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成人脑室胶质瘤患者预后列线图模型的构建与评价

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【摘要】 目的 探究成人脑室胶质瘤（adult ventricle glioma, AVG）患者的预后因素，进一步构建和评价预后列线图模型，为该类患者的临床管理提供一定的参考。 **方法** 本研究纳入SEER数据库（1973–2016）中经组织学明确诊断的AVG患者，用随机数字表法按2∶1比例分为训练集和验证集进行分析。使用Kaplan-Meier进行生存分析，Cox回归分析确定总生存（OS）和癌症特异性生存（CSS）的独立预后因素，结合患者基本特征，分别构建训练集中针对OS率和CSS率的生存相关列线图预测模型，再依次通过训练集和验证集进行模型的内部交叉验证和外部验证。C指数（C-index）用来评估列线图模型的真实性和可靠性，校准图用来评估训练集和验证集中预测值和观察值之间的一致性。 **结果** 本研究共纳入369例AVG患者，其中男性218例，女性151例，所有患者中位年龄为53岁。根据WHO分级，66例（17.9%）为Ⅱ级胶质瘤，73例（19.8%）为Ⅲ级胶质瘤，230例（62.3%）为Ⅳ级胶质瘤。根据手术切除程度，59 例（16.0%）为肿瘤全切，145例（39.3%）为次全切或部分切除。所有患者中，167例（45.3%）术后接受了放疗，143例（38.8%）术后接受了化疗。患者随机分为训练集（n=246）和验证集（n=123），训练集和验证集之间的基本临床特征的差异均无统计学意义（P>0.05）。训练集中Cox回归分析显示，年龄≥65岁、肿瘤分级III级和Ⅳ级、未接受放疗均是OS和CSS的独立预后因素。在训练集中，使用5个变量（年龄、性别、WHO 分级、手术和放疗）分别构建用于预测术后6个月、1年和2年OS率和CSS率的列线图模型。训练集内部交叉验证结果显示，OS率和CSS率的C指数分别为0.758和0.765；验证集外部验证结果显示，OS率和CSS率的C指数分别为0.733和0.719。训练集中6个月、1年和2年OS率的校准图均表现出良好的一致性，而在验证集中一致性相对较低。6个月、1年和2年CSS率的校准图与OS率校准图具有相似的结果。 **结论** OS率和CSS率的列线图预测模型具有中等可靠的预测效能，可为临床医生简易评估AVG患者的生存概率提供参考。

【关键词】 脑室胶质瘤　列线图　预后模型　SEER　总生存期　癌症特异性生存期

Development and Evaluation of Prognostic Nomogram Model for Adult Ventricle Glioma Patients

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【Abstract】 Objective To explore the prognostic factors of adult ventricle glioma (AVG) and to construct and evaluate a survival-related prognostic nomogram model, which could provide further reference for the clinical management of AVG patients. **Methods** The patients covered in the study were selected from the Surveillance Epidemiology and End Results (SEER) database (1973–2016). They all had definite histological diagnosis of AVG. They were assigned randomly to the training cohort and the validation cohort by random number table at a 2/1 ratio. Survival analysis was performed by Kaplan-Meier analysis. Cox regression analysis was employed to determine the independent prognostic factors for overall survival (OS) and cancer-specific survival (CSS). Then, integrating the basic characteristics of patients, the survival-related nomogram predictive model for OS and CSS in the training cohort was constructed, respectively. After that, internal cross validation and external validation of the model were carried out with the training cohort and the validation cohort in succession. The authenticity and reliability of the nomogram model were evaluated by calculating the concordance index (C-index). Calibration plots were constructed to assess the agreement between the predicted values and the observed values in the training cohort and the validation cohort. **Results** A total of 369 AVG patients, including 218 males and 151 females, were included. The median age of the patients was 53. According to the WHO classification of gliomas, 66 (17.9%) patients had grade Ⅱ gliomas, 73 (19.8%) had grade Ⅲ gliomas, and 230 (62.3%) had grade Ⅳ gliomas. Regarding the extent of resection (EOR), 59 (16.0%) had gross total resection (GTR) and 145 (39.3%) had subtotal resection (STR) or partial resection (PR). Of all the patients, 167 (45.3%) received postoperative radiotherapy and 143 (38.8%) received postoperative chemotherapy. Patients were randomized into the training cohort (n=246) and the validation cohort (n=123), and there was no significant difference (P>0.05) in the basic clinical characteristics between the training cohort and the validation cohort. In the training cohort, Cox regression analysis revealed that the independent prognostic factors for OS and CSS included age≥65, grades Ⅲ and Ⅳ according to the

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WHO classification of gliomas, and not receiving radiotherapy. Furthermore, 5 variables, including age, gender, WHO grades, surgery, and radiotherapy, were used to construct the nomogram model for predicting 6-month, 1-year, and 2-year OS and CSS. The results of internal cross validation in the training cohort showed that the C-indexes of OS and CSS were 0.758 and 0.765, respectively. The external validation results of the validation cohort showed that the C-indexes of OS and CSS were 0.733 and 0.719, respectively. Calibration plots for 6-month, 1-year, and 2-year OS in the training cohort showed relatively good agreement, while in the validation cohort the agreement was relatively low. The 6-month, 1-year, and 2-year CSS calibration plots had results similar to the calibration plots of OS. **Conclusion** This nomogram predictive model of OS and CSS showed moderately reliable predictive performance, providing helpful reference information for clinicians to make quick and simple assessment of the survival probability of AVG patients.

