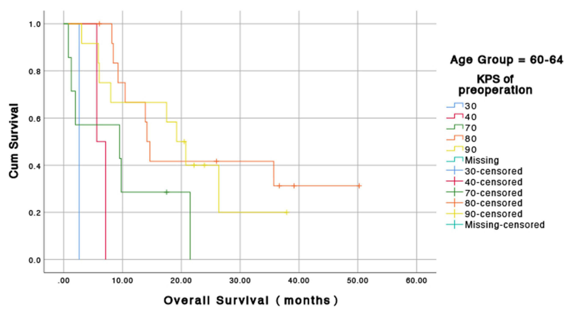
Discussion

The optimal management of elderly patients with GBM remains a significant clinical challenge, requiring a delicate balance between treatment efficacy and potential toxicity. Our study provides important insights into prognostic stratification in this population, confirming several established predictors while uncovering a novel, age-dependent role for performance status. The primary findings are threefold: (1) male gender is an independent negative prognostic factor, whereas maximal safe resection and CCRT are robust positive prognostic factors; (2) preoperative KPS is a significant predictor of survival only in the "young-elderly" (60–64 years), losing its prognostic utility in patients aged 65 and older; and (3) postoperative KPS is a powerful and consistent prognostic indicator across the entire elderly spectrum.

Our confirmation of EOR and CCRT as key determinants of survival aligns with the current standards of care and extensive existing literature.[4,17,18] These findings reinforce the principle that aggressive, multi-modal therapy should be offered to appropriately selected elderly patients, as it confers a substantial survival benefit. The unexpected finding of male gender as a strong independent risk factor warrants further investigation. The finding of male gender as a risk factor should be interpreted with caution. While consistent with some literature,[2] it may be influenced by unmeasured confounding variables such as molecular subtypes (eg, MGMT methylation distribution), which were not available for this analysis. This finding also aligns with recent epidemiological data suggesting a survival advantage for females in GBM.[19–22] Potential mechanisms include the neuroprotective effects of estrogen, which may inhibit glioma cell proliferation,[23–25] and sex-specific differences in immune regulation within the tumor microenvironment.[26,27]

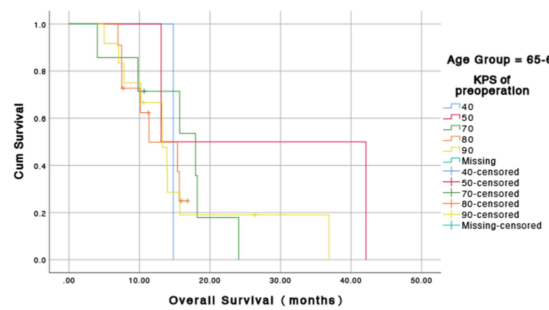
The most compelling finding of our study is the differential prognostic impact of preoperative KPS based on age. The observation that preoperative KPS is prognostic for patients aged 60–64 but not for those ≥65 provides a potential explanation for the conflicting reports in the literature, which often group all elderly patients together.[9,28] We hypothesize that in the "young-elderly," preoperative KPS accurately reflects underlying functional reserve. However, in older

A



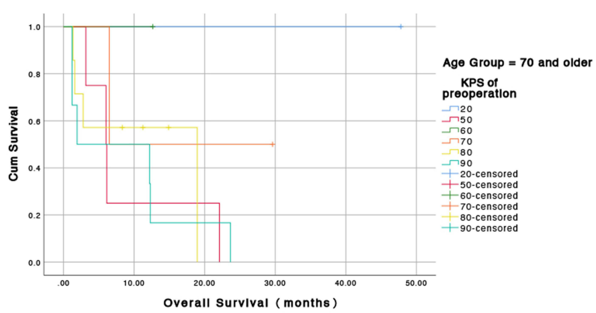
60-64	Follow-Up Time (months)						
KPS	0	10	20	30	40	50	60
30	1	0	0	0	0	0	0
40	2	0	0	0	0	0	0
70	7	2	1	0	0	0	0
80	13	9	5	4	1	1	0
90	12	8	6	1	0	0	0
Total	35	19	12	5	1	1	0

B



65-69	Follow-Up Time (months)					
KPS	0	10	20	30	40	50
40	1	1	0	0	0	0
50	2	2	1	1	1	0
70	7	5	1	0	0	0
80	11	7	0	0	0	0
90	12	9	2	1	0	0
Total	33	24	4	2	1	0

