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• 专题报道 •

急性缺血性脑卒中患者认知障碍的危险因素分析

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[摘要] **目的** 探讨急性缺血性脑卒中(AIS)患者发生认知障碍的危险因素。**方法** 选择2022年8月至12月海军军医大学(第二军医大学)第一附属医院脑血管病中心收治的AIS患者100例作为研究对象,根据简易智能精神状态检查量表(MMSE)评分分为认知功能正常组(59例)和认知障碍组(41例)。采集并比较两组患者的基本临床资料、实验室检查结果、影像学检查结果及蒙特利尔认知评估量表(MoCA)、9条目患者健康问卷抑郁量表(PHQ-9)、Lubben 社会网络量表(LSNS-6)、加利福尼亚大学洛杉矶分校孤独量表第3版(UCLA-3)评估资料。采用二元logistic回归模型分析AIS患者发生认知障碍的危险因素。**结果** 与认知功能正常组相比,认知障碍组患者年龄较大($P=0.012$),受教育年限较低($P=0.045$),有糖尿病病史的患者比例较高($P=0.026$),MMSE评分($P<0.001$)、MoCA评分($P<0.001$)和LSNS-6评分($P=0.012$)较低,PHQ-9评分($P<0.001$)和UCLA-3评分较高($P=0.002$)。两组患者的牛津郡社区卒中规划(OCSP)临床表现分型($P=0.031$)差异有统计学意义。二元logistic回归分析结果显示,年龄($OR=1.070$, 95% CI 1.020~1.123, $P=0.005$)和完全前循环梗死($OR=55.633$, 95% CI 2.041~1 516.526, $P=0.017$)是AIS患者发生认知障碍的危险因素。**结论** 年龄和完全前循环梗死是AIS患者发生认知障碍的危险因素。

[关键词] 急性缺血性脑卒中; 认知障碍; 危险因素; 年龄; 完全前循环梗死

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Risk factors of cognitive impairment in patients with acute ischemic stroke

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[Abstract] **Objective** To investigate the risk factors of cognitive impairment in patients with acute ischemic stroke (AIS). **Methods** A total of 100 AIS patients in Neurovascular Center, The First Affiliated Hospital of Naval Medical University (Second Military Medical University) from Aug. to Dec. 2022 were enrolled. According to the mini mental status evaluation (MMSE) score, the patients were divided into normal cognitive group (59 cases) and impaired cognitive group (41 cases). The basic clinical data, laboratory and imaging examination data, Montreal cognitive assessment (MoCA), patient health questionnaire-9 (PHQ-9), Lubben social network scale (LSNS-6) and University of California, Los Angeles loneliness scale-version 3 (UCLA-3) of the patients in the 2 groups were collected. Binary logistic regression model was used to analyze the risk factors of cognitive impairment in AIS patients. **Results** Compared with the normal cognitive group, the impaired cognitive group was older ($P=0.012$), had lower level of education ($P=0.045$), higher proportion of diabetes mellitus history ($P=0.026$), and lower MMSE score ($P<0.001$), MoCA score ($P<0.001$) and LSNS-6 score ($P=0.012$), and higher PHQ-9 score ($P<0.001$) and UCLA-3 score ($P=0.002$). Moreover, there was significant difference in Oxfordshire Community Stroke Project (OCSP) classification ($P=0.031$) between the

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2 groups. Binary logistic regression analysis showed that age (odds ratio [OR]=1.070, 95% confidence interval [CI] 1.020-1.123, $P=0.005$) and total anterior circulation infarct ($OR=55.633$, 95% CI 2.041-1 516.526, $P=0.017$) were risk factors for cognitive impairment in AIS patients. **Conclusion** Age and total anterior circulation infarct are risk factors of cognitive impairment in AIS patients.