【Key words】 Ventricleglioma Nomogram Prognostic model SEER Overall survival Cancer-specific survival.

弥漫性胶质瘤(diffuse glioma)是成人最常见的恶性脑肿瘤[1]。在2016年世界卫生组织(World Health Organization, WHO)中枢神经系统(central nervous system, CNS)肿瘤分类中,弥漫性胶质瘤包括WHO Ⅱ级和Ⅲ级的星形细胞瘤和少突胶质细胞瘤,以及Ⅳ级的胶质母细胞瘤(glioblastoma, GBM)[2]。弥漫性胶质瘤可发生在CNS的任何部位,其中以大脑半球(尤其是额颞叶)最为常见,而发生于脑室系统内的肿瘤相对少见。目前,关于成人脑室胶质瘤(adult ventricle glioma, AVG)患者临床特征和预后因素等相关的研究报道较少[3-6]。此外,目前尚无此类胶质瘤患者预后相关预测模型的研究报道。为了进一步了解AVG患者的临床和预后特征,以及预测生存相关概率,本研究从SEER(Surveillance Epidemiology and End Results)数据库中提取AVG患者的临床和预后特征等数据,分析与总生存(overall survival, OS)和癌症特异性生存(cancer-specific survival, CSS)相关的独立预后因素,并进一步构建生存预测模型,为该类患者的临床诊疗提供参考。

1　对象与方法

1.1　研究对象

使用SEER*Stat 8.3.6软件从SEER数据库(1973–2016)中检索并提取AVG患者的临床和生存特征等数据。采用国际肿瘤疾病分类第三版(the third edition of the International Classification of Diseases for Oncology, ICD-O-3)定义的部位代码和组织学代码进行数据筛选。本研究纳入经组织学诊断确诊的AVG患者,组织学类型包括少突胶质细胞瘤、弥漫性星形细胞瘤(diffuse astrocytoma, DA)、间变性少突胶质细胞瘤 (anaplastic oligodendroglioma, AO)、间变性星形细胞瘤(anaplastic astrocytoma, AA)和GBM。如果患者缺失主要数据(包括年龄、性别、手术、生存时间和状态),则在数据筛选中排除。本研究共纳入AVG患者369例,通过随机数字表法按2∶1的比例分为两个数据集,其中训练集246例,验证集123例。病例数据筛选流程图如图1所示。本研究获四川大学华西医院生物伦理审查委员会批准(批准号2022审973号)。

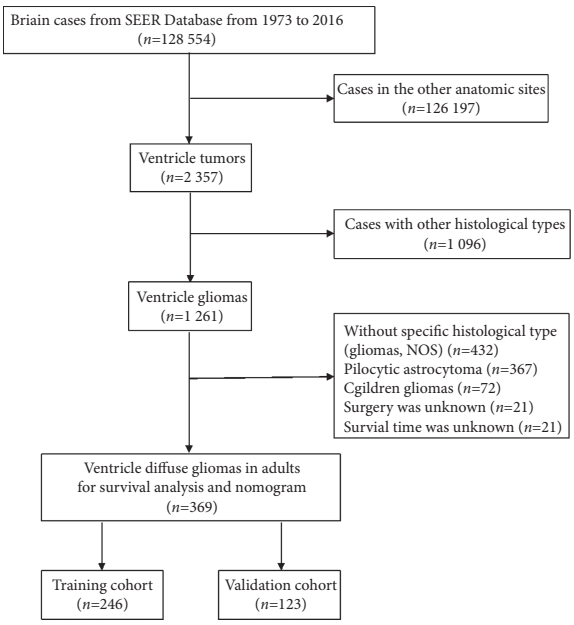

图 1 SEER数据库AVG患者筛选流程图

Fig 1 The flow diagram of how cases were selected from the SEER database

NOS: Not otherwise specified.

