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Prognostic significance of preoperative serum albumin, albumin-to-globulin ratio, and prognostic nutritional index for patients with glioma

A meta-analysis

Mingchang Liu, MM, Liwen Wang, BM* iD

Abstract

Background: The serum albumin, albumin-to-globulin ratio (AGR), and prognostic nutritional index (PNI) have been recommended to represent the nutritional and inflammatory status. Thus, they may be potential prognostic biomarkers for cancer. However, contradictory results were reported in different studies on glioma. The goal of this study was to perform a meta-analysis to re-evaluate their prognostic potential for glioma.

Methods: Databases of PubMed, EMBASE, and Cochrane Library were systematically searched to enroll all the studies investigating the prognostic significance of albumin, AGR, and PNI for glioma. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using STATA 13.0 software to indicate the intensity of association.

Results: Eleven studies with 2928 cases were included. Overall meta-analysis showed that the prognostic values of albumin, AGR, and PNI were limited for glioma ($P > .05$). However, subgroup analysis demonstrated a high preoperative serum albumin was significantly related with excellent OS of patients with GBM (HR = 0.95, 95% CI: 0.91–0.99, $P = .018$), while high PNI (HR = 0.56, 95% CI: 0.43–0.73, $P < .001$) and AGR (HR = 0.57, 95% CI: 0.34–0.96, $P = .034$) may be a protective factor of favorable OS for patients with high-grade gliomas. Furthermore, integration of all studies with multivariate analysis and clear cut-off also proved reduced preoperative serum albumin, AGR, and PNI were predictors of poor prognosis for patients with gliomas.

Conclusion: Preoperative serum albumin, AGR, and PNI may represent promising biomarkers to predict the prognosis in patients with glioma, especially for high-grade.

Abbreviations: AGR = albumin-to-globulin ratio, CI = confidence interval, GBM = glioblastoma multiforme, HR = hazard ratio, IL = interleukin, NOS = Newcastle-Ottawa Scale, OS = overall survival, PNI = prognostic nutritional index, PRISMA = Preferred Reporting Items for Systematic Review and Meta-analysis.

Keywords: albumin, albumin-to-globulin ratio, glioma, prognosis, prognostic nutritional index

1. Introduction

Glioma is one of the most common primary central nervous system tumors, with age-adjusted annual incidence of 7.3 cases/100,000 persons.[1] Clinically, gliomas are subdivided into 4

grades, with the malignant degree gradually increasing from grade I to grade IV (glioblastoma multiforme, GBM). Despite advance has been made in the treatment of glioma (including radical surgery, radiotherapy, and chemotherapy), some patients still face a poor prognosis, especially for the high-grade population [the 5-year overall survival (OS) rate: grade I, 82%; grade II, 54%; grade III, 22%; and grade IV, 3%].[1] Therefore, it is very important to early identify patients who may have an unfavorable outcome and then schedule individualized treatment regimens for them in order to further improve OS, in which exploring an effective prognostic biomarker is the first demand.

There is increasing evidence to suggest preoperative malnutrition and inflammatory status are associated with the OS of patients with cancer.[2–4] Albumin synthesized by the liver is a major component (accounting for 50%–65%) of the total protein in human serum and thus serum albumin has been recommended as an indicator to represent the nutritional status of patients.[5] Patients with hypoalbuminemia were considered to be malnourished.[5] Furthermore, supplementation of long-term high-dose albumin was found to reduce the levels of inflammatory cytokines [interleukin (IL)-6, granulocyte colony-stimulating factor, interleukin 1 receptor antagonist, and vascular endothelial growth factor] in patients with decompensated cirrhosis[6]; in vitro albumin dialysis experiments also demonstrated albumin added

to the dialysate solution induced a significant decrease of IL-6,[7] indicating albumin may also be an anti-inflammatory protein. Moreover, there was direct evidence to show that tumor-bearing animals became hypoalbuminemic, which was reported to be resulted from depressed albumin synthesis and increased albumin degradation.[8] According to these findings, we hypothesize serum albumin may be a potential prognostic biomarker for glioma, with low level predicting poor survival. This hypothesis had been confirmed in the study of Han et al [9] and Wang et al.[10] However, there were also some contradictory conclusions, showing no significant associations between serum albumin level and OS in patients with glioma.[11–15] These inconsistent results may be attributed to 2 aspects:

1. small sample size of each individual study; and
2. possible limited predictive ability of serum albumin.

To resolve these 2 problems, on one hand, a meta-analysis that integrates all the evidence should be performed to enhance the statistical power; on the other hand, biomarkers that combined with serum albumin should be investigated. For the latter, recent studies put forward to use prognostic nutritional index [PNI, calculated as albumin (g/L) + 5 × total lymphocyte count (10^9/L)] and albumin-to-globulin ratio (AGR). As expected, most of the known studies proved preoperative AGR[9,10,14–16] and PNI[10,12,18,19] were independent prognostic factors of OS for patients with glioma. Unfortunately, there were still occasional studies to indicate PNI was not associated with prognosis.[13,14,20] Hereby, their prognostic significance also needs further assessment.[21]

In present study, we aimed to re-evaluate the prognostic significance of preoperative serum albumin, AGR, and PNI for patients with glioma by performing a meta-analysis.

2. Materials and methods

This meta-analysis was conducted under the guidelines developed in The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). Ethical approval and patient consent were not required since this study was a meta-analysis based on published studies.

2.1. Search strategy

All relevant literatures published up to December 31, 2019 were retrieved by searching the databases of PubMed, EMBASE, and Cochrane Library. The search keywords and terms included: ("albumin" OR "hyperalbuminemia" OR "hypoalbuminemia" OR "albumin-to-globulin ratio" OR "albumin/globulin ratio" OR "prognostic nutritional index") AND ("glioblastoma" OR "gliomas"). Meanwhile, the references listed in all included articles and reviews were also manually screened to identify additional related articles.