[**Key words**] acute ischemic stroke; cognitive impairment; risk factors; age; total anterior circulation infarct

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脑卒中是引起国人死亡和残疾的首位疾病,其中缺血性脑卒中占大部分,不仅给社会、家庭带来沉重的经济负担,也是我国公共卫生和健康管理的重要难题^[1-2]。卒中后认知障碍是脑卒中后最常见的并发症之一,严重影响患者的神经功能恢复和生存时间^[3-5]。因此,迫切需要深入探讨急性缺血性脑卒中(acute ischemic stroke, AIS)后发生认知障碍的危险因素,以制定有效的干预策略。但目前对于 AIS 患者发生认知障碍影响因素的研究结论不一^[6]。本研究通过回顾 AIS 患者的基本临床资料、实验室及影像学检查结果、量表资料,从多层次系统分析 AIS 患者发生认知障碍的危险因素,为 AIS 防治提供新的思路和理论依据。

1 资料和方法

1.1 研究对象 回顾性分析 2022 年 8 月至 12 月海军军医大学(第二军医大学)第一附属医院脑血管病中心收治的 100 例 AIS 患者的病例资料。纳入标准:(1)符合《中国急性缺血性脑卒中诊治指南 2018》诊断标准^[7],并经头颅 CT 或 MRI 检查证实为 AIS;(2)年龄 ≥ 18 岁;(3)发病至入院时间 < 14 d;(4)能配合完成神经心理评估及影像学检查;(5)签署知情同意书。排除标准:(1)患有严重的精神疾病,如精神分裂症或精神发育迟滞等;(2)患有恶性肿瘤或严重的心、肝、肺、肾功能衰竭;(3)患有严重的躯体疾病且很可能是认知损害的主要原因;(4)有严重的视觉或听力障碍,无法完成神经心理测验;(5)有严重失语或意识障碍等而无法配合检查。本研究获得海军军医大学(第二军医大学)第一附属医院伦理委员会审批。

1.2 研究方法

1.2.1 临床资料收集 收集患者的发病年龄、受教育年限、性别、户口类型、婚姻状况、居住状态、日常运动情况、高血压病史、糖尿病病史、高脂血症病史、冠心病史、脑卒中家族史、吸烟史、饮酒史、BMI 等基本资料,记录入院时的收缩压和舒张压、

入院 24 h 内美国国立卫生研究院卒中量表(National Institute of Health stroke scale, NIHSS)评分^[8-9]、发病至医院就诊时间(onset to door time)。

1.2.2 实验室检查资料收集 患者入院次日采集空腹静脉血,检测空腹血糖、糖化血红蛋白、总胆固醇、甘油三酯、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、同型半胱氨酸等实验室指标。

1.2.3 影像学检查资料收集 对患者进行头颅 MRI、CT 灌注成像检查,并采用磁共振血管造影、CT 血管成像、颈动脉超声或数字减影血管造影评估血管病变。记录所有研究对象的梗死灶面积、梗死灶数量,了解有无脑白质病变、有无微出血、有无低灌注。由具有临床经验的神经内科医师对患者进行临床表现分型[牛津郡社区卒中规划(Oxfordshire Community Stroke Project, OCSF)分型]^[10]和病因分型[Org 10172 急性脑卒中治疗试验(Trial of Org 10172 in Acute Stroke Treatment, TOAST)分型]^[11]。

1.2.4 量表评估 患者在发病 2 周内,由经过统一培训的医师进行标准化量表评估,评估项目包括:(1)简易智能精神状态检查量表(mini mental status evaluation, MMSE)^[12],包含时间定向力、地点定向力、即刻记忆力、注意力及计算力、延迟记忆力、语言、视空间 7 个方面,总分为 0~30 分,用于评估患者的总体认知功能。

(2)蒙特利尔认知评估量表(Montreal cognitive assessment, MoCA)^[13],用于广泛的认知功能筛查,总分为 0~30 分,分值越高表示认知功能越好。

