

## · 临床研究 ·

## 高龄老年住院患者谵妄发生的危险因素

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**【摘要】目的** 观察高龄老年住院患者谵妄的发生情况,对相关危险因素进行分析。**方法** 选择2018年2月至2020年2月于徐州医科大学附属老年科住院的365例年龄 $\geq 80$ 岁的患者为研究对象。应用老年综合评估(CGA)评估患者入院时情况,采用意识模糊评估表(CAM)评估患者入院后7d内谵妄的发生情况,并将患者分为谵妄组(43例)和非谵妄组(322例)。采用SPSS 24.0统计软件进行数据分析。根据数据类型,分别采用 $t$ 检验或 $\chi^2$ 检验进行组间比较。采用logistic回归分析谵妄发生的独立危险因素。**结果** 365例老年患者中有43例发生谵妄,发生率为11.8%。谵妄组患者的居家环境、居住方式、多重用药率、抑郁症、营养不良发生率、多病共存发生率、衰弱状态、简易智能状态检查量表(MMSE)评分、老年综合征发生情况及入院时血清中枢神经特异蛋白100 $\beta$ (S100 $\beta$ )水平与非谵妄组相比,差异均有统计学意义( $P < 0.05$ )。多因素logistic回归分析显示,年龄( $OR = 2.683, 95\%CI 1.005 \sim 4.019, P < 0.05$ )、营养状况( $OR = 2.212, 95\%CI 1.101 \sim 5.212, P < 0.05$ )、衰弱( $OR = 3.108, 95\%CI 1.005 \sim 5.015, P < 0.05$ )、MMSE评分( $OR = 2.694, 95\%CI 0.705 \sim 3.117, P < 0.05$ )、老年综合征数量( $OR = 1.412, 95\%CI 1.025 \sim 4.041, P < 0.05$ )、S100 $\beta$ 蛋白( $OR = 1.919, 95\%CI 1.789 \sim 4.664, P < 0.05$ )是谵妄发生的独立危险因素。**结论** 高龄老年住院患者谵妄发生率与营养状态、衰弱、认知功能障碍及S100 $\beta$ 蛋白的升高相关,需要在临床上加以重视并及时干预。

**【关键词】** 谵妄;高龄老年;危险因素**【中图分类号】** R749.2**【文献标志码】** A**【DOI】** 10.11915/j.issn.1671-5403.2022.06.094

## Risk factors of delirium in the elderly inpatients

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**【Abstract】 Objective** To observe the delirium of the elderly inpatients and analyze the related risk factors. **Methods** A total of 365 patients aged  $\geq 80$  years were selected, who were admitted to the Geriatric Department of Affiliated Hospital of Xuzhou Medical University from February 2018 to February 2020. On admission the patients were assessed using the comprehensive geriatric assessment (CGA), and the incidence of delirium was assessed within 7 days after admission using the confusion assessment method (CAM). The patients were divided into delirium group ( $n = 43$ ) and non-delirium group ( $n = 322$ ) by CAM. SPSS statistics 24.0 was used for data analysis. Depending on the data type,  $t$ -test or  $\chi^2$  test were used for comparison between groups. Logistic regression analysis was used to analyze the independent risk factors. **Results** Of 365 elderly patients, 43 developed delirium with an incidence of 11.8%. The delirium group differed significantly from the non-delirium group in home environment, living style, polypharmacy rate, depression, malnutrition rate, coexistence rate, frail status, mini-mental state examination (MMSE) score, geriatric syndrome and serum central nervous system specific protein (S100 $\beta$ ) level on admission ( $P < 0.05$ ). Multivariate logistic regression analysis showed that age ( $OR = 2.683, 95\%CI 1.005 \sim 4.019; P < 0.05$ ), nutritional status ( $OR = 2.212, 95\%CI 1.101 \sim 5.212; P < 0.05$ ), frailty ( $OR = 3.108, 95\%CI 1.005 \sim 5.015; P < 0.05$ ), MMSE score ( $OR = 2.694, 95\%CI 0.705 \sim 3.117; P < 0.05$ ), number of geriatric syndromes ( $1.412, 95\%CI 1.025 \sim 4.041; P < 0.05$ ), S100 $\beta$  ( $OR = 1.919, 95\%CI 1.789 \sim 4.664; P < 0.05$ ) were all independent risk factors of delirium. **Conclusion** The incidence of delirium in the elderly inpatients is related to nutritional status, frailty, cognitive impairment and the increase of S100 $\beta$  protein, which requires clinical attention and intervention.

**【Key words】** delirium; advanced age; risk factors

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谵妄是一组由于各种原因引起患者意识和知觉、注意力、记忆力、思维能力、精神及运动行为、情

绪和睡眠-觉醒周期紊乱的急性脑代谢综合征。它是高龄老年住院患者容易出现的临床综合征

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之一<sup>[1]</sup>,根据临床表现可将谵妄分为抑制型、兴奋型和混合型<sup>[2]</sup>。老年住院患者以抑制型和混合型最为常见<sup>[3,4]</sup>,其发生率高达50%<sup>[5]</sup>。意识模糊评估表(confusion assessment method, CAM)作为临床上最常用的谵妄评估