1.2　研究变量

基于以下变量对AVG患者进行描述: 患者基本特征(年龄、性别、婚姻状况和保险)、肿瘤特征(肿瘤分级、直径和范围)和治疗方案(手术类型、放疗和化疗)。纳入患者根据年龄分布分为两组: 18 ~ < 65岁和≥65岁。诊断年份分为三个时间段: 1973–1999、2000–2009 和 2010–2016。肿瘤直径的中位值作为切分值(cut-off)。肿瘤范围定义为局部和远处受累。根据WHO中CNS肿瘤分类标准,将肿瘤级别分为Ⅱ、Ⅲ、Ⅳ级。手术治疗中,切除范围分为完全切除(gross total resection, GTR)、次全切除(subtotal resection,

STR)、部分切除(partial resection, PR)和未切除。

1.3 Cox回归分析和预测模型构建

使用单变量和多变量Cox回归分析确定训练集OS和CSS的独立预后因素,结合患者基本特征(年龄、性别等),分别构建训练集中针对OS率和CSS率的生存相关列线图预测模型。在模型构建过程中,先通过训练集进行模型构建,并依次通过训练集和验证集进行模型的内部和外部验证。通过1 000次重复抽样计算方式进行内部验证和外部验证评估列线图模型的预测效能。通过C指数(Concordance index, C-index)来评估列线图模型的真实性和可靠性,C-index越高表示区分能力越好(范围为0.5 ~ 1.0)。通过校准图评估训练集和验证集中预测值和观察值之间的一致性。

1.4 统计学方法

所有统计分析均使用SPSS(Version 24)和R(Version 4.0.1, http://www.R-project.org)软件进行。对于连续性变量,使用$\bar{x}\pm s$来表示。比较分类变量和连续变量分别采用卡方检验和t检验。构建Kaplan-Meier曲线,使用log-rank检验比较不同组间的生存差异。使用单变量和多变量Cox回归分析分别确定OS和CSS的独立预后因素。使用R语言包“survival”和“rms”构建列线图模型。$P<0.05$为差异有统计学意义。

2 结果

2.1 AVG患者临床特征

本研究共纳入369例患者,其中男性218例(59.1%),女性151例(40.9%);中位年龄为53岁;230例(62.3%)为Ⅳ级胶质瘤;关于手术切除范围,145例(39.3%)为PR/STR,占比最高。有167例(45.3%)接受放疗,143例(38.8%)接受化疗。见表1。训练集和验证集之间的基本临床特征差异无统计学意义($P>0.05$)。

2.2 预后分析

本研究纳入的所有AVG患者中位OS期为8.0个月,其中训练集为8.0个月,验证集为7.0个月。在训练集中OS的Kaplan-Meier分析结果显示,年龄较小、低级别、最大范围切除以及接受放疗的患者具有更好的生存结果(图2)。进一步分析结果表明(图3),在低级别胶质瘤(lowgrade glioma, LGG)患者中,不论术后放疗与否,接受GTR的患者具有最大的生存获益;对于高级别胶质瘤(high grade glioma, HGG)患者,接受GTR和放疗治疗策略的患者OS最优,具有最大生存获益。进一步的多变量Cox回归分析显示,年龄≥65岁、肿瘤分级Ⅲ级和Ⅳ级、未采用放疗是OS的独立预后危险因素(表2)。同样,在训练集中

表 1 AVG患者的临床病理特征和治疗情况

Table 1 Summary of clinicopathologic features and treatments of in patients with AVG

Variable	All (n=369)	Training cohort (n=246)	Validation cohort (n=123)
Age at diagnosis			
Mean/yr.	51.44±17.53	51.73±17.55	50.88±17.54
Median/yr.	53	53	52
18-<65 yr./case	272	182	90
≥65 yr./case	97	64	33
Sex/case			
Male	218	147	71
Female	151	99	52
Race/case			
White	313	206	107
Black	24	13	11
Other	32	27	5
Year at diagnosis			
1973–1999	143	105	38
2000–2009	124	75	49
2010–2016	102	66	36
Marital status/case			
Single or divorced	124	79	45
Married	233	158	75
Unknown	12	9	3
Insurance/case			
Insured	117	76	41
Medicaid	22	13	9
No/unknown	230	157	73
WHO grade/case			
Ⅱ	66	44	22
Ⅲ	73	51	22
Ⅳ	230	151	79
Tumor diameter/mm			
$\bar{x}\pm s$	39.93±16.03	39.90±16.56	40.00±15.10
Median	40.00	40.00	40
Surgery/case			
GTR	59	43	16
PR/STR	145	90	55
No	88	57	31
Surgery, NOS	77	56	21
Radiotherapy/case			
Yes	167	115	52
No/unknown	202	131	71
Chemotherapy/case			
Yes	143	96	47
No/unknown	226	150	76
OS/month			
Median	8.0	8.0	7.0

GTR: Gross total resection; STR: Subtotal resection; PR: Partial resection; NOS: Not otherwise specified.

CSS的Kaplan-Meier分析结果显示，年龄较小、低级别、最大范围切除以及接受放疗的患者具有更好的生存结果（图4），多变量Cox回归分析显示，肿瘤分级Ⅲ级和Ⅳ级、未采用放疗是其独立的预后危险因素（表2）。