(3)9 条目患者健康问卷抑郁量表(patient health questionnaire-9, PHQ-9)^[14],共有 9 个条目,每个条目采用 0~3 分的 4 级评分(完全不会出现症状计 0 分,好几天出现症状计 1 分,一半以上的天数出现症状计 2 分,几乎每天都出现症状计 3 分),总分为 0~27 分,其中 0~4 分为无抑郁,5~9 分为轻度抑郁,10~14 分为中度抑郁,15~19 分为中重度抑郁,20~27 分为重度抑郁。(4)Lubben 社会网络量表(Lubben social network scale,

LSNS-6)^[15],包含家庭网络和朋友网络2个维度,每个维度有3个条目,共6个条目,采用0~5分计分,计分方式为“当您需要时,有几个家人/亲戚可以给您提供帮助?”回答0个计0分,1个计1分,2个计2分,3~4个计3分,5~8个计4分,9个或更多计5分,总分为0~30分,分数越低表示社会隔离风险越高,总得分<12分视为社会隔离状态,各维度得分<6分视为家庭或朋友隔离状态。

(5)加利福尼亚大学洛杉矶分校(University of California, Los Angeles; UCLA)孤独量表第3版(UCLA loneliness scale-version 3, UCLA-3)^[16],该量表有3个项目,选项分为“几乎没有”“有时”“经常”3个等级,依次对应1~3分,总分为3~9分,分值越高表示孤独感越强。

1.2.5 分组 MMSE总分为0~30分,评分越低患者认知功能越差。按以下标准定义认知障碍:文盲≤17分、小学(受教育年限≤6年)≤20分、初中以上文化(受教育年限>6年)≤24分^[12]。

根据患者有无认知障碍,将其分为认知功能正常组和认知障碍组。

1.3 统计学处理 应用SPSS 26.0软件进行统计学分析。呈正态分布的计量资料以 $\bar{x}\pm s$ 表示,组间比较采用Student *t*检验;呈偏态分布的计量资料以中位数(下四分位数,上四分位数)表示,组间比较采用Mann-Whitney *U*检验。计数资料以例数和百分数表示,组间比较采用 χ^2 检验。应用二元logistic回归模型分析影响AIS患者发生认知障碍的危险因素。所有检验均为双侧检验,检验水准(α)为0.05。

2 结果

2.1 两组患者临床资料比较 共纳入100例AIS患者,男73例、女27例,年龄为(61.37±11.85)岁,其中认知功能正常组59例、认知障碍组41例。与认知功能正常组相比,认知障碍组患者年龄较大($P=0.012$),受教育年限较低($P=0.045$),有糖尿病病史的患者比例较高($P=0.026$)。见表1。

