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Letter to Editor

Meta-analysis of the correlation between glioma prognosis and PD-1/PD-L1 expression

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To the editor,

Cerebral glioma is a common adult primary central nervous system tumor with the highest mortality rate.[1] Although in recent years, the continuous progress of medicine has been greatly improved. However, the prognosis of glioma remains unimproved, due to limited options for standard therapy.[2] With the advent of immunotherapy, glioma patients have seen the dawn of hope. Among them, the most widely studied in glioma immunotherapy is PD-1/PD-L1 immune checkpoint inhibitor therapy for glioma.[3] However, PD-1/PD-L1 inhibitors have not been found to have as good an effect in glioma treatment studies as other solid tumors.[4] Therefore, studies on PD-1/PD-L1 inhibitors in glioma are facing great challenges. However, recent studies on the prognosis of PD-1/PD-L1 in the treatment of glioma have mixed results, and many studies have yet to reach a consistent conclusion. Therefore, this study aimed to search for studies related to glioma prognosis and PD-1/PD-L1 expression for meta-analysis to evaluate the relationship between PD-1/PD-L1 expression and glioma.

Databases such as PubMed, The Cochrane Library, Web of Science, and Embase were searched. The initial search yielded 2238

Table 1
Basic information of the 24 included studies.

Author (year)	country	Sample size	WHO grading	PD-L1(+/−)/NO	PD-1(+/−)/NO	Comparison with normal brain tissue	Outcome indicators	HR(95%CI)	NOS
Ohno (2022)	Japan	71	I-IV	21/71	NO	no	①⑥	NR	6
Knudsen (2021)	Denmark	163	I-IV	NR	NO	no	④	1.03(0.70−1.60)	5
Sun (2020)	China	94	I-IV	69/25	NO	yes	①③⑤	NR	7
Jia (2019)	China	43	I-IV	30/13	NO	no	①③	NR	6
Partt (2019)	USA	183	I-IV	43/140	NO	no	①④⑥	1.52(1.22−1.88)	7
Jha (2019)	India	126	II-IV	40/86	NO	no	①④⑥	1.29(0.58−4.52)	5
Yang (2019)	China	86	I-IV	47/39	NO	yes	①③⑤	NR	7
Hwang (2018)	Korea	41	II-IV	8/33	11/30	no	①②	NO	7
Song (2018)	China	64	I-IV	28/36	NO	no	①③	NO	7
Li (2018)	China	80	I-IV	34/46	NO	yes	①③④⑤	2.61(1.27−5.35)	5
Xue (2017)	China	64	I-IV	50/14	NO	no	①③	NR	8
Hodges (2017)	USA	295	I-IV	24/271	59/93	no	①②⑥	NR	6
Han (2017)	Korea	54	IV	17/37	27/27	no	①②④	3.06(1.16−8.06)	5
Berghoff (2017)	Australia	174	II-IV	NR	20/154	no	①②⑥	NR	7
Lee (2017)	Korea	115	IV	37/78	NO	no	①④⑥	1.79(1.10−2.91)	8
Majzner (2017)	USA	14	IV	5/9	NO	no	①	1.13(0.78−1.64)	6
Zeng (2016)	China	229	I-IV	117/112	NO	no	①③④	1.76(1.09−2.84)	8
Nduom (2016)	USA	94	IV	36/58	NO	no	①④	1.99 (1.05−2.28)	7
Garber (2016)	USA	345	I-IV	21/324	74/161	no	①②③⑥	NR	6
Berghoff (2015)	Australia	117	IV	44/73	34/83	no	①②④	1.22 (0.83−1.80)	7
Liu (2013)	Denmark	17	III-IV	13/4	NO	no	①④	4.67(1.42 −15.43)	7
Avril (2010)	France	20	IV	9/11	NO	no	①	NR	5
Yao (2009)	China	48	I-IV	36/11	NO	no	①	NR	6
Wilmotte (2005)	Switzerland	54	II-IV	27/27	NO	yes	①	NR	6

Note: NR: not mentioned; NO: none; NOS: Newcastle−Ottawa Scale; ①: PD-L1 positive rate of glioma tissue; ②: PD-1 positive rate of glioma tissue; ③: PD-L1 positive rate of glioma tissue of different WHO grades; ④: OS of patients with PD-L1 positive or negative/high expression and low expression; ⑤: PD-L1 positive rate of glioma tissue and normal brain tissue; ③: PD-L1 positive rate of IDH1 mutation and IDH1 wild-type glioma tissue.