2.2. Inclusion and exclusion criteria

The study selection process was performed by 2 independent investigators, with any disagreements being discussed. Publications that met the following inclusion criteria were included:

1. the prognostic value of serum albumin, AGR, or PNI was investigated for glioma patients;
2. the related clinical indicators (level of serum albumin, globulin, and lymphocyte count) were collected preoperatively;

3. the hazard ratio (HR) with 95% confidence interval (CI) were provided or can be estimated from Kaplan–Meier curve;
4. published in English; and
5. had full text.

The studies were excluded according to exclusion criteria:

1. duplicated or with overlapped data;
2. observational study;
3. abstracts, letters, case reports, reviews, and comments;
4. performed on animals;
5. focusing on the association between postoperative serum albumin and prognosis; and
6. no sufficient data for calculating HRs and 95%CIs.

2.3. Data extraction

Two authors extracted the following data independently: the surname of the first author, year of publication, country, case number, study design, follow-up, cancer type, cut-off value, HR source and HR with 95%CI for prognosis outcomes. HRs and 95%CIs were preferentially extracted from the multivariable analysis if both univariate and multivariate analyses were available. The survival data were estimated using a digitizing software-Engauge Digitizer (version 4.1; http://digitizer.source forge.net/) if only Kaplan–Meier curve was included in studies.

2.4. Quality assessment

The quality of enrolled studies was evaluated by 2 independent researchers using the Newcastle-Ottawa Scale (NOS) criteria.[22] NOS score ranged from 0 to 9. A study was regarded as high quality if its NOS was higher than 7.

2.5. Statistical analysis

The association between serum albumin/AGR/PNI and prognostic outcomes (such as OS) of glioma patients was assessed by pooled HR and 95% CI. HR < 1 indicated a protective effect for prognosis in patients with high albumin, AGR, or PNI; otherwise, it indicated a risk effect. Statistical difference was determined by using z test ($P < .05$) with 95%CI (not overlapping 1). Heterogeneity among studies was evaluated using Cochranes Q (Chi-Squared) and I^2 tests. The random-effects model was used to calculate the pooled HR and 95%CI when P was less than .10 and I^2 was more than 50% (that is, significant heterogeneity among studies); otherwise, a fixed-effects model was chosen. Subgroup analyses were performed according to country (Asian or Non-Asian), sample size (<200 or >200), cut-off (Yes or No), cancer type (GBM, all gliomas, high-grade glioma, or low-grade gliomas) and source of HR (univariate or multivariate). Egger linear regression test was used to detect the publication bias, with $P < .05$ indicating the presence of publication bias.[23] All analyses were performed or figures were generated using STATA 13.0 (STATA Corporation, College Station, TX, USA).

3. Results

3.1. Study search

Figure 1 provides detailed strategy of search and selection for relevant studies used in this meta-analysis. The initial literature search in available databases yielded 623 records. A total of 156 articles were found to be duplicated and then removed. After
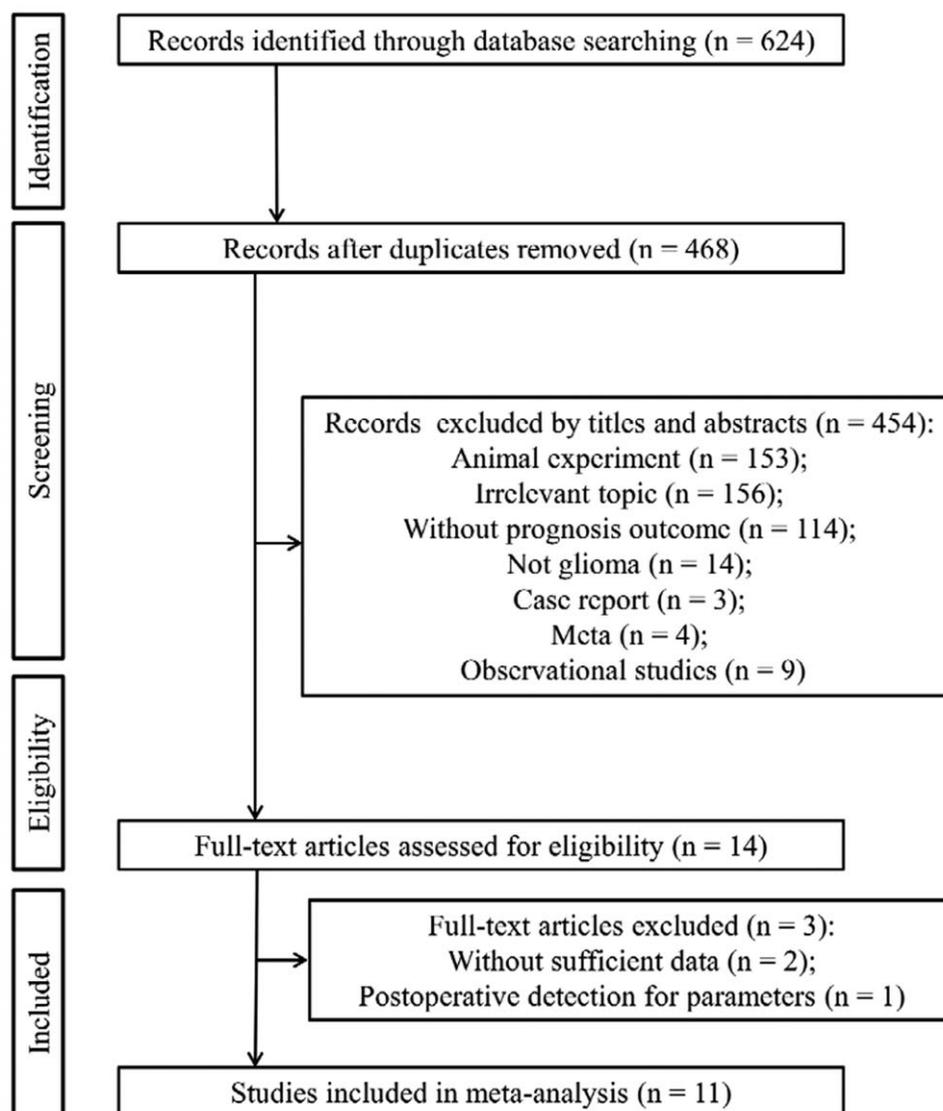
Figure 1. Flow diagram of included studies.