表1 两组AIS患者临床资料比较

Tab 1 Comparison of clinical data of AIS patients between 2 groups

Characteristic	Normal cognitive <i>N</i> =59	Impaired cognitive <i>N</i> =41	Statistic	<i>P</i> value
Age/year, <i>M</i> (<i>Q_L</i> , <i>Q_U</i>)	61 (49, 70)	66 (59, 72)	<i>Z</i> = -2.504	0.012
Education/year, <i>M</i> (<i>Q_L</i> , <i>Q_U</i>)	9 (9, 13)	9 (9, 12)	<i>Z</i> = -2.000	0.045
Male, <i>n</i> (%)	47 (79.7)	26 (63.4)	$\chi^2=3.239$	0.072
Type of household, <i>n</i> (%)			$\chi^2=1.801$	0.180
Agriculture	13 (22.0)	14 (34.1)		
Non-agriculture	46 (78.0)	27 (65.9)		
Marital status, <i>n</i> (%)			$\chi^2=0.000$	1.000
Married	55 (93.2)	39 (95.1)		
Unmarried/divorced/widowed	4 (6.8)	2 (4.9)		
Living status, <i>n</i> (%)			$\chi^2=0.000$	1.000
Living alone	2 (3.4)	2 (4.9)		
Not living alone	57 (96.6)	39 (95.1)		
Physical activity, <i>n</i> (%)	24 (40.7)	12 (29.3)	$\chi^2=1.367$	0.242
Hypertension, <i>n</i> (%)	40 (67.8)	32 (78.0)	$\chi^2=1.261$	0.261
Diabetes mellitus, <i>n</i> (%)	16 (27.1)	20 (48.8)	$\chi^2=4.927$	0.026
Hyperlipidemia, <i>n</i> (%)	17 (28.8)	14 (34.1)	$\chi^2=0.322$	0.571
CHD, <i>n</i> (%)	8 (13.6)	7 (17.1)	$\chi^2=0.234$	0.628
Family history of stroke, <i>n</i> (%)	17 (28.8)	8 (19.5)	$\chi^2=1.116$	0.291
Smoking, <i>n</i> (%)	28 (47.5)	19 (46.3)	$\chi^2=0.012$	0.912
Drinking, <i>n</i> (%)	25 (42.4)	14 (34.1)	$\chi^2=0.688$	0.407
BMI/(kg·m ⁻²), $\bar{x}\pm s$	25.21±3.23	24.48±2.87	<i>t</i> = 1.153	0.252
SBP/mmHg, $\bar{x}\pm s$	143.39±20.14	144.54±22.45	<i>t</i> = -0.267	0.790
DBP/mmHg, <i>M</i> (<i>Q_L</i> , <i>Q_U</i>)	85 (78, 92)	80 (76, 92)	<i>Z</i> = -0.913	0.361
NIHSS score at admission, <i>M</i> (<i>Q_L</i> , <i>Q_U</i>)	2 (1, 4)	3 (2, 5)	<i>Z</i> = 0.056	0.056
Onset to door time, <i>n</i> (%)				
<4.5 h	7 (11.9)	8 (19.5)	$\chi^2=1.110$	0.292
≥4.5 h	52 (88.1)	33 (80.5)		

1 mmHg=0.133 kPa. AIS: Acute ischemic stroke; CHD: Coronary heart disease; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; NIHSS: National Institute of Health stroke scale; *M* (*Q_L*, *Q_U*): Median (lower quartile, upper quartile).

2.2 两组患者实验室检查结果比较 认知障碍组和认知功能正常组空腹血糖、糖化血红蛋白、总胆固醇、甘油三酯、高密度脂蛋白胆固醇、低密度脂

蛋白胆固醇、同型半胱氨酸差异均无统计学意义 (P 均 >0.05)。见表2。

表2 两组 AIS 患者实验室指标比较

Tab 2 Comparison of laboratory data of AIS patients between 2 groups

Index	Normal cognitive $N=59$	Impaired cognitive $N=41$	Statistic	P value
FBG/(mmol·L ⁻¹), $M(Q_L, Q_U)$	5.7 (5.1, 7.2)	6.5 (5.2, 8.3)	$Z=-1.315$	0.189
HbA1c/%, $M(Q_L, Q_U)$	6.2 (5.5, 7.1)	6.6 (5.8, 7.9)	$Z=-0.859$	0.390
TC/(mmol·L ⁻¹), $\bar{x} \pm s$	4.65 ± 1.22	4.59 ± 1.12	$t=0.240$	0.811
Triglyceride/(mmol·L ⁻¹), $M(Q_L, Q_U)$	1.48 (1.03, 1.92)	1.45 (1.16, 2.20)	$Z=-0.599$	0.549
HDL-C/(mmol·L ⁻¹), $M(Q_L, Q_U)$	1.16 (0.98, 1.28)	1.14 (1.03, 1.34)	$Z=-0.287$	0.774
LDL-C/(mmol·L ⁻¹), $\bar{x} \pm s$	2.95 ± 1.11	2.85 ± 0.93	$t=0.507$	0.613
Homocysteine/(mmol·L ⁻¹), $M(Q_L, Q_U)$	11.3 (8.9, 15.1)	12.1 (9.9, 12.4)	$Z=-0.053$	0.958

AIS: Acute ischemic stroke; FBG: Fasting blood glucose; HbA1c: Glycosylated hemoglobin; TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; $M(Q_L, Q_U)$: Median (lower quartile, upper quartile).

