XGBoost algorithm and logistic regression to predict the postoperative 5-year outcome in patients with glioma

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These authors contributed equally to this work.

Background: Glioma is the most common primary intracranial tumor with poor prognosis. The prediction of glioma prognosis has not been well investigated. XGBoost algorithm has been widely used in and data analysis. The predictive value of XGBoost algorithm in glioma remains unclear. This current study used the XGBoost algorithm to construct a predictive model for postoperative outcomes of glioma patients.

Methods: Patients with glioma who underwent surgery from January 2006 to April 2017 were retrospectively included in this study. Clinical and follow-up data were collected. The XGBoost model and multivariate logistic regression analysis model were used to screen the factors related to postoperative outcomes, and the results of the two models were compared. The area under the receiver operating characteristic (ROC) curve (AUC), sensitivity, specificity, and Youden index were calculated to evaluate the predictive value of the XGBoost model.

Results: A total of 638 patients were included. In total, 336 (52.7%) cases died within 5 years after the operation. Multivariate logistic regression analysis showed that age, gender, World Health Organization (WHO) grade, extent of tumor resection, Karnofsky performance score (KPS), tumor diameter, and whether postoperative radiotherapy and chemotherapy were administered, were the most important risk factors for death within 5 years after surgery in glioma patients. The XGBoost model showed that the top 5 factors related to death of glioma patients within 5 years after surgery were WHO grade (30 points), extent of tumor resection (19 points), postoperative radiotherapy and chemotherapy (16 points), KPS (14 points), and age (11 points). The AUC of the XGBoost model for predicting the death of glioma patients within 5 years after surgery was 0.803 [95% confidence interval (CI): 0.718–0.832], and the sensitivity and specificity were 0.894 and 0.581, respectively. The Youden index was 0.475. The AUC of the multivariate logistic regression model was 0.738 (95% CI: 0.704–0.781), the sensitivity and specificity were 0.785 and 0.632, respectively, and the Youden index was 0.417.

Conclusions: Compared with multivariate logistic regression model, XGBoost model has better performance in predicting the risk of death within 5 years after surgery in patients with glioma.

Keywords: Glioma; XGBoost model; multivariate logistic analysis; death; risk factors
Introduction

Gliomas originate from brain glial cells and ranks the first in primary intracranial tumor (1). The World Health Organization (WHO) classifies gliomas into low grade (grades I and II) and high grade (grades III and IV) tumors. In clinical practice, patients with grade I glioma are often misdiagnosed. More than 80% of brain malignancies are gliomas (2). Glioblastoma (GBM), which is classified as WHO grade IV, accounts for about 50% of primary malignant central nervous system gliomas (3). The annual incidence of gliomas and malignant gliomas in China is 3.0–6.4 per 100,000 and 5.8 per 100,000, respectively, with 7,000–10,000 new cases diagnosed each year (4,5). The incidence of glioma has only increased slightly in the past 20 years, especially among the elderly, possibly due to advances in imaging diagnostic techniques, improved quality of life, and increased knowledge and awareness of diseases and demand for medical services. Malignant gliomas are 40% more common in men than women, and twice as common in Caucasians and people of African descent. The median age of patients when first diagnosed with GBM and anaplastic glioma is 64 years and 45 years, respectively (6). The 5-year mortality rate of glioma patients is very high and only rank after pancreatic cancer and lung cancer, and it is one of the malignant tumors with the worst prognosis. While the pathogenesis remains unclear, high-dose ionizing radiation exposure is believed to be a major risk factor. Previous studies have mostly used multivariate logistic regression models or Cox proportional hazard models to analyze factors related to end-point events (7,8). These models have high requirements on the sample size and related parameters of the study, which greatly limits the development of clinical research. The XGBoost algorithm is based on gradient boosting decision-making, has low data requirements, fast training speed, and accurate training results. It has been widely used in artificial intelligence and the data analysis fields, and has been increasingly used in clinical research (9,10). This study retrospectively analyzed patients who received surgical treatment for glioma for the first time. The XGBoost algorithm and logistic regression model were used to identify the factors associated with death within 5 years after glioma surgery. We present the following article in accordance with the STARD reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3384/rc).