2.3　列线图预测模型的构建与验证

见图5。在训练集中，使用5个变量（年龄、性别、WHO 分级、手术和放疗）分别构建用于预测术后6个月、1年和2年OS率和CSS率的列线图预测模型。OS率和

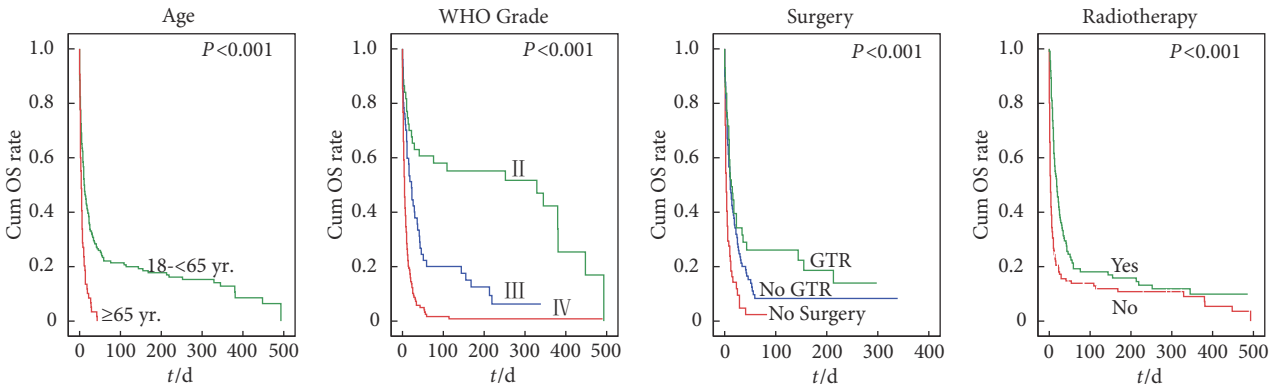

图 2　训练集Kaplan-Meier分析显示不同预后因素对OS的影响

Fig 2　Kaplan-Meier analysis was conducted to determine the impact of variables on OS in the training cohort

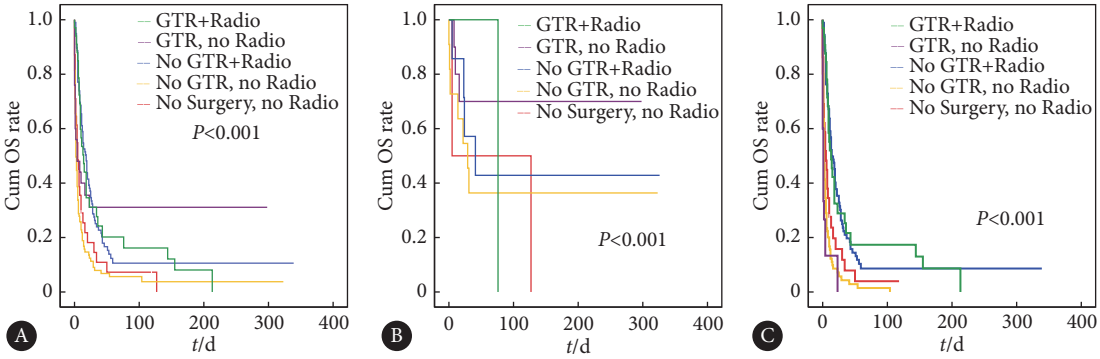

图 3　Kaplan-Meier分析不同治疗方案对AVG患者OS的影响

Fig 3　Kaplan-Meier analysis was conducted to determine the impact of treatment regimens on the OS of AVG patients

A: All patients; B: LGG patients; C: HGG patients. Radio: Radiotherapy.

表 2　训练集中OS和CSS的多变量Cox回归分析（*n*=246）

Table 2　Multivariate Cox regression analysis of OS and CSS in the training cohort (*n*=246)

Variable	OS			CSS		
	HR	95% *CI*	*P*	*HR*	95% *CI*	*P*
Age at diagnosis						
18-<65 yr.	1	Ref		1	Ref	
⩾65 yr.	1.529	1.075-2.177	0.018	1.309	0.886-1.934	0.176
WHO grade						
Ⅱ	1	Ref		1	Ref	
Ⅲ	5.166	2.339-11.412	<0.001	4.667	1.908-11.417	0.001
Ⅳ	12.208	5.662-26.323	<0.001	13.339	5.725-31.077	<0.001
Surgery						
No	1	Ref		1	Ref	
PR/STR	1.004	0.628-1.605	0.986	1.255	0.766-2.056	0.367
GTR	1.021	0.577-1.805	0.944	1.176	0.634-2.181	0.607
Radiotherapy						
No	1	Ref		1	Ref	
Yes	0.328	0.213-0.506	<0.001	0.295	0.189-0.461	<0.001

HR: Hadds ratio; *CI*: Confidence interval; OS: Overall survival; CSS: Cancer-specific survival.