2.3 两组患者影像学检查结果比较 认知障碍组和认知功能正常组 OSCP 分型差异有统计学意义 ($P=0.031$), 而 TOAST 病因分型、梗死灶面积、

梗死灶数量、脑白质病变、微出血、低灌注差异均无统计学意义 (P 均 >0.05)。见表3。

表3 两组 AIS 患者影像学检查结果比较

Tab 3 Comparison of imaging findings of AIS patients between 2 groups

Index	Normal cognitive $N=59$	Impaired cognitive $N=41$	χ^2 value	n (%) P value
OCSP classification			8.900	0.031
Total anterior circulation infarct	1 (1.7)	5 (12.2)		
Partial anterior circulation infarct	34 (57.6)	28 (68.3)		
Posterior circulation infarct	19 (32.2)	7 (17.1)		
Lacunar circulation infarct	5 (8.5)	1 (2.4)		
TOAST classification			1.811	0.770
Large-artery atherosclerosis	15 (25.4)	12 (29.3)		
Cardioembolism	5 (8.5)	2 (4.9)		
Small vessel occlusion	31 (52.5)	21 (51.2)		
Stroke of other determined etiology	5 (8.5)	2 (4.9)		
Stroke of undetermined etiology	3 (5.1)	4 (9.8)		
Infarct size			0.429	0.513
<1.5 cm	10 (16.9)	5 (12.2)		
≥1.5 cm	49 (83.1)	36 (87.8)		
Number of infarcts			0.381	0.826
Single infarction	11 (18.6)	7 (17.1)		
Multiple infarcts in the same location	20 (33.9)	12 (29.3)		
Multiple infarcts in multiple locations	28 (47.5)	22 (53.7)		
White matter hyperintensity	28 (47.5)	25 (61.0)	1.775	0.183
Cerebral microbleed	6 (10.2)	3 (7.3)	0.018	0.893
Cerebral hypoperfusion	6 (10.2)	9 (22.0)	2.634	0.105

AIS: Acute ischemic stroke; OSCP: Oxfordshire Community Stroke Project; TOAST: Trial of Org 10172 in Acute Stroke Treatment.

2.4 两组患者量表评估结果比较 认知障碍组 MMSE 评分 ($P<0.001$)、MoCA 评分 ($P<0.001$) 和 LSNS-6 评分 ($P=0.012$) 均低于认知功能正常组, 而 PHQ-9 评分 ($P<0.001$) 和 UCLA-3 评分 ($P=0.002$) 均高于认知功能正常组。见表4。

2.5 AIS 患者发生认知障碍的二元 logistic 回归分析结果 将是否发生认知障碍作为因变量,

两组间临床资料、实验室指标、影像学检查结果比较差异有统计学意义的因素作为自变量, 进行二元 logistic 回归分析。结果显示年龄 ($OR=1.070$, 95% CI 1.020~1.123, $P=0.005$) 和完全前循环梗死 ($OR=55.633$, 95% CI 2.041~1 516.526, $P=0.017$) 是 AIS 患者发生认知障碍的危险因素。见表5。

表4 两组 AIS 患者量表评估结果比较

Tab 4 Comparison of scale assessment results of AIS patients between 2 groups

Index	Median (lower quartile, upper quartile)		Z value	P value
	Normal cognitive n=59	Impaired cognitive n=41		
Mini mental status evaluation (MMSE)	26 (25, 28)	20 (15, 22)	-8.314	<0.001
Montreal cognitive assessment (MoCA)	23 (21, 26)	13 (11, 18)	-7.199	<0.001
Patient health questionnaire-9 (PHQ-9)	1 (0, 3)	3 (1, 6)	-3.752	<0.001
Lubben social network scale (LSNS-6)	17 (15, 21)	15 (12, 19)	-2.527	0.012
UCLA loneliness scale-version 3 (UCLA-3)	3 (3, 3)	3 (3, 4)	-3.162	0.002

AIS: Acute ischemic stroke; UCLA: University of California, Los Angeles.