C



70 and older	Follow-Up Time (months)					
KPS	0	10	20	30	40	50
20	1	1	1	1	1	0
50	4	1	1	0	0	0
60	1	1	0	0	0	0
70	2	1	1	0	0	0
80	7	3	0	0	0	0
90	6	3	1	0	0	0
Total	21	10	4	1	1	0

Figure 1 Kaplan-Meier analysis of overall survival stratified by preoperative Karnofsky Performance Status (KPS). Number-at-risk tables are provided below the X-axis. **Note**: 95% confidence bands were omitted to maintain visual clarity given the multiple KPS strata. (**A**) Significant separation in 60–64 group. (**B** and **C**) No significant separation in older groups.

patients (≥65), the prognostic signal of KPS may become obscured by the cumulative burden of age-related physiological decline and comorbidities, which themselves become dominant drivers of outcome. This finding has direct clinical implications: for patients over 65, a poor preoperative KPS alone should perhaps not be an absolute contraindication to

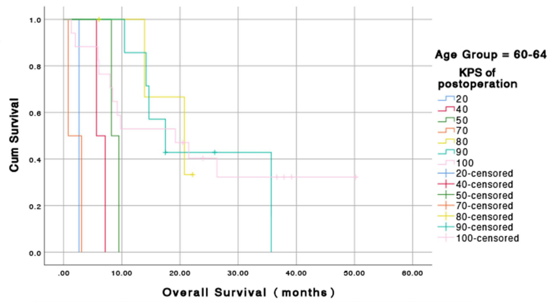
Table 5 Log Rank Test for Equality of Survival Distributions by Postoperative KPS

Age Group (years)	Test	Chi-Square	df	P-value (Sig.)
60-64	Log Rank (Mantel-Cox)	35.317	6	<0.001*
	Breslow (Generalized Wilcoxon)	32.433	6	<0.001*
	Tarone-Ware	33.703	6	<0.001*
65-69	Log Rank (Mantel-Cox)	22.141	6	0.001*
	Breslow (Generalized Wilcoxon)	19.728	6	0.003*
	Tarone-Ware	20.931	6	0.002*
≥70	Log Rank (Mantel-Cox)	23.905	6	<0.001*
	Breslow (Generalized Wilcoxon)	21.232	6	0.002*
	Tarone-Ware	22.515	6	0.001*

Note: *P < 0.05 indicates statistical significance.

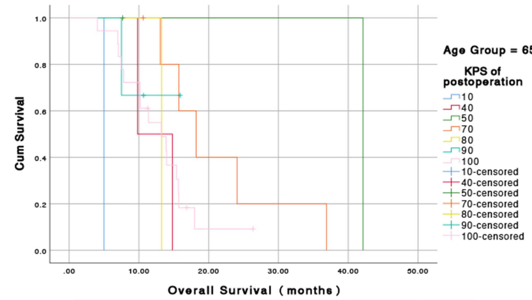
https://doi.org/10.2147/CIA.S574787

A



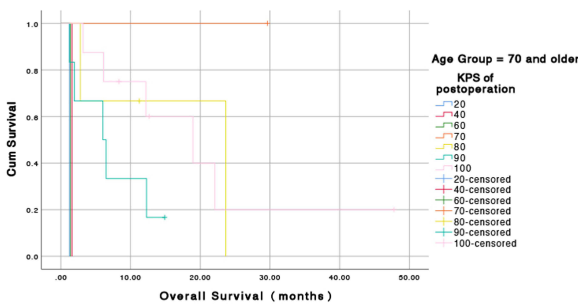
60-64	Follow-Up Time (months)						
KPS	0	10	20	30	40	50	60
20	1	0	0	0	0	0	0
40	2	0	0	0	0	0	0
50	2	0	0	0	0	0	0
70	2	0	0	0	0	0	0
80	4	3	2	0	0	0	0
90	7	7	2	1	0	0	0
100	17	9	8	4	1	1	0
Total	35	19	12	5	1	1	0