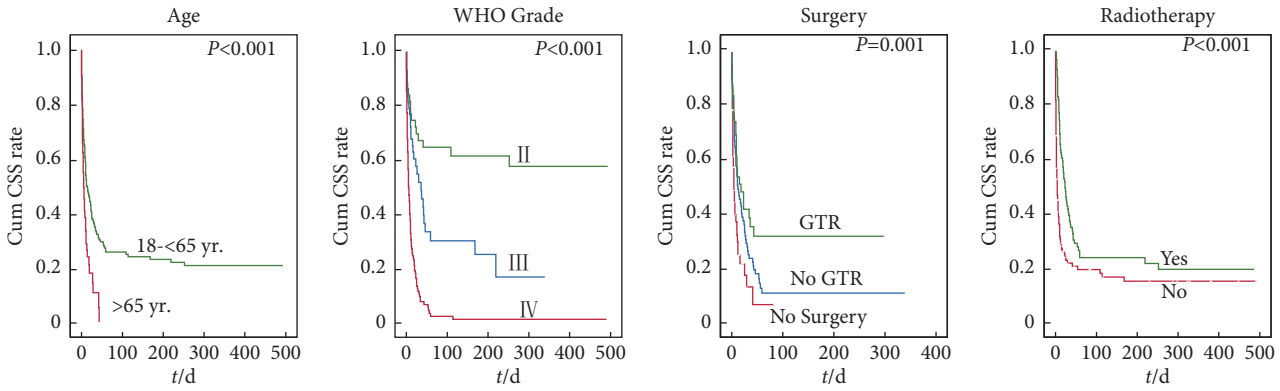

图 4 训练集Kaplan-Meier分析显示不同预后因素对CSS的影响

Fig 4 Kaplan-Meier analysis was conducted to determine the impact of variables on CSS in the training cohort

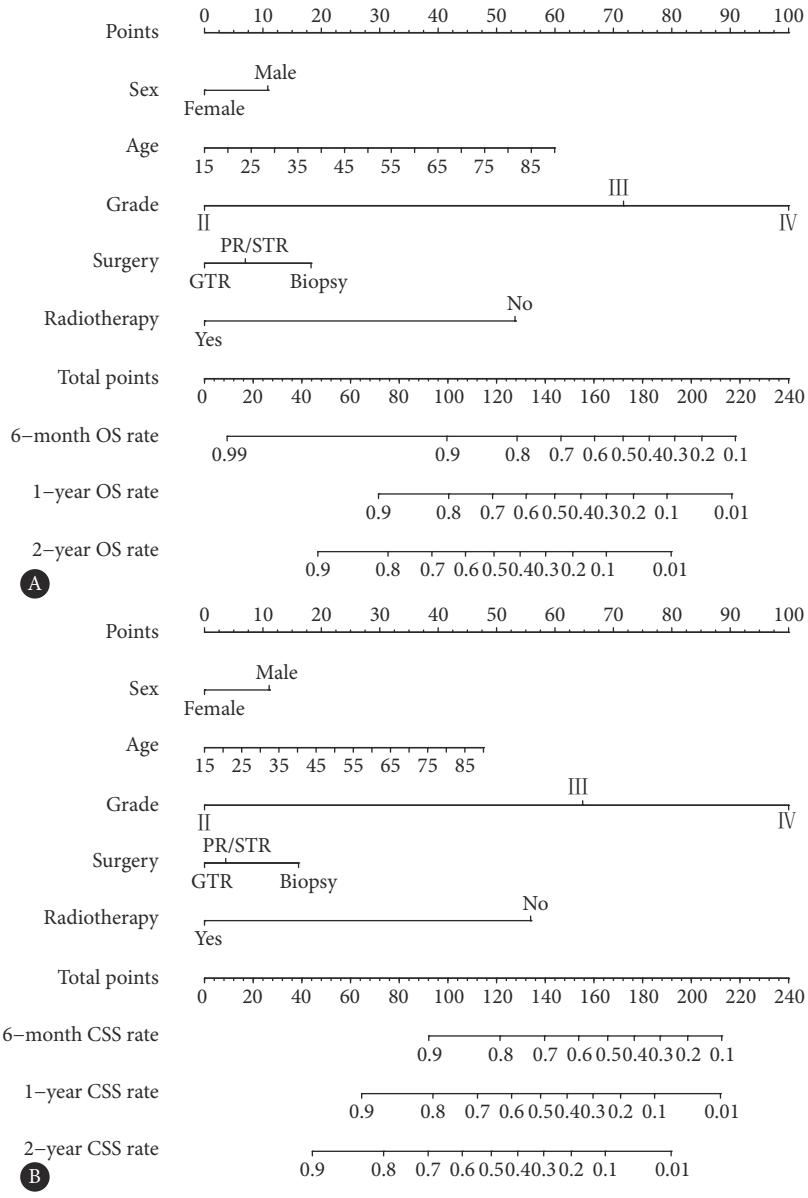

图 5 训练集中6个月、1年和2年OS率和CSS率的列线图预测模型

Fig 5 Nomogram prediction model of 6-month, 1-year, and 2-year OS rates and CSS rates in the training cohort

A: Nomogram model of 6-month,1-year, and 2-year OS rates in the training cohort; B: Nomogram model of 6-month, 1-year, and 2-year CSS rates in the training cohort.