reading the titles and abstracts, 453 studies were excluded because they did not meet the eligibility criteria, including animal experiment (n=153); irrelevant topic (n=156); without prognosis outcome (n=114); not glioma (n=14); case report (n=3); meta-analysis (n=4); and observational studies (n=9). The full text of the remaining 14 studies were downloaded and then read. Of them, 3 studies were further discarded because no sufficient data could be obtained (n=2) and serum albumin was collected postoperatively (n=1). Finally, 11 studies with 2928 cases were included in this meta-analysis.[9–17,19,20]

3.2. Study characteristics and quality assessment

The main characteristics of eligible studies are summarized in Table 1. Among these 11 studies, the study of Han et al [9] contained 2 multivariate analysis results due to different adjusted variables; the study of He et al[19] included the training and validation cohorts for prognosis analysis; the study of Wang e

al[10] independently analyzed all the gliomas and GBM samples; thus, in fact, 14 datasets were used for this meta-analysis. Seven studies with 9 datasets[9–15] assessed the prognostic value of serum albumin on OS; 5 studies with 6 datasets[10,11,15–17] investigated the association between AGR and OS; 7 studies with 9 datasets[10,12–14,18–20] focused the predictive ability of PNI for OS; and 1 study with 2 datasets reported the relationship between PNI and PFS.[19] Six studies evaluated patients belonging to GBM (IV), 2 evaluated high-grade patients (III-IV), 1 focused on low-grade cases (II-III), and 3 studies evaluated all glioma types (I-IV). All these studies were retrospectively conducted in population from China (n=10) and Italy (n=1). HRs and 95%CIs were directly obtained from 9 studies; there were 2 articles[16,17] only providing Kaplan–Meier curves and their HRs were estimated by Engauge Digitizer. Cut-off values of albumin ranged from 30 to 42; AGR ranged from 1.35 to 1.79; PNI ranged from 44.4 to 52.55. The NOS was 9 for 4 articles and 8 for 7 studies, indicating the quality of all eligible studies was high (Table 1).

Table 1

Characteristics of included studies.

Study	Year	Country	No.	Age	Male	Design	Follow-up	Cancer type	Parameters	Cut-off	Outcome	HR source	NOS
Ding JD	2018	China	300	49.9±14.0	182	R	–	GBM (IV)	PNI	44	OS (non-significant)	M	8
Wang PF	2018	China	706	45.2±13.4	407	R	–	All gliomas (II-IV), GBM (IV)	AGR, albumin, PNI	–	OS (significant)	U	8
Xu WZ	2017	China	166	50.4±14.5	84	R	14 m	GBM (IV)	AGR, albumin, PNI	AGR, 1.75; albumin, 42; PNI, 48	OS (AGR/PNI, significant; albumin, non-significant)	M	9
Zhou XW	2016	China	84	53 (43–62)	50	R	–	GBM (IV)	Albumin, PNI	Albumin, 38.9; PNI, 44.4	OS (PNI, significant; albumin, non-significant)	M	8
Han S	2015	China	214	52.3±12.8	120	R	13.7 m	GBM (IV)	Albumin	30	OS (significant; 2 adjusted variables)	M	9
Yang T	2019	China	128	47.8±14.0	71	R	–	Gliomas (I-IV)	Albumin, PNI	Albumin, 35; PNI, 45	OS (non-significant)	M	9
He ZQ	2017	China	318	–	–	R	–	High-grade gliomas (III-IV)	PNI	52.55	OS (training, significant; validation, non-significant)	M	8
Rigamonti A	2019	Italy	282	66.4 (28.5–83.3)	178	R	3.3 y	GBM (IV)	Albumin, PNI	Albumin, -; PNI, 45.9	OS (non-significant)	U	8
Liang R	2019	China	169	53 (21–91)	99	R	–	High-grade gliomas (III-IV)	AGR, albumin	AGR, 1.35; albumin, 40	OS (albumin, non-significant; AGR, significant)	U (albumin); M (AGR)	9
Zhang ZY	2019	China	358	–	–	R	32 m	Low-grade gliomas (II-III)	AGR	1.79	OS (significant)	U (K-M)	8
Wu Y	2019	China	203	44±14.61	114	R	–	Glioma (I-IV)	AGR	1.9	OS (significant)	U (K-M)	8

AGR = albumin-to-globulin ratio, GBM = glioblastoma multiforme, HR = hazard ratio, K–M = Kaplan–Meier curve, m = month, M = multivariate analysis, NOS = Newcastle-Ottawa Scale, OS = overall survival, PNI = prognostic nutritional index, R = retrospective, U = univariate analysis, y = year.

3.3. Impact of preoperative serum albumin on postoperative OS

Since an obvious heterogeneity was found between included studies ($I^2=69.7\%$, $P=.001$), a random-effect model was used for meta-analysis. Pooled results demonstrated that there was no significant difference in OS between the patients with high- and low-level of serum albumin (HR=0.96, 95% CI: 0.89–1.04, $P=.276$) (Table 2). To explore the source of heterogeneity, the subgroup analysis was performed. The results showed that a high preoperative serum albumin was significantly related with excellent OS in subgroups with sample size less than 200 (HR=0.77, 95% CI: 0.59–0.99, $P=.047$), having clear cut-off (HR=0.77, 95% CI: 0.59–0.99, $P=.047$), undergoing multivariate analysis (HR=0.96, 95% CI: 0.94–0.98, $P<.001$; Fig. 2)

and belonging to GBM grade (HR=0.95, 95% CI: 0.91–0.99, $P=.018$; Fig. 3) (Table 2).