B



65-69	Follow-Up Time (months)					
KPS	0	10	20	30	40	50
10	1	0	0	0	0	0
40	2	1	0	0	0	0
50	2	1	1	1	1	0
70	6	6	2	1	0	0
80	1	1	0	0	0	0
90	3	2	0	0	0	0
100	18	13	1	0	0	0
Total	33	24	4	2	1	0

C



70 and older	Follow-Up Time (months)					
KPS	0	10	20	30	40	50
20	1	0	0	0	0	0
40	1	0	0	0	0	0
60	1	0	0	0	0	0
70	1	0	0	0	0	0
80	3	2	1	0	0	0
90	6	2	0	0	0	0
100	8	5	2	1	1	0
Total	21	9	3	1	1	0

Figure 2 Kaplan-Meier analysis of overall survival stratified by postoperative KPS. Higher postoperative KPS significantly predicted survival across all age groups. Number-at-risk tables are provided below the X-axis. (**A**) 60–64 years; (**B**) 65–69 years; (**C**) ≥70 years.

considering aggressive surgery. Instead, surgical candidacy should be based on the potential for functional preservation rather than preoperative status alone, incorporating frailty indices and comprehensive geriatric assessments.[29,30]

In contrast to its preoperative counterpart, postoperative KPS emerged as a universally powerful prognostic marker. This underscores that a patient's functional status following surgical recovery is a critical determinant of their ability to tolerate and benefit from subsequent adjuvant therapies, ultimately influencing their survival trajectory.[31,32] Therefore, the surgical goal in the elderly must balance cytoreduction with the preservation of eloquent function. This emphasizes the importance of advanced surgical techniques, such as awake craniotomy, intraoperative neuromonitoring, and brain mapping, alongside meticulous perioperative care and early integration of neuro-rehabilitation services.[33] The RANO resect group recently validated the pivotal role of postoperative KPS, alongside residual tumor and molecular markers, in a novel risk model, further cementing its status as a cornerstone of postoperative prognostication.[34]

Limitations

This study has several important limitations that must be acknowledged. First, its retrospective, single-center design is susceptible to selection bias and limits the generalizability of our findings. Second, the modest sample size of 89 patients, when stratified into age and KPS subgroups, results in small numbers within certain strata, which can reduce statistical power and increase the risk of spurious findings. While our results for the KPS subgroup analysis were highly significant,

https://doi.org/10.2147/CIA.S574787

they require validation in a larger, multicenter cohort. Third, and most significantly, our analysis lacks data on IDH1/2 mutation and MGMT promoter methylation status for the majority of patients (Supplementary Table S1), as these tests were not standard of care in our region during the early study period. Consequently, our results should be interpreted as reflecting the prognostic landscape based on clinical factors alone.

Conclusions

In conclusion, this study reaffirms the central roles of maximal safe resection and concurrent chemoradiation in prolonging survival for elderly patients with GBM. Our key contribution is the demonstration of an age-dependent divergence in the prognostic utility of KPS. While preoperative KPS appears to be a reliable prognosticator for patients younger than 65 years, its value diminishes thereafter. Postoperative KPS, however, stands out as a robust and universally applicable prognostic indicator across all elderly age groups. These findings suggest that surgical decision-making in the older-elderly should not be based solely on preoperative presentation but rather on the likelihood of achieving a favorable postoperative functional state.

Abbreviation

CCRT, Concurrent Chemoradiation; CI, Confidence Interval; EOR, Extent of Resection; GBM, Glioblastoma; GTR, Gross Total Resection; HR, Hazard Ratio; KPS, Karnofsky Performance Status; OS, Overall Survival; STR, Subtotal Resection; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author, Dr. Jing Tong, on reasonable request.

Ethics Approval and Consent to Participate

The study protocol received full approval from the Institutional Committee on Human Research of the Fourth Hospital of Hebei Medical University (Reference No. 2024KS147). The committee granted a waiver for the requirement of individual patient informed consent due to the retrospective nature of the research, the use of de-identified data, and the confirmation that the study posed no more than minimal risk to subjects. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for Publication

Not applicable. The manuscript does not contain any individual person's data in any form (including individual details, images, or videos).

Acknowledgments

We would like to thank Professor Xiaolin Zhang from the Department of Epidemiology and Statistics, School of Public Health, Hebei Medical University for valuable statistical consultation.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by Medical Science Research Project of Hebei (Grant number: 20170152, 2021KY196, and 20240026). The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Disclosure

The authors declare that they have no competing interests in this work.