CSS率的列线图显示, 肿瘤分级与预后具有最强的相关性, 其次是年龄和放疗。

此外, 除了在训练集中进行内部验证列线图的预测效能, 还在验证集中进行外部验证。训练集中内部验证结果显示, OS率和CSS率列线图预测模型的C指数分别为0.758(95%*CI*: 0.706 ~ 0.810)和0.765(95%*CI*: 0.712 ~ 0.818)。验证集中外部验证结果显示, OS率和CSS率列线图预测模型的C指数分别为0.733(95%*CI*: 0.654 ~ 0.812)和0.719(95%*CI*: 0.628 ~ 0.810)。在训练集和验证集中分别构建了列线图预测模型的校准图(图6、图7)。结果显示, 在训练集中, 6个月、1年和2年OS率的校准图均表现出相对较好的一致性(图6A ~ 6C), 而在验证集中一致性相对较低(图6D ~ 6F)。6个月、1年和2年CSS率的校准图与OS率校准图具有相似的结果(图7)。

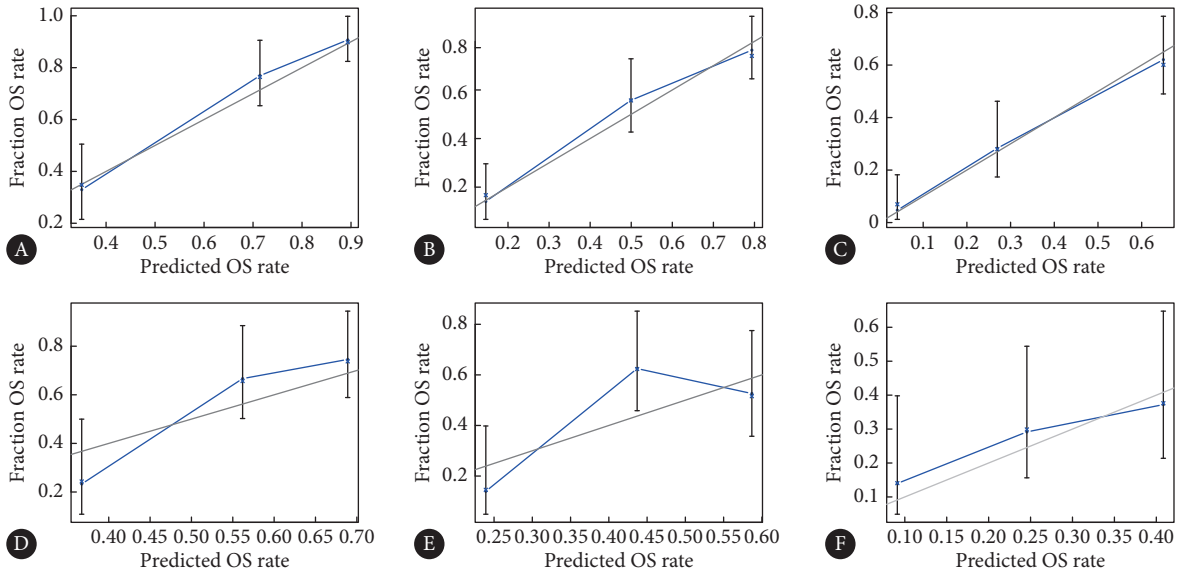

图 6 训练集和验证集中6个月、1年和2年OS率的校准图

Fig 6 Calibration plots of 6-month, 1-year, and 2-year OS rate in the training cohort and validation cohort

A-C: Calibration plots of 6-month, 1-year, and 2-year OS rates in the training cohort. D-F: Calibration plots of 6-month, 1-year, and 2-year OS rates in the validation cohort. The grey curve is the ideal curve, the blue curve is the actual curve, and the black line indicates the error margin.