Methods

Study population

This is a retrospective study. Consecutive patients who received surgical treatment for glioma for the first time in our hospital from January 2006 to April 2017 were retrospectively enrolled. The following inclusion criteria were applied: (I) adult patients; (II) with definite diagnosis of primary glioma of grade II or above; (III) no previous surgery for glioma. Exclusion criteria: (I) presentation brain tumors of other types or cancer in other organs and tissues; (II) co-existence of heart dysfunction, renal dysfunction, liver dysfunction, etc.; and (III) co-existence of rheumatic diseases. According to these criteria, a total of 638 patients were included in the statistical analysis. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Xijing Hospital (Approval No. KY20222151) and individual consent for this retrospective analysis was waived.

Treatment methods

All patients received surgical resection, and the operations were formulated and completed by the same glioma surgical team. A total of 291 (45.6%) patients underwent extended tumor resection or total resection, and 347 (54.4%) patients had partial resection, including 289 (45.3%) patients who underwent subtotal resection and 58 (9.1%) patients who had local excision. There were 426 patients (66.8%) who received radiotherapy after surgery, 434 patients (68.0%) who received chemotherapy, 337 patients (52.8%) who received both radiotherapy and chemotherapy, and 115 patients (18.0%) who did not receive radiotherapy nor chemotherapy.

Observation indicators

The baseline data was collated for each patient prior to their first operation. The demographic data included age, gender, family income, and medical history included underlying diseases, smoking and drinking history, blood pressure, heart rate, weight, and height. Laboratory indicators included blood cell count, level of hemoglobin, indicators of liver function, and renal function, and levels of electrolyte. Information of imaging examination included that obtained at the first diagnosis of glioma and the latest preoperative.
imaging examination results, including the location and diameter of glioma. Surgical information and Karnofsky performance score (KPS) were also collated.

Follow-up

All the last follow-ups were conducted during this study, and the time from the baseline operation to the latest follow-up was not less than 5 years. Follow-up data included survival (including tumor-related death and all-cause death) within 5 years after baseline surgery, rehospitalization for glioma (due to recurrence or progression), or any other treatment.

Statistical analysis

The SPSS 22.0 statistical software was used for statistical processing. Quantitative data were tested for normal homogeneity. Data that conformed to the normal distribution are expressed as the mean ± standard deviation (SD), and the comparison between groups was conducted using the Student’s t-test. Data that did not conform to normal distribution are expressed as the median (percentile). The rank sum test was used for comparison between groups. Qualitative data are expressed as numerical values and percentages, and comparison between groups was performed using the χ² test or Fisher’s exact test. The XGBoost algorithm and multivariate logistic regression model were used to analyze the factors associated with death within 5 years after surgery. The receiver operating characteristic (ROC) was used to analyze the predictive value of different models. The area under the ROC curve (AUC) and the Youden index for the two models was compared. When performing XGBoost analysis, qualitative data was converted into numerical data, that is, “yes” and “no” are converted into “1” and “0”. A two-sided P value <0.05 was considered statistically significant.

Results

Follow-up results

At the last follow-up, there were 336 cases of all-cause deaths within 5 years after glioma surgery, with a mortality rate of 52.7%, and 295 cases (46.2%) of tumor-related deaths. Among all patients, 189 (29.6%) underwent reoperation due to tumor recurrence or progression, and 88 (13.8%) received non-surgical treatment. According to the postoperative 5-year survival, the patients were divided into a deceased group (n=336) and a survival group (n=302). The comparison of baseline data between the two groups is shown in Tables 1,2. There were statistically significant differences in multiple indicators between the two groups at baseline, including age, sex, body mass index (BMI), proportion of smoker and drinker, tumor diameter, WHO classification, postoperative radiotherapy and chemotherapy ratios, and surgical method.

Multivariate logistic regression analysis related to death within 5 years after surgery

Univariate and multivariate analysis showed that age, gender, WHO grade, extent of tumor resection, KPS, tumor diameter, and postoperative radiotherapy and chemotherapy were closely related to death during the 5-year follow-up period (Table 3).

Risk prediction model of death within 5 years after operation based on the XGBoost algorithm

The XGBoost model demonstrated that multiple factors were related to the death of glioma patients within 5 years after operation. The top 5 factors were WHO classification (30 points), extent of tumor resection (19 points), postoperative radiotherapy and chemotherapy (16 points), KPS (14 points), and age (11 points) (Figure 1).