References

1. Chen B, Chen C, Zhang Y, Xu J. Recent incidence trend of elderly patients with glioblastoma in the United States, 2000-2017. *BMC Cancer*. 2021;21(1):54. doi:10.1186/s12885-020-07778-1
2. Nunna RS, Khalid SI, Patel S, et al. Outcomes and patterns of care in elderly patients with glioblastoma multiforme. *World Neurosurg*. 2021;149: e1026–e1037. doi:10.1016/j.wneu.2021.01.028
3. Okada M, Miyake K, Tamiya T. Glioblastoma Treatment in the Elderly. *Neurol Med Chir*. 2017;57(12):667–676. doi:10.2176/nmc.ra.2017-0009
4. Conti Nibali M, Gay LG, Sciortino T, et al. Surgery for glioblastoma in elderly patients. *Neurosurg Clin N Am*. 2021;32(1):137–148. doi:10.1016/j.nec.2020.08.008
5. Mazarakis NK, Robinson SD, Sinha P, et al. Management of glioblastoma in elderly patients: A review of the literature. *Clin Transl Radiat Oncol*. 2024;46:100761. PMID: 38500668; PMCID: PMC10945210. doi:10.1016/j.ctro.2024.100761
6. Bruno F, Pellerino A, Palmiero R. Glioblastoma in the elderly: review of molecular and therapeutic aspects. *Biomedicines*. 2022;10(3):644. doi:10.3390/biomedicines10030644
7. Dobran M, Nasi D, Della Costanza M, et al. Characteristics of treatment and outcome in elderly patients with brain glioblastoma: a retrospective analysis of case series. *Acta Clin Croat*. 2019;58(2):221–228. doi:10.20471/acc.2019.58.02.04
8. Roth P, Gramatzki D, Weller M. Management of elderly patients with glioblastoma. *Curr Neurol Neurosci Rep*. 2017;17(4):35. doi:10.1007/s11910-017-0740-3
9. Rigamonti A, Imbesi F, Silvani A, et al. Pattern of care and outcome in elderly patients with glioblastoma: data in 151 patients from 3 lombardia hospitals. *J Neurol Sci*. 2017;378:3–8. doi:10.1016/j.jns.2017.04.030
10. Karsy M, Yoon N, Boettcher L, et al. Surgical treatment of glioblastoma in the elderly: the impact of complications. *J Neuro-oncol*. 2018;138 (1):123–132. doi:10.1007/s11060-018-2777-9
11. Rabin EE, Huang J, Kim M, et al. Age-stratified comorbid and pharmacologic analysis of patients with glioblastoma. *Brain Behav Immun Health*. 2024;38:100753. doi:10.1016/j.bbih.2024.100753
12. Chaichana KL, Chaichana KK, Olivi A, et al. Surgical outcomes for older patients with glioblastoma multiforme: preoperative factors associated with decreased survival. Clinical article. *J Neurosurg*. 2011;114(3):587–594. doi:10.3171/2010.8.JNS1081
13. Wildiers H, Heeren P, Puts M, et al. International society of geriatric oncology consensus on geriatric assessment in older patients with cancer. *J clin oncol*. 2014;32(24):2595–2603. doi:10.1200/JCO.2013.54.8347
14. Liu J, Li C, Wang Y, et al. Prognostic and predictive factors in elderly patients with glioblastoma: a single-center retrospective study. *Front Aging Neurosci*. 2021;13:777962. doi:10.3389/fnagi.2021.777962
15. von Elm E, Altman DG, Egger M. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2007;60(6):344–349.
16. Ostrom QT, Price M, Neff C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2015-2019. *Neuro Oncol*. 2022;24(Suppl 5):v1–v95. doi:10.1093/neuonc/noac202
17. Klingenschmid J, Krigers A, Kerschbaumer J, Thome C, Pinggera D, Freyschlag CF. Surgical management of malignant glioma in the elderly. *Front Oncol*. 2022;12:900382. doi:10.3389/fonc.2022.900382
18. Kalra B, Kannan S, Gupta T. Optimal adjuvant therapy in elderly glioblastoma: results from a systematic review and network meta-analysis. *J Neuro-oncol*. 2020;146(2):311–320. doi:10.1007/s11060-019-03375-w