3.4. Impact of preoperative AGR on postoperative OS

It was noticeable that a large heterogeneity was present between included studies ($I^2=88.4\%$, $P<.001$), thus a random-effect model was used for the pooled analysis. The meta-analysis result showed that AGR was not associated with OS (HR=0.90, 95% CI: 0.56–1.46, $P=.670$) (Table 3). Subsequently, subgroup analysis was further conducted to explore the sources of heterogeneity. Subgroup analysis of studies with sample size less than 200 (HR=0.68, 95% CI: 0.47–0.97, $P=.033$), having clear cut-off (HR=0.64, 95% CI: 0.51–0.79, $P<.001$) and undergoing multivariate analysis (HR=0.96, 95% CI: 0.94–0.98, $P<.001$;

Table 2

Meta-analyses for the prediction ability of albumin for OS.

Comparison	Studies	HR (95%CI)	P_A-value	I^2	P_H-value	Model
Overall	9	0.96 (0.89,1.04)	.276	69.7	.001	R
Subgroup						
Country						
Asian	8	0.96 (0.89,1.04)	.352	73.3	<.001	R
Non-Asian	1	0.89 (0.66,1.21)	.456	–	–	R
Sample size						
<200	4	0.77 (0.59,0.99)	**.047**	0.0	.790	F
>200	5	0.98 (0.90,1.06)	.586	82.3	<.001	R
Cut-off						
Yes	4	0.77 (0.59,0.99)	**.047**	0.0	.790	F
No	5	0.98 (0.90,1.06)	.586	82.3	<.001	R
HR source						
M	5	0.96 (0.94,0.98)	**<.001**	0.0	.509	F
U	4	0.86 (0.52,1.42)	.542	86.7	<.001	R
Cancer type						
GBM	6	0.95 (0.91,0.99)	**.018**	42.4	.122	F
All gliomas	2	1.21 (0.54,2.72)	.647	62.0	.105	R
High-grade gliomas	1	0.68 (0.45,1.02)	.061	–	–	R

CI = confidence interval, F = fixed-effects, GBM = glioblastoma multiforme, HR = hazard ratio, M = multivariate analysis, OS = overall survival, P_A = P value for association, P_H = P value for heterogeneity, R = random-effects, U = univariate analysis.
Bold indicated the significant results pooled by at least 2 studies.
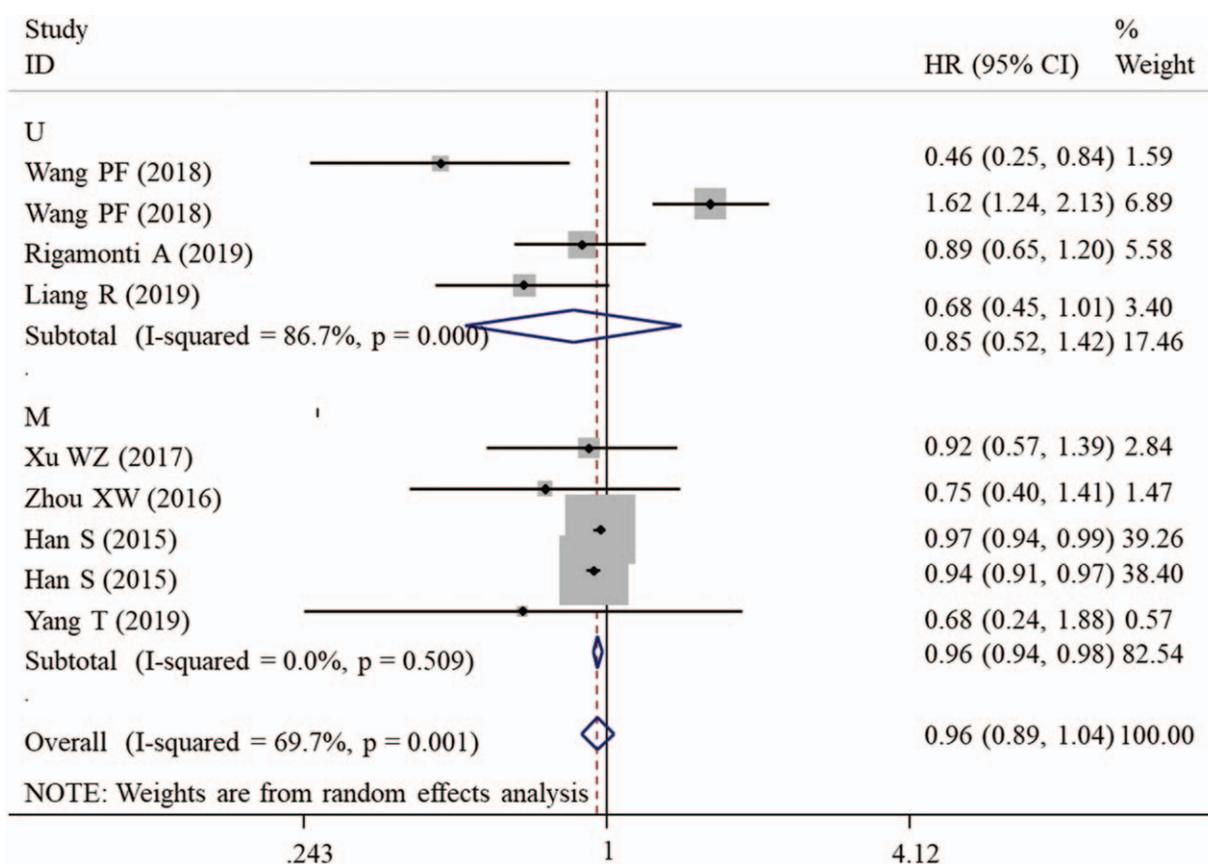
Figure 2. Forest plots to investigate the correlation between albumin and overall survival based on HR source subgroup analyses. CI = confidence interval, HR = hazard ratio, M = multivariate analysis, U = univariate analysis.