A comparison of the predictive ability between the XGBoost algorithm and the logistic regression model

The AUC of the multivariate logistic regression model was 0.738 [95% confidence interval (CI): 0.704–0.781], with sensitivity and specificity of 0.785 and 0.632, respectively, and a Youden index of 0.417. The AUC of the XGBoost model for predicting death within 5 years after surgery in glioma patients was 0.803 (95% CI: 0.718–0.832), with sensitivity and specificity of 0.894 and 0.581, respectively, and a Youden index of 0.475. The AUC of the XGBoost model increased by 0.065 compared with that of the logistic model (Figure 2), and the Youden index increased by 0.058.

Discussion

This study retrospectively analyzed the clinical data and follow-up results of glioma patients. Logistic multivariate regression analysis revealed that the factors associated with the death of glioma patients within 5 years after...
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Deceased (n=336)</th>
<th>Survived (n=302)</th>
<th>t/χ² value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>44.6±10.3</td>
<td>38.5±9.9</td>
<td>7.607</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>141 (64.4)</td>
<td>215 (51.3)</td>
<td>9.963</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>23.6±2.9</td>
<td>22.7±2.6</td>
<td>4.109</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>112 (33.3)</td>
<td>77 (25.5)</td>
<td>4.685</td>
<td>0.030</td>
</tr>
<tr>
<td>Alcohol, n (%)</td>
<td>124 (36.9)</td>
<td>76 (25.2)</td>
<td>10.185</td>
<td>0.001</td>
</tr>
<tr>
<td>WBC (x10⁹/L), mean ± SD</td>
<td>6.5±2.2</td>
<td>6.3±2.1</td>
<td>1.171</td>
<td>0.242</td>
</tr>
<tr>
<td>NEU (x10⁹/L), mean ± SD</td>
<td>3.8±1.7</td>
<td>3.7±1.6</td>
<td>0.763</td>
<td>0.446</td>
</tr>
<tr>
<td>LYM (x10⁹/L), mean ± SD</td>
<td>2.0±0.7</td>
<td>2.1±0.6</td>
<td>1.927</td>
<td>0.055</td>
</tr>
<tr>
<td>RBC (x10¹²/L), mean ± SD</td>
<td>4.7±0.9</td>
<td>4.8±0.8</td>
<td>1.477</td>
<td>0.143</td>
</tr>
<tr>
<td>Hb (g/L), mean ± SD</td>
<td>143.4±13.9</td>
<td>144.1±13.2</td>
<td>0.650</td>
<td>0.516</td>
</tr>
<tr>
<td>PLT (x10³/L), mean ± SD</td>
<td>176.7±31.5</td>
<td>173.9±30.2</td>
<td>1.143</td>
<td>0.253</td>
</tr>
<tr>
<td>Cr (μmol/L), mean ± SD</td>
<td>68.7±18.2</td>
<td>70.1±19.8</td>
<td>0.931</td>
<td>0.352</td>
</tr>
<tr>
<td>UA (μmol/L), mean ± SD</td>
<td>242.6±70.3</td>
<td>251.5±61.6</td>
<td>1.692</td>
<td>0.091</td>
</tr>
<tr>
<td>ALT (U/L), mean ± SD</td>
<td>25.3±6.8</td>
<td>26.1±6.3</td>
<td>1.536</td>
<td>0.125</td>
</tr>
<tr>
<td>AST (U/L), mean ± SD</td>
<td>21.8±4.7</td>
<td>22.4±4.4</td>
<td>1.659</td>
<td>0.098</td>
</tr>
<tr>
<td>DBIL (μmol/L), mean ± SD</td>
<td>5.7±1.9</td>
<td>5.8±1.7</td>
<td>0.697</td>
<td>0.486</td>
</tr>
<tr>
<td>BUN (mmol/L), mean ± SD</td>
<td>7.2±2.3</td>
<td>7.0±2.0</td>
<td>1.166</td>
<td>0.244</td>
</tr>
<tr>
<td>K (mmol/L), mean ± SD</td>
<td>4.54±0.36</td>
<td>4.55±0.33</td>
<td>0.364</td>
<td>0.716</td>
</tr>
<tr>
<td>Na (mmol/L), mean ± SD</td>
<td>143.5±11.2</td>
<td>144.0±10.7</td>
<td>0.575</td>
<td>0.566</td>
</tr>
<tr>
<td>Cl (mmol/L), mean ± SD</td>
<td>106.8±12.3</td>
<td>107.5±12.1</td>
<td>0.723</td>
<td>0.470</td>
</tr>
<tr>
<td>Ca (mmol/L), mean ± SD</td>
<td>2.2±0.7</td>
<td>2.1±0.6</td>
<td>1.927</td>
<td>0.055</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>23 (6.8)</td>
<td>20 (6.6)</td>
<td>0.013</td>