19. Smits A, Lysiak M, Magnusson A, Rosell J, Söderkvist P, Malmström A. Sex disparities in MGMT promoter methylation and survival in glioblastoma: further evidence from clinical cohorts. *J Clin Med*. 2021;10(4):556. doi:10.3390/jcm10040556
20. Tian M, Ma W, Chen Y, et al. Impact of gender on the survival of patients with glioblastoma. *Biosci. Rep*. 2018;38(6). doi:10.1042/BSR20180752
21. Claus EB, Black PM. Survival rates and patterns of care for patients diagnosed with supratentorial low-grade gliomas: data from the SEER program, 1973-2001. *Cancer*. 2006;106(6):1358–1363. doi:10.1002/cncr.21733
22. Innocenti L, Ortenzi V, Scarpitta R, et al. The prognostic impact of gender, therapeutic strategies, molecular background, and tumor-infiltrating lymphocytes in glioblastoma: a still unsolved jigsaw. *Genes*. 2023;14(2):501. doi:10.3390/genes14020501
23. Barone TA, Gorski JW, Greenberg SJ, Plunkett RJ. Estrogen increases survival in an orthotopic model of glioblastoma. *J Neuro-oncol*. 2009;95 (1):37–48. doi:10.1007/s11060-009-9904-6
24. Li Q, Jedlicka A, Ahuja N, et al. Concordant methylation of the ER and N33 genes in glioblastoma multiforme. *Oncogene*. 1998;16 (24):3197–3202. doi:10.1038/sj.onc.1201831
25. Hönikl LS, Lämmer F, Gempt J, Meyer B, Schlegel J, Delbridge C. High expression of estrogen receptor alpha and aromatase in glial tumor cells is associated with gender-independent survival benefits in glioblastoma patients. *J Neuro-oncol*. 2020;147(3):567–575. doi:10.1007/s11060-020-03467-y
26. Franceschi E, Tosoni A, Minichillo S, et al. The prognostic roles of gender and o6-methylguanine-dna methyltransferase methylation status in glioblastoma patients: the female power. *World Neurosurg*. 2018;112:e342–e347. doi:10.1016/j.wneu.2018.01.045
27. Carrano A, Juarez JJ, Incontri D, Ibarra A, Guerrero Cazares H. Sex-specific differences in glioblastoma. *Cells*. 2021;10(7):1783. doi:10.3390/cells10071783
28. Heiland DH, Haaker G, Watzlawick R, et al. One decade of glioblastoma multiforme surgery in 342 elderly patients: what have we learned? *J Neuro-oncol*. 2018;140(2):385–391. doi:10.1007/s11060-018-2964-8
29. Nabors LB, Portnow J, Ahluwalia M, et al. Central nervous system cancers, version 3.2020, NCCN clinical practice guidelines in oncology. *J National Compr Cancer Netw*. 2020;18(11):1537–1570. doi:10.6004/jnccn.2020.0052
30. Krenzlin H, Jankovic D, Alberter C, et al. Frailty in glioblastoma is independent from chronological age. *Front Neurol*. 2021;12:777120. doi:10.3389/fneur.2021.777120
31. Al Feghali KA, Buszek SM, Elhalawani H, Chevli N, Allen PK, Chung C. Real-world evaluation of the impact of radiotherapy and chemotherapy in elderly patients with glioblastoma based on age and performance status. *Neurooncol Pract*. 2021;8(2):199–208. doi:10.1093/nop/npaa064

32. Deguchi S, Mitsuya K, Oishi T, Nakasu Y, Sugino T, Hayashi N. Editors' Choice Impact of maintenance of postoperative performance status on survival in elderly patients over 70 with high-grade astrocytoma. *Nagoya J Med Sci*. 2020;82(3):533–543. doi:10.18999/nagjms.82.3.533
33. Sanai N, Berger MS. Glioma extent of resection and its impact on patient outcome. *Neurosurgery*. 2008;62(4):753–764. doi:10.1227/01.neu.0000318159.21731.cf
34. Karschnia P, Young JS, Youssef GC, Dono A. Development and validation of a clinical risk model for postoperative outcome in newly diagnosed glioblastoma: a report of the RANO resect group. *Neuro-Oncology*. 2025;27(4):1046–1060. doi:10.1093/neuonc/noae231