Table 3

Meta-analyses for the prediction ability of AGR for OS.

Comparison	Studies	HR (95%CI)	P_A-value	I^2	P_H-value	Model
Overall		0.90 (0.56,1.46)	.670	88.4	<.001	R
Subgroup						
Country						
Asian	6	0.90 (0.56,1.46)	.670	88.4	<.001	R
Non-Asian	0	–	–	–	–	–
Sample size						
<200	2	0.68 (0.47,0.97)	**.033**	0.0	.375	F
>200	4	1.03 (0.55,1.93)	.930	91.7	<.001	R
Cut-off						
Yes	4	0.64 (0.51,0.79)	**<.001**	0.0	.452	F
No	2	1.79 (1.41,2.28)	**<.001**	20.4	.262	F
HR source						
M	2	0.68 (0.47,0.97)	**.033**	0.0	.375	F
U	4	1.03 (0.55,1.93)	.930	91.7	<.001	R
Cancer type						
GBM	2	1.12 (0.59,2.10)	.735	75.4	.044	R
All gliomas	2	1.01 (0.26,3.92)	.992	96.3	<.001	R
High-grade gliomas	1	0.57 (0.34,0.96)	.034	–	–	R
Low-grade gliomas	1	0.72 (0.50,1.03)	.071	–	–	R

AGR = albumin-to-globulin ratio, CI = confidence interval, F = fixed-effects, GBM = glioblastoma multiforme, HR = hazard ratio, M = multivariate analysis, OS = overall survival, P_A = P value for association, PFS = progression free survival, P_H = P value for heterogeneity, R = random-effects, U = univariate analysis.
Bold indicated the significant results pooled by at least 2 studies.
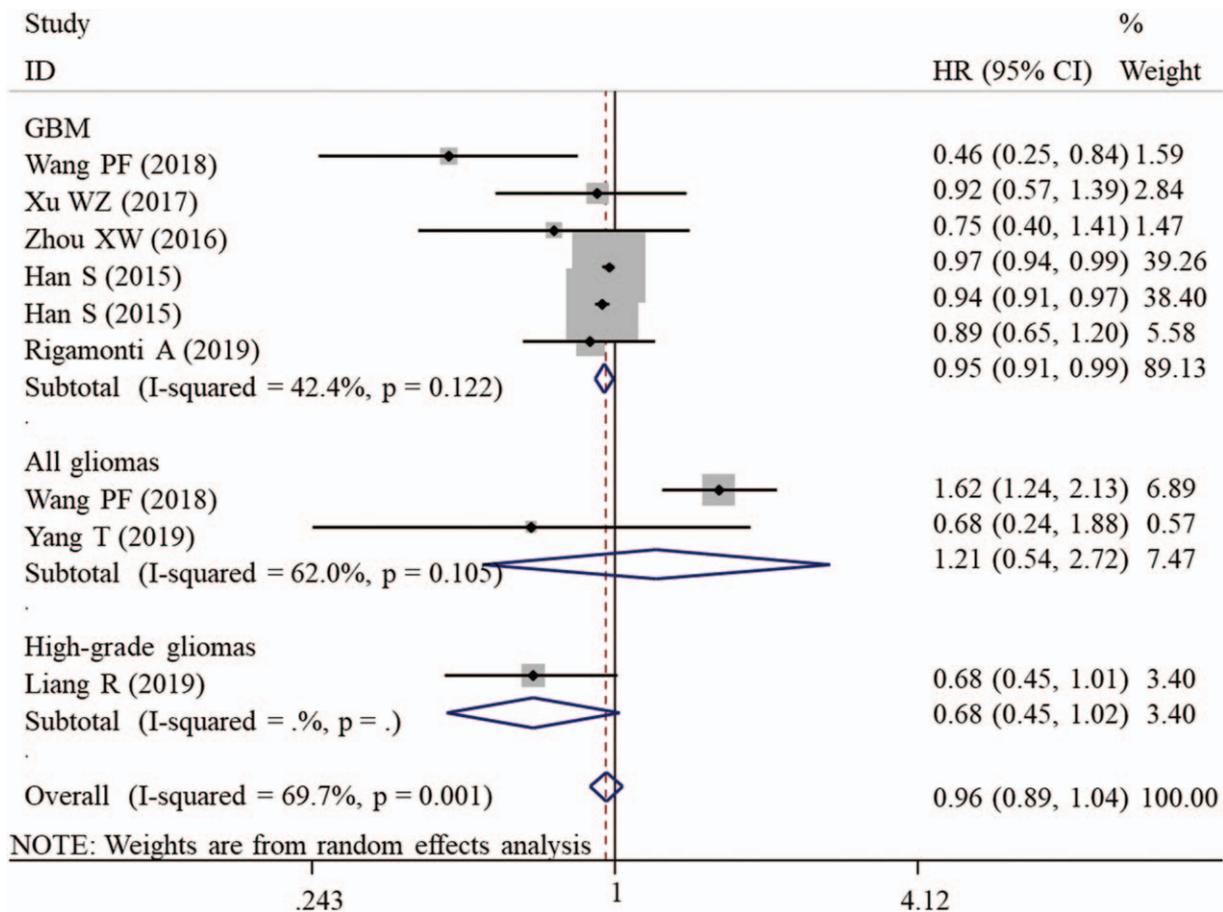
Figure 3. Forest plots to investigate the correlation between albumin and overall survival based on cancer type subgroup analyses. CI = confidence interval, GBM = glioblastoma multiforme, HR = hazard ratio.

Fig. 4) revealed that a low preoperative AGR predicted poor OS (Table 3).