<td>0.911</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>31 (9.2)</td>
<td>27 (8.9)</td>
<td>0.016</td>
<td>0.900</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>11 (3.3)</td>
<td>9 (3.0)</td>
<td>0.045</td>
<td>0.832</td>
</tr>
<tr>
<td>CAD, n (%)</td>
<td>9 (2.7)</td>
<td>7 (2.3)</td>
<td>0.085</td>
<td>0.771</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>5 (1.7)</td>
<td>4 (1.3)</td>
<td>0.026</td>
<td>0.872</td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>16 (4.8)</td>
<td>11 (3.6)</td>
<td>0.526</td>
<td>0.468</td>
</tr>
<tr>
<td>Statins, n (%)</td>
<td>15 (4.5)</td>
<td>12 (4.0)</td>
<td>0.095</td>
<td>0.759</td>
</tr>
<tr>
<td>ADDs, n (%)</td>
<td>11 (3.3)</td>
<td>9 (3.0)</td>
<td>0.045</td>
<td>0.832</td>
</tr>
<tr>
<td>KPS, mean ± SD</td>
<td>64.8±2.6</td>
<td>68.3±2.3</td>
<td>17.924</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SD, standard deviation; BMI, body mass index; WBC, white blood cell; NEU, neutrophils; LYM, lymphocyte; RBC, red blood cell; Hb, hemoglobin; PLT, platelet; Cr, creatine; UA, uric acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; BUN, blood urea nitrogen; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ADD, anti-diabetic drug; KPS, Karnofsy performance score.
Table 2 A comparison of tumor characteristics and medical treatment between the deceased group and the survival group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Deceased (n=336)</th>
<th>Survived (n=302)</th>
<th>$\chi^2$ value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location, n (%)</td>
<td></td>
<td></td>
<td>21.352</td>
<td>0.0001</td>
</tr>
<tr>
<td>Upper lobe (n=484)</td>
<td>252 (75.0)</td>
<td>232 (76.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper brain midline (n=76)</td>
<td>55 (16.4)</td>
<td>21 (7.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebellum (n=63)</td>
<td>21 (6.3)</td>
<td>42 (13.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain stem (n=15)</td>
<td>8 (2.4)</td>
<td>7 (2.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm), mean ± SD</td>
<td>32.7±9.3</td>
<td>29.4±8.8</td>
<td>4.590</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHO class, n (%)</td>
<td></td>
<td></td>
<td>378.245</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>II</td>
<td>25 (7.4)</td>
<td>248 (82.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>86 (25.6)</td>
<td>36 (11.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>225 (67.0)</td>
<td>18 (6.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery, n (%)</td>
<td></td>
<td></td>
<td>171.477</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Partial resection</td>
<td>265 (78.9)</td>
<td>82 (27.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total/extensive resection</td>
<td>71 (21.1)</td>
<td>220 (72.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy, n (%)</td>
<td></td>
<td></td>
<td>8.532</td>
<td>0.004</td>
</tr>
<tr>
<td>Yes</td>
<td>207 (61.6)</td>
<td>219 (72.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>129 (38.4)</td>
<td>83 (27.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy, n (%)</td>
<td></td>
<td></td>
<td>9.962</td>
<td>0.002</td>
</tr>
<tr>
<td>Yes</td>
<td>210 (62.5)</td>
<td>224 (74.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>126 (37.5)</td>
<td>78 (25.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD, standard deviation; WHO, World Health Organization.