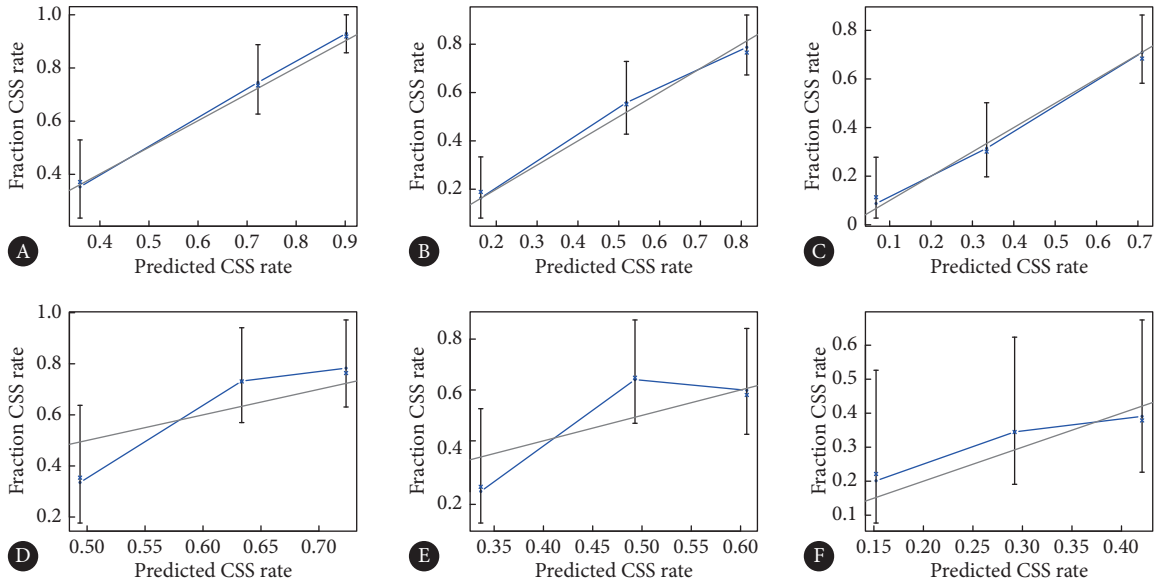

图 7 训练集和验证集中6个月、1年和2年CSS率的校准图

Fig 7 Calibration plots of 6-month, 1- year, and 2-year CSS rates in the training cohort and validation cohort

A-C: Calibration plots of 6-month, 1-year, and 2-year CSS rates in the training cohort; D-F: Calibration plots of 6-month, 1-year, and 2-year CSS rates in the validation cohort. The grey curve is the ideal curve, the blue curve is the actual curve, and the black line means the error margin.

3 讨论

弥漫性胶质瘤通常发生在大脑皮层,在脑室系统内较为少见。AVG可位于侧脑室、第三脑室和第四脑室[4-6]。研究表明,脑室受累是影响胶质瘤总生存期的一个不良预后因素[7-9]。同样,与发生于大脑皮层的弥漫性胶质瘤相比,位于脑室的弥漫性胶质瘤预后更差,这可能与脑室位置深、周围结构复杂以及容易引起较为严重的并发症等主要因素有关,例如脑积水[9-10]。近期,一项多中心的回顾性研究显示,侵犯室管膜下区域的幕上高级别胶质瘤与生存率降低之间存在明显的相关性[11]。由于AVG患者在临床上较为少见,截至目前,对其综合特征、治疗方案以及生存预后等方面的认识尚不足。本研究纳入了较大样本量的AVG患者,总结并分析与OS和CSS相关的独立预后因素,以及进一步构建可用于预测个体患者生存概率的列线图预测模型。本研究中所有AVG患者的中位OS期为8.0个月,总体预后很差,甚至比弥漫性中线胶质瘤(diffuse midline glioma, DMG)和小脑HGG的中位OS期还差[12-13]。

弥漫性胶质瘤可发生在任何年龄阶段。根据文献报道,大多数脑室胶质瘤发生在成人,而儿童相对更为少见[4, 14-16]。BEN NSIR等[4]在2016年报道了一项关于脑室GBM的研究,共包括29例病例,其中23例(79.3%)为成人,6例(20.7%)为儿童。在23例成人患者中,中年有17例(73.9%),老年有5例(26.1%)。本研究中,大部分AVG患者是中年人(73.7%),其余患者是老年人(26.3%)。年龄通常是胶质瘤患者一个重要的预后因素,与年轻患者相比,老年患者预后更差。本研究中,生存分析显示老年AVG患者预后较差,年龄是OS和CSS的独立预后因素。

肿瘤级别也是弥漫性胶质瘤重要的预后因素。相比LGG,HGG患者的预后更差[2, 17]。同样,相比于较低级别(Ⅱ级和Ⅲ级)胶质瘤,Ⅳ级GBM具有最差的预后[18-20]。本研究中,Cox回归分析显示不同肿瘤级别AVG患者的OS和CSS差异有统计学意义,与Ⅱ和Ⅲ级胶质瘤相比,Ⅳ级GBM患者的预后最差。此外,肿瘤范围(局部或远处转移)和肿瘤直径也可能是胶质瘤的重要预后因素,具有远处转移和更大肿瘤的患者预后较差[21]。然而,本研究结果表明在AVG患者中,肿瘤范围和肿瘤直径并不是OS和CSS的独立预后因素,这可能与脑室肿瘤具有特殊性有关。对于脑室肿瘤,脑积水是术前或术后常见的继发性改变,但由于这些数据无法从SEER数据库获得,本研究未能评估脑积水对预后的影响。

已有研究表明,与部分切除和活检相比,肿瘤全切的弥漫性胶质瘤患者预后更佳[22-23]。然而,关于手术切除范围在脑室胶质瘤的预后作用仍存在争议,且目前尚无专门针对脑室胶质瘤的诊疗共识或指南[4]。有研究表明,在非中线以及部分中线部位脑胶质瘤患者中,最大范围的肿瘤切除均发挥了重要的作用,手术切除范围被认为是OS的独立预后因素[17, 22]。本研究结果表明,尽管手术切除范围不是OS和CSS的独立预后因素,但最大范围的肿瘤切除有助于AVG患者的生存获益。BEN NSIR等[4]的一项研究报道了8例脑室GBM,与未接受肿瘤全切的患者相比,接受肿瘤全切的3例患者预后更好。