3.5. Impact of preoperative PNI on postoperative OS

A random-effect model was used to calculate the HR and 95% CI because a significant heterogeneity existed between included studies ($I^2 = 84.4\%$, $P < .001$). Overall meta-analysis showed that the OS was not significantly different between the patients with high PNI and those with low PNI (Table 4). However, the subgroup study proved that high PNI may be a protective factor of favorable OS for patients with high-grade gliomas (HR = 0.56, 95% CI: 0.43–0.73, $P < .001$; Fig. 5). Also, the prognostic value of PNI was significant if the studies enrolled less than 200 samples (HR = 0.60, 95% CI: 0.49–0.74, $P < .001$), had defined cut-off (HR = 0.63, 95% CI: 0.52–0.77, $P < .001$) and performed multivariate analysis (HR = 0.63, 95% CI: 0.52–0.77, $P < .001$; Fig. 6) (Table 4).

3.6. Publication bias

Although heterogeneities were observed among studies for investigating the prognostic values of serum albumin, AGR, and PNI, Egger test results showed there was no obvious evidence of publication bias (albumin, $P = .596$; AGR, $P = .134$; PNI, $P = .206$).

4. Discussion

There have numerous articles to use the meta-analysis to confirm the prognostic significance of preoperative serum albumin for patients with urothelial carcinoma,[24] epithelial ovarian cancer,[25] bladder cancer[26]; AGR for digestive system cancers,[27] or combined all cancer types[28,29]; and PNI for lung cancer,[30,31] hepatocellular carcinoma,[32] esophageal cancer,[33] and pancreatic cancer.[34] All these studies revealed the cancer patients with decreased albumin, AGR, and PNI held a worse OS compared with those who carried a higher albumin, AGR, and PNI. In line with these reports, our analysis of studies with multivariate association tests and clear cut-off also found a higher preoperative serum albumin, AGR, and PNI indicated a better OS, especially for patients with GBM or high-grade gliomas.

Although the exact protective mechanisms of albumin for gliomas remain unclear, we speculated its association with malnutrition and inflammation may be possible contributors. Clinically, weight loss of >10% of normal body weight is considered to represent protein-energy malnutrition.[35] Albumin protein concentrations were reported to be positively correlated with the percent ideal body weight ($r = 0.390$, $P < .05$) and negatively associated with extent of reported weight loss ($r = -0.492$, $P < .01$).[36] Multivariate analysis in the study of Ehrsson et al [37] revealed tumor stage was the only independent factor of maximum weight loss. Weight gain increased the survival and
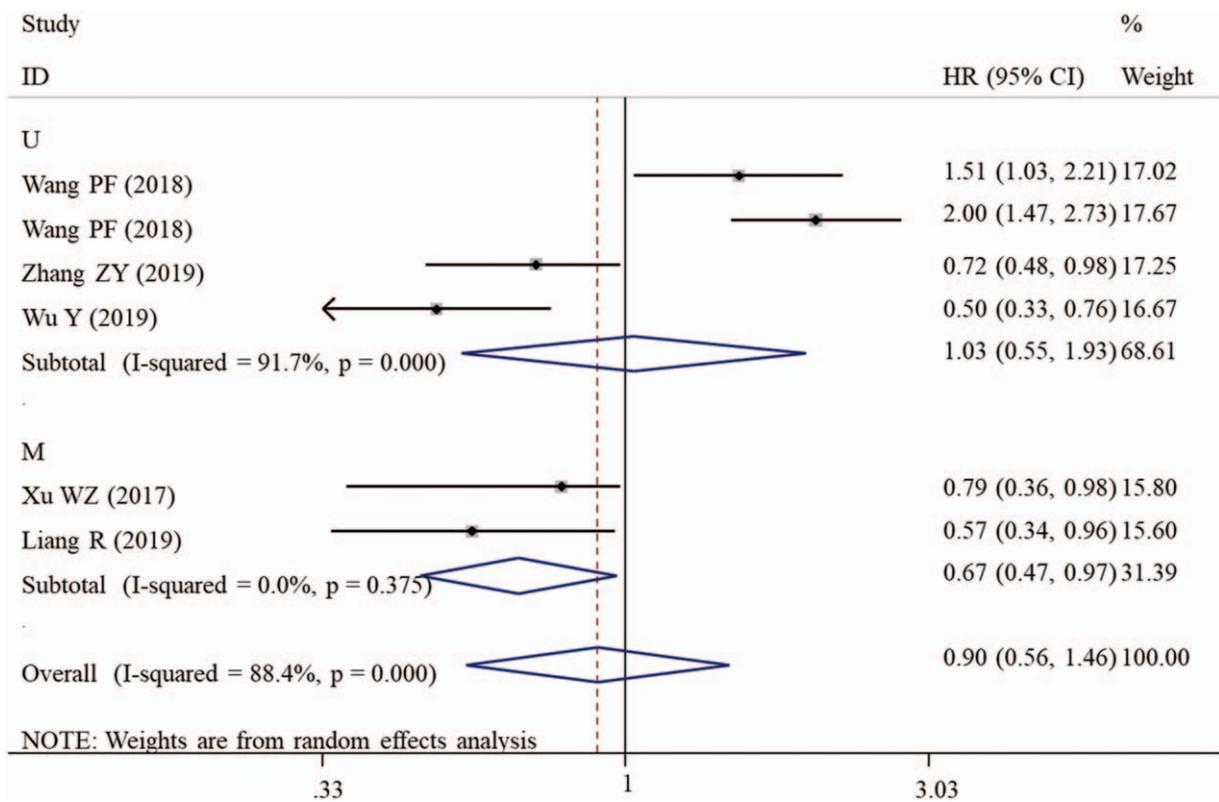
Figure 4. Forest plots to investigate the correlation between albumin-to-globulin ratio and overall survival based on HR source subgroup analyses. CI = confidence interval, HR = hazard ratio, M = multivariate analysis, U = univariate analysis.

quality of life of patients with cancer.[38] Furthermore, cytokine tumor necrosis factor α concentrations were also observed to be significantly higher in cancer patients with severe weight loss than in those with moderate or light weight loss (26.3 ± 8.3 vs 8.9 ± 4.2 or 3.8 ± 2.1).[39] Serum C-reactive protein (CRP) was also proved

to be an independent variable in determining degree of weight loss (estimate of effect, 34%).[40] Therefore, low albumin-weight loss-inflammation may be the possible mechanism for the development and progression of gliomas. This hypothesis can be indirectly reflected by the negative correlation between

Table 4

Meta-analyses for the prediction ability of PNI for OS.