Table 3 Factors associated with tumor progression at the 5-year follow-up

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>1.09</td>
<td>1.04–1.15</td>
</tr>
<tr>
<td>Male</td>
<td>1.12</td>
<td>1.06–1.29</td>
</tr>
<tr>
<td>WHO class</td>
<td>1.37</td>
<td>1.23–1.96</td>
</tr>
<tr>
<td>Extent of resection</td>
<td>1.40</td>
<td>1.19–2.27</td>
</tr>
<tr>
<td>KPS</td>
<td>0.94</td>
<td>0.88–0.98</td>
</tr>
<tr>
<td>Diameter</td>
<td>1.66</td>
<td>1.31–3.42</td>
</tr>
<tr>
<td>Chemotherapy/radiotherapy</td>
<td>0.84</td>
<td>0.57–0.96</td>
</tr>
</tbody>
</table>

WHO, World Health Organization; KPS, Karnofsky performance score; OR, odds ratio; CI, confidence interval.

surgery included age, gender, WHO grade, extent of tumor resection, preoperative KPS, tumor diameter, and postoperative radiotherapy and chemotherapy. The XGBoost model analysis showed that the top factors related to the death of glioma patients within 5 years after surgery are WHO grade, extent of tumor resection, postoperative
radiotherapy and chemotherapy, preoperative KPS, and age. A comparison of the two models demonstrated that the area under ROC was larger with the XGBoost model compared to the logistic model, and the Youden index was also greater.

Brain gliomas usually occur between the ages of 20 and 40 years. Clinical presentations vary with the location and volume of glioma and are largely related to the compressive effects of the tumor. The most often seen clinical presentation is seizure, which can be found in about 60–80% of patients. Other often seen symptoms include headaches, cognitive dysfunction, abnormal behavior, motor dysfunction, and sensory dysfunction. In most patients, seizures can be treated effectively with antiepileptic drugs. Symptoms usually can be improved following the resection of tumor in most patients. In previous study conducted by Robe et al., the results showed that early wide resection improved outcomes in patients with glioma (11). If surgical treatment is delayed or the tumor tissue is unreseactable, the growth of tumor should be intensively monitored with imaging [especially magnetic resonance imaging (MRI)] within 6 months after the first time of glioma diagnosis.

The prognosis of gliomas with different WHO grades varies greatly. Gliomas of WHO grade I–II gliomas are usually high-differentiated with slow progression. These gliomas are usually clinically stable over a long period of time, their slow progression can only be detected by imaging examination at longer intervals (12). A significant proportion of WHO grades I–II gliomas eventually progress into advanced stage at some point in the disease process if not treated with timely and effective surgical treatment (13). Standard treatments include surgical resection and radiation therapy. Radiation therapy is often used in patients with symptomatic and/or progressive disease or in patients with poor prognosis (14). Although the early role of surgery and extent of resection have not been demonstrated in randomized studies, retrospective studies have suggested that wide resection improves outcomes (15). However, in clinical practice, the operation time and surgery strategy are often decided according to the characteristics of the patient’s condition, and some patients eventually will relapse and quickly progress after the surgery.

Some previous studies outlined the predictors of glioma prognosis (16-18), including patient’s history of diseases, such as the results of preoperative laboratory test results, the patient’s living habits, co-existing diseases, and other often-used information (including age and gender, etc.); preoperative information of imaging examination, including the location and volume of tumor, and its relationship with adjacent tissues; and results of pathological examination, such as pathological type. In recent years, a large number of research have investigated the correlation between glioma and some genetic biomarkers such as isocitrate dehydrogenase 1 (IDH1) and IDH2 genotypes, microRNAs, and protein biomarkers. These investigations have brought the clinicians with various new perspectives on gliomas, and evoked novel ideas for the development of effective and timely clinical diagnosis and treatments. However, some of these studies focused on all glioma patients without distinguishing between WHO grades, while others focused only on patients at advanced stages. In addition,
Cote found that there was no definite relationship.

The 1,734 expression, and positive. This study included 2,469. However, a meta-

At the same time,

Our present study examined glioma patients who

and the difference lies

However,

and the risk of deaths due to cancers

and statins may have a protective effect

Findings of our present study

In contrast, a study by

never used statins [hazard ratio (HR) =1.43; 95% CI: 1.10–

developing glioma when compared with patients who have

were treated with statins had a significantly higher risk of

Study (HPFS, n=50,223). They found that patients who

and the Men's Health Professionals Follow-

(NHS, n=114,419), the Nurses' Health Study II (NHSII,

outcome

statins and the occurrence, progression and long-term

In many previous clinical studies, statins have been shown to

patients with glioma. According to some previous studies,

the effectiveness of some drug therapy on the prognosis of

patients with glioma. According to some previous studies,

statins have received extensive attention in clinical practice.

patients with glioma. According to some previous studies,

the major underlying reason is that although these

parameters have high predictive value, it is temporarily
difficult to popularize in clinical practice. In clinical

practice, simple, convenient, and cheap biomarkers are

essential to provide clinical value of implication.