表5 AIS 患者发生认知障碍的二元 logistic 回归分析结果

Tab 5 Binary logistic regression analysis of cognitive impairment in AIS patients

Variable	b	SE	Wald	OR (95% CI)	P value
Age	0.068	0.024	7.764	1.070 (1.020, 1.123)	0.005
Education	-0.125	0.069	3.215	0.883 (0.770, 1.012)	0.073
Diabetes mellitus	0.704	0.493	2.041	2.023 (0.770, 5.317)	0.153
OCSF classification				1	
Lacunar circulation infarct					
Total anterior circulation infarct	4.019	1.686	5.679	55.633 (2.041, 1 516.526)	0.017
Partial anterior circulation infarct	1.657	1.184	1.959	5.242 (0.515, 53.329)	0.162
Posterior circulation infarct	0.778	1.252	0.387	2.178 (0.187, 25.318)	0.534

AIS: Acute ischemic stroke; OCSF: Oxfordshire Community Stroke Project; b: Regression coefficient; SE: Standard error; OR: Odds ratio; CI: Confidence interval.

3 讨论

本研究结果显示, AIS 后认知障碍组患者年龄较大、受教育年限较低、有糖尿病病史的患者比例较高, MMSE 评分、MoCA 评分和 LSNS-6 评分较低, PHQ-9 评分和 UCLA-3 评分较高。此外, 两组患者的 OCSF 分型亦差异显著。进一步 logistic 回归分析显示, 年龄和完全前循环梗死是 AIS 患者发生认知障碍的危险因素。

高龄是卒中后认知障碍的独立危险因素。随着年龄的增长, 脑细胞发生不同程度的衰退, 脑组织可塑性降低, 并且脑组织因动脉硬化处于低灌注状态, 导致高龄人群容易发生认知损害^[6,17-20]。大量研究表明教育水平和认知障碍密切相关^[6,17,19], 较高的教育水平意味着更好的认知储备, 可以延缓认知功能的下降^[21-23]。糖尿病是公认的脑血管疾病的危险因素之一, 有研究认为, 糖尿病引起的内皮功能障碍和微血管损伤通过脑白质高信号变化加速认知障碍或痴呆^[24-27]。此外, 本研究结果表明, 缺血性脑卒中的 OCSF 分型与认知功能损伤有密切关系, 与既往研究结果^[28]一致。临床上不同 OCSF 分型的 AIS 患者发生认知障碍的比例不尽相同, 前循环梗死的患者认知障碍发生率较高^[29-30]。近年来, 越来越多的证据表明社会因素(包括社会网

络)和心理因素(包括抑郁、孤独感)与缺血性脑卒中的发病风险相关^[31-37], 并影响患者的生活质量, 但目前对其干预尚未得到重视。本研究结果显示, AIS 后认知障碍组 LSNS-6 评分低于认知功能正常组, PHQ-9 评分和 UCLA-3 评分高于认知功能正常组。因此, 对于 AIS 患者, 应积极改善社会网络水平、提高心理健康水平, 预防认知障碍的发生与发展。

综上所述, 年龄和完全前循环梗死为 AIS 后患者认知障碍的危险因素, 对 AIS 后认知障碍的早期识别和管理具有重要意义。本研究为单中心、小样本、回顾性病例分析, 具有一定的局限性。在未来将开展多中心、大样本、随访研究, 以明确缺血性脑卒中后认知障碍的危险因素, 从而为缺血性脑卒中后认知障碍的诊治与干预提供新的策略和靶点。

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