Comparison	Studies	HR (95%CI)	P_A-value	I^2	P_H-value	Model
Overall for OS	9	0.83 (0.60,1.16)	.282	84.4	<.001	R
Subgroup for OS						
Country						
Asian	8	0.83 (0.56,1.25)	.375	85.8	<.001	R
Non-Asian	1	0.79 (0.61,1.03)	.078	–	–	R
Sample size						
<200	5	0.60 (0.49,0.74)	**<.001**	0.0	.732	F
>200	4	1.18 (0.75,1.87)	.476	86.5	<.001	R
Cut-off						
Yes	6	0.63 (0.52,0.77)	**<.001**	0.0	.611	F
No	3	1.31 (0.75,2.27)	.346	89.9	<.001	R
HR source						
M	6	0.63 (0.52,0.77)	**<.001**	0.0	.611	F
U	3	1.31 (0.75,2.27)	.346	89.9	<.001	R
Cancer type						
GBM	5	0.87 (0.61,1.23)	.422	66.1	.019	R
All gliomas	2	1.15 (0.50,2.65)	.740	85.9	.008	R
High-grade gliomas	2	0.56 (0.43,0.73)	**<0.001**	–	–	–

CI = confidence interval, F = fixed-effects, GBM = glioblastoma multiforme, HR = hazard ratio, M = multivariate analysis, OS = overall survival, P_A = P value for association, P_H = P value for heterogeneity, PNI = prognostic nutritional index, R = random-effects, U = univariate analysis.
Bold indicated the significant results pooled by at least 2 studies.
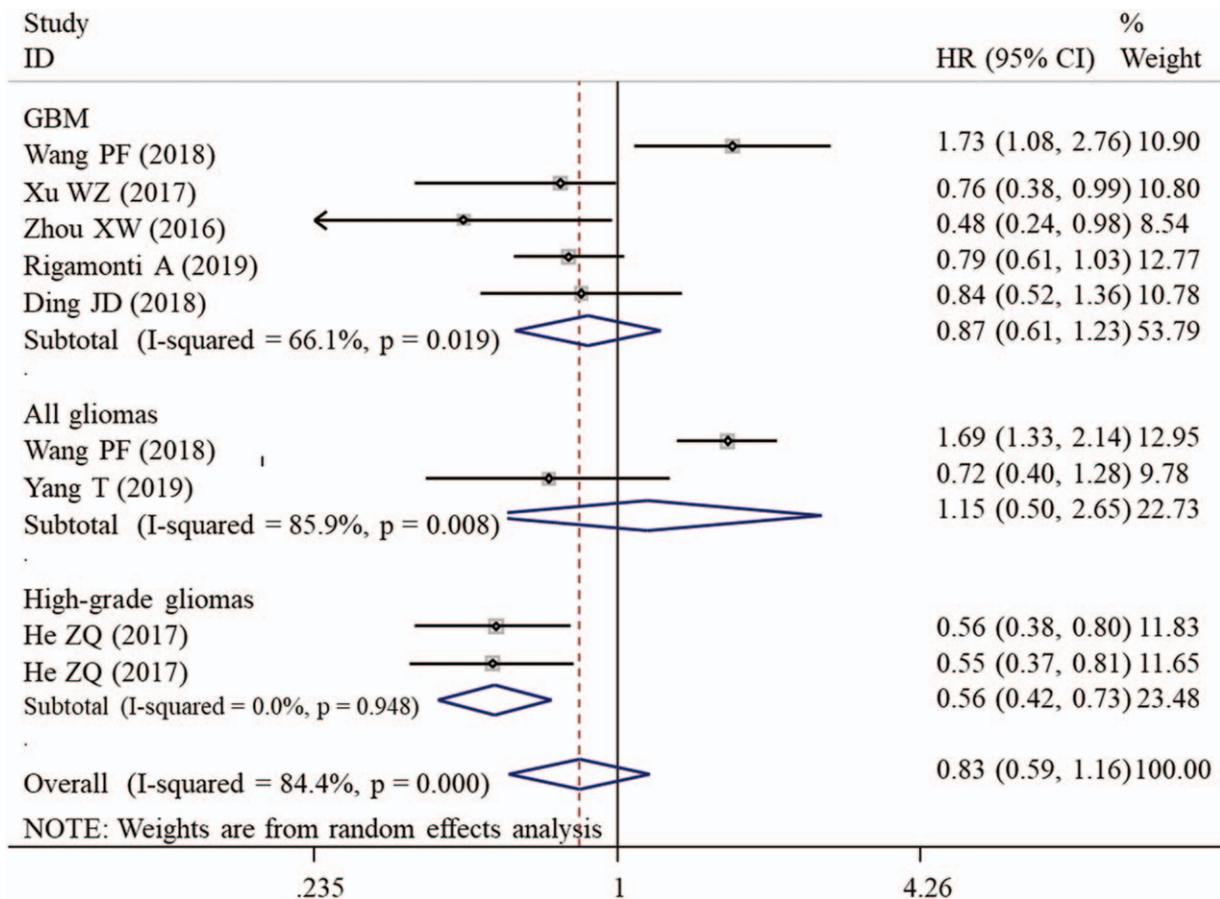
Figure 5. Forest plots to investigate the correlation between prognostic nutritional index and overall survival based on cancer type subgroup analyses. CI = confidence interval, GBM = glioblastoma multiforme, HR = hazard ratio.

albumin protein level and C-reactive protein concentration in cancer.[36,41]