放疗和替莫唑胺化疗是弥漫性胶质瘤术后的主要辅助治疗手段,手术以及术后辅助放化疗等的综合治疗是弥漫性胶质瘤(尤其是HGG)的标准治疗方案[24-26]。本研究结果表明,放疗能使AVG患者生存获益,是OS和CSS独立的预后因素,然而,化疗不是独立的预后因素。从以上结果得知,放疗可能是AVG患者术后主要的辅助治疗选择,但放疗的具体剂量和疗程等有待进一步研究。对于脑室胶质瘤,化疗不能显著延长AVG的总生存期,这可能与替莫唑胺在脑脊液中的分布差异有关。此外,一项关于手术和放疗的综合生存分析表明,在LGG患者中接受GTR但不进行放疗能够取得最大的生存获益,在HGG患者中GTR联合术后放疗的综合治疗能够取得最大的生存获益[13, 18, 26]。

弥漫性胶质瘤的分子病理特征,如IDH1/2、MGMT启动子甲基化等,与肿瘤的级别,对放化疗的敏感性和预后密切相关[25, 27-28]。近期一项研究表明,在高风险胶质瘤患者中,MGMT启动子甲基化与胶质瘤的生存结果存在显著相关性,MGMT启动子甲基化是总生存期有利的预后因素[25]。由于SEER数据库未纳入分子病理数据,故本研究无法评估分子标志物在AVG患者中的预后作用。

列线图能够将预测模型进行简易图形化展示,故在临床上广泛用于预测肿瘤等患者疾病相关事件概率的风险评估[29]。目前已有研究为多种类型的恶性肿瘤构建了列线图的生存预测模型,并具有一定的临床应用价值[30-35]。在本研究中,AVG患者OS率和CSS率列线图预测模型的有效性和可靠性通过C指数和校准图进行验证和评价,其中训练集中内部验证结果和验证集中外部验证结果显示出该预测模型具有中等可靠的预测效能,这与之前几项重要的关于GBM和LGG列线图模型的预测能力具有相似性,同样也具有中等的预测效能(C指数在0.7~0.9区间)[31-35]。2017年GITTLEMAN等[31]通过两个国际GBM队列数据(训练集RTOG 0525和验证集RTOG 0825)分别构建并验证生存预测列线图模型,结果显示该

预测模型的C指数为0.657。我国CHENG等[32]进一步对CGGA数据库中191例原发GBMs中国队列进行分析，筛选出包括KPS评分、MGMT启动子甲基化以及*IDH*1突变分子指标等预后因子并构建列线图预测模型，显示出该模型的C指数为0.69，略高于GITTLEMAN的GBM列线图预测模型。同样，2020年GITTLEMAN等[33]对两个国际LGG队列数据（训练集TCGA和验证集OBTS）分别构建并验证生存预测列线图模型，结果显示该预测模型的C指数为0.844。由于IDH分子在LGG队列具有重要的预后作用，相比之前GBM列线图预测模型，LGG列线图预测模型中还纳入IDH分子指标，该模型显示出较高的预测效能（C指数：0.844 vs. 0.657）。近期，我们团队基于华西脑胶质瘤中心多年积累的成人丘脑胶质瘤（adult thalamic glioma, ATG）患者数据构建生存相关列线图预测模型，该模型的C指数为0.736，具有中等可靠的预测效能[34]。此外，ZHAO等[35]基于SEER数据库数据构建了LGG队列的生存相关列线图模型，同本研究类似，该列线图模型也缺少与胶质瘤患者预后情况紧密相关的KPS评分及分子标志物等数据。

从以上不同类型胶质瘤的列线图预测模型来看，尽管不同研究队列纳入的预后因素会略有不同，但这些预测模型均显示出中等可靠的预测效能。基于目前构建的列线图预测模型，可以通过扩大样本量以及纳入其他重要预后因素尽可能地提高该模型的预测能力。然而，目前尚无法非常准确地预测胶质瘤患者的生存概率，这可能与模型本身具有一定的局限性以及胶质瘤患者的临床异质性较大等因素有关。对于本研究中AVG列线图预测模型，我们认为主要还存在以下局限性。首先，胶质瘤相关临床指标，如KPS评分和分子标志物（如IDH1/2、1p/19q和MGMT启动子甲基化）未纳入SEER数据库，故无法评估这些指标在AVG患者中的预后作用以及模型构建。其次，由于AVG病例临床上较为少见，目前尚无法在其他独立的数据队列中进行外部验证来明确该预测模型预测效能的稳定性。需要补充说明的是，性别因素在生存差异中虽然无统计学意义，但作为常规基线，我们也予以纳入预测模型。尽管该预测模型中已经纳入较大样本量的数据分析，然而仍需多中心更大样本量的数据积累优化该模型。

综上所述，本研究全面总结和分析AVG患者的临床特征以及独立预后因素，进一步构建了OS和CSS的列线图预测模型。尽管该列线图预测模型具有中等可靠的预测效能，然而依然有助于临床医生简易地对AVG个体患者的生存概率进行风险评估，对此类患者的临床管理具有一定的参考价值。

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利益冲突　所有作者均声明不存在利益冲突

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