In recent years, there have been many studies examining

the effectiveness of some drug therapy on the prognosis of

patients with glioma. According to some previous studies,

statins have received extensive attention in clinical practice.

In many previous clinical studies, statins have been shown to

have favorable effect on the reduction of the risk of cancers

(20-22) and the risk of deaths due to cancers (23). However,

there have also been reports of increased tumor risk (24,25)

and others showing no definite relationship between

statins and the occurrence, progression and long-term

outcome (26). Cote et al. conducted a meta-analysis based

on three large studies including the Nurses’ Health Study

(NHS, n=114,419), the Nurses’ Health Study II (NHSII,

n=115,813), and the Men's Health Professionals Follow-

up Study (HPFS, n=50,223). They found that patients who

were treated with statins had a significantly higher risk of
developing glioma when compared with patients who have

never used statins [hazard ratio (HR) =1.43; 95% CI: 1.10–

1.86], and the risk was higher in patients with longer time of

statin treatment (HR =1.72; 95% CI: 1.21–2.45, for >8 years

of use; P-trend =0.003). Further subgroup analysis revealed

that water-soluble statins (e.g., rosuvastatin and pravastatin)

were closely associated with the risk of gliomas, while fat-
soluble statins (such as simvastatin and atorvastatin) did

not show statistical significance (27). However, a meta-

analysis combining the three earlier studies found that

taking statins was associated with a lower risk of developing

gliomas during follow-up [odds ratio (OR) =0.75; 95%

CI: 0.62–0.90; P=0.0016] (28). In contrast, a study by

Seliger et al. found that there was no definite relationship

between the statins treatment and the risk of occurrence

or progression of glioma (29). This study included 2,469

glioma patients and 24,690 control patients, which is a large

sample size and has good representation (29). The 1,734

(70.2%) glioma patients in this study were over the age

of 50, and nearly half of the patients were elderly. Some

previous studies did not distinguish the grades of gliomas,

while the developmental biology and prognosis of gliomas

with different grades vary widely (27-29). At the same time,

surgery also has a certain impact on the biological behavior

of tumor cells (30) and statins may have a protective effect

on this process. In addition, statins may have a certain

impact on the local tumor microenvironment. Therefore,

the results of studies on the risk of developing gliomas with

statins remain inconclusive and this may be related to the

significant differences in the included patients. Moreover,

the vast majority of patients enrolled in the above-

mentioned studies were non-Asian patients, and there may

be differences between patients with different human race

(27-29). Our present study examined glioma patients who

received surgical treatment. These patients are relatively

inoperable and may have a positive response to drugs.

However, since most of the patients in this study are young

and middle-aged, there were few patients taking statins.

Therefore, the benefit of statins could not be analyzed. The

effect of tumor size and the extent of tumor resection on

death within 5 years after surgery in glioma patients was

consistent with another study (19), and the difference lies

in the specific numerical range. In general, the larger the

volume of tumor, the poorer the postoperative prognosis,

and the more extension the tumor resection, the better the

postoperative outcome.

Our present study had some limitations. First, this was

a single-center, retrospective study conducted over a large

time span, and there may be different treatment tendencies

for the patients over that period of time, and the surgical
experience of the surgical team may also change over time, resulting in certain differences or bias between cases. Second, the findings of this study could not be validated in additional case cohorts. In particular, risk prediction models that produce results in one case cohort should be validated with a different cohort to demonstrate model fitness. Third, this study used common clinical indicators, and failed to include gene parameters and molecular parameters which may be more related to the prognosis of glioma patients. The results of this study should be further validated using a prospective cohort, and genetic and molecular testing of patients should be performed to increase the accuracy of the risk prediction models.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3384/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3384/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3384/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Xijing Hospital (Approval No. KY20222151) and individual consent for this retrospective analysis was waived.

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