In addition to albumin, the protective effects of PNI and AGR may also result from the secretion of more lymphocytes and production of less globulin. Lymphocytes and globulin were also reported to respectively exert anti-tumor or proto-oncogenic roles in previous studies on cancer. For example, Quattrocchi et al demonstrated that local infusion of autologous tumor infiltrating lymphocytes was effective for treatment of some patients with recurrent malignant gliomas, with the partial response of 50% after a long term follow-up.[42] Misao et al observed that treatment of an endometrial cancer cell line with oestradiol-17 beta (E2) significantly increased corticosteroid-binding globulin mRNA expression in a dose-dependent manner. E2 was implied to promote endometrial carcinoma progression via activating the IL-6 pathway.[43]

There were some limitations that should be acknowledged. First, the number of eligible studies remained relatively small, which may result in low statistical power for some of the subgroup analyses. Thus, the effect size may be overestimated or underestimated. Second, the HRs and 95%CIs were obtained from univariate analysis in some included studies in which the effect size may also be overestimated. Third, some HRs and 95% CI were estimated from Kaplan–Meier curve, which may be different from the actual data and may introduce potential errors. Fourth, all these studies were retrospectively performed, which may introduce unavoidable bias in patient selection and data collection. Fifth, the populations in a majority of the studies were Chinese and thus its applicability to other ethnicities remained discussed. Sixth, the cut-off value was not unified in different articles, which influenced its generalization in clinical practice. Seventh, significant heterogeneity was observed in the overall analysis which may affect the robustness of the pooled analysis. However, Egger test results showed there was no obvious evidence of publication bias and most of subgroup analyses with significant results were obtained from studies without heterogeneity. So our conclusion still may be believable. Accordingly, more studies with prospective design, larger sample size and cases from other ethnicities are needed to further confirm the prognostic values of albumin, AGR, and PNI for glioma in the future.

5. Conclusion

This meta-analysis indicated that preoperative serum albumin, AGR, and PNI may represent promising biomarkers to predict the prognosis in patients with glioma, especially for high-grade. Decreased serum albumin, AGR, and PNI were correlated with worse survival in patients with glioma.
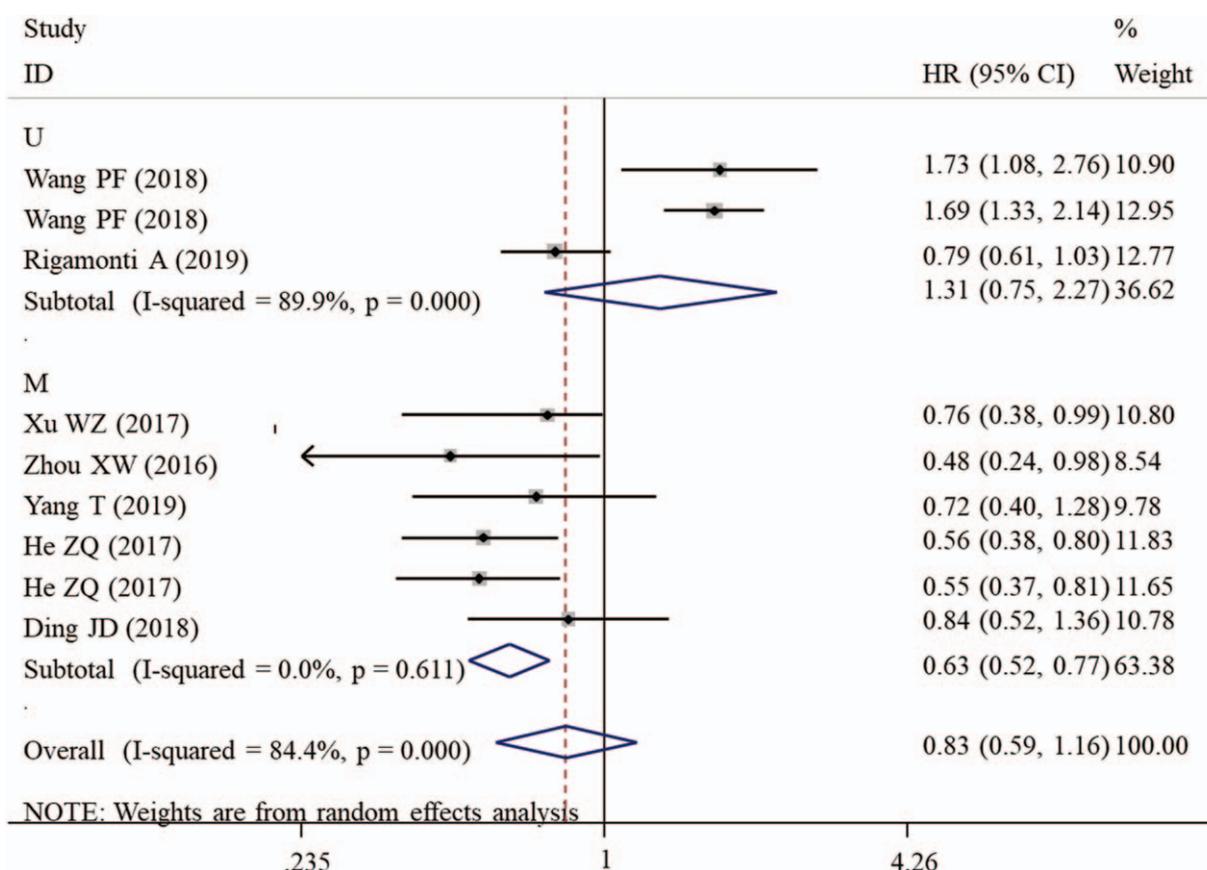
Figure 6. Forest plots to investigate the correlation between prognostic nutritional index and overall survival based on HR source subgroup analyses. CI = confidence interval, HR = hazard ratio, M = multivariate analysis, U = univariate analysis.

Author contributions

Conceptualization: Mingchang Liu, Liwen Wang.
Data curation: Mingchang Liu.
Formal analysis: Mingchang Liu, Liwen Wang.
Methodology: Mingchang Liu.
Writing – original draft: Mingchang Liu.
Writing – review & editing: Liwen Wang.

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