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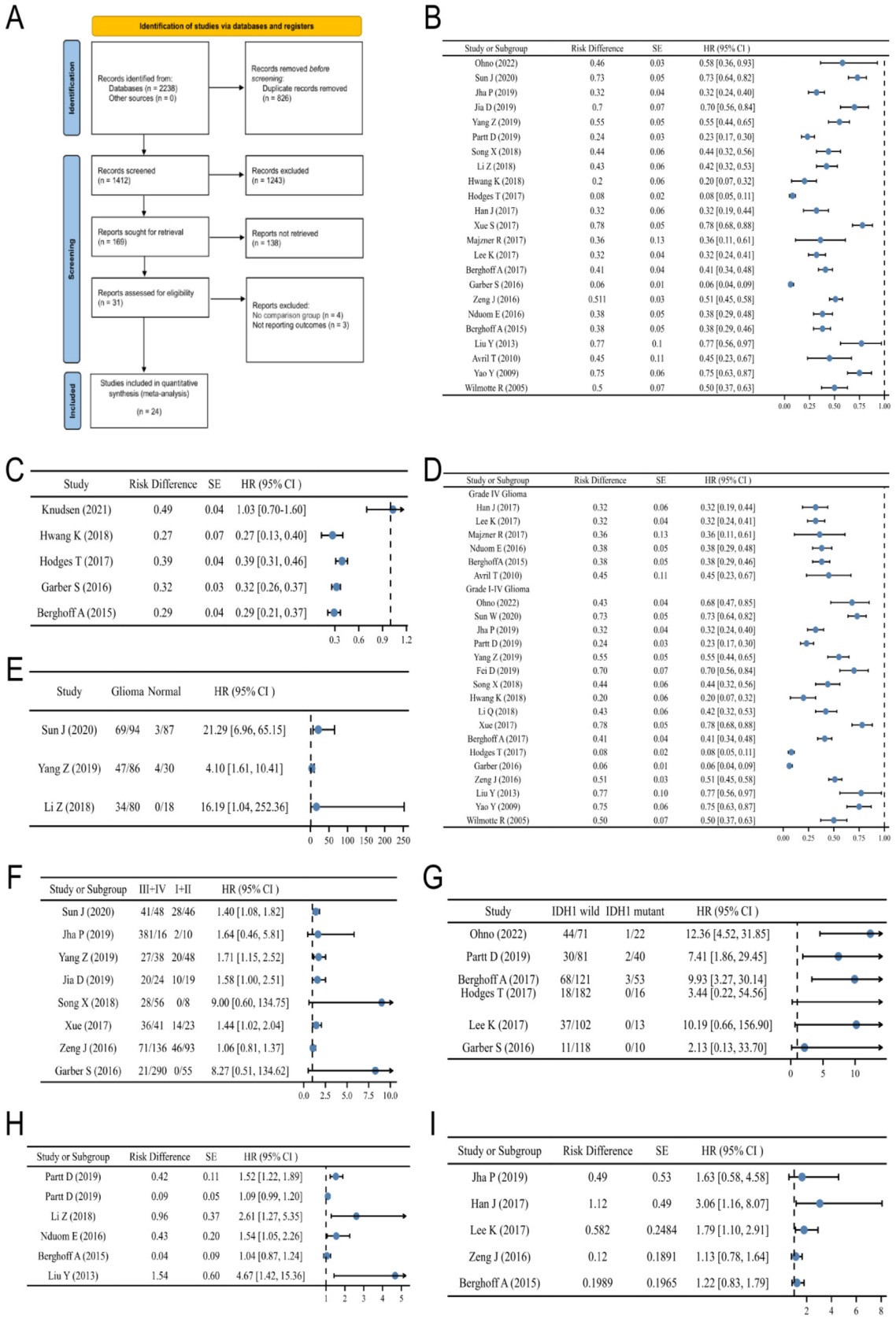

Fig. 1. Forest plot of correlation between prognosis of glioma and PD-1/PD-L1 expression. (A) Flowchart; (B) The expression of PD-L1; (C) The expression of PD-1; (D) Subgroup analysis of PD-L1 expression in different tumor grades; (E) PD-L1 expression in glioma compared to normal control brain tissue; (F) PD-L1 expression in grade III-IV versus grade I-II glioma tissues; (G) Differential expression between IDH1 mutant and wild type; (H) OS difference between high and low PDL1 expression groups; (I) PD-L1 positive versus negative.

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relevant articles, and 24 relevant studies (2591 patients) were finally included (Table 1). The literature screening process is shown in Fig. 1A. Twenty-three included studies reported PD-L1 expression in glioma. The analysis showed that the PD-L1 expression rate in glioma tissues was higher than that in normal tissues (Fig. 1B), and the difference was statistically significant ($P < 0.05$). The PD-1 expression rate in glioma tissues was also higher than normal (Fig. 1C). Subgroup analysis of tumor grade showed a disappearance of heterogeneity between studies with grade IV glioma samples (Fig. 1D), indicating that the source of heterogeneity between studies may be due to different grades of tumor specimens between studies. Compared with normal brain tissue, glioma tissues had higher PD-L1 expression (Fig. 1E), and the difference was statistically significant ($P < 0.05$). Compared with WHO grade I-II glioma tissues, grade III-IV glioma had a higher PD-L1 expression rate (Fig. 1F). IDH1 wild-type glioma had higher PD-L1 expression than IDH1 mutant glioma (Fig. 1G). The overall survival rate of patients with high PD-L1 expression was lower than low PD-L1 expression (Fig. 1H). The overall survival rate of patients with positive PD-L1 expression was lower than negative PD-L1 expression (Fig. 1I).

PD-1/PD-L1 expression has also been increasingly studied in glioma, and many studies have confirmed that PD-1/PD-L1 have higher expression in gliomas.[5] Some studies suggest that PD-L1/PD-1 expression levels are negatively correlated with the prognosis of patients, but the results of Berghoff et al show that PD-L1 expression is not correlated with the prognosis of glioma patients. In our study, glioma tissues showed higher PD-L1 expression compared with normal brain tissues; High-grade glioma had higher PD-L1 expression compared with low-grade glioma; IDH1 wild-type glioma had higher PD-L1 expression rate than IDH1 mutant; Patients with positive PD-L1 expression had lower overall survival rate than negative PD-L1 expression. In summary, it showed that PD-L1 expression may be an important factor in the prognosis of glioma patients.

Author contributions

Chang-cheng Ren and Bo Xu designed the study. Min-shu Wang, Feng He, Jun-hui Chen, and Liang Liao searched articles, extracted the data. Wu Liang wrote and reviewed the manuscript. All the authors approved the final manuscript.

Data availability statement

All data relevant to this study are included in this article.

Ethics approval

Not applicable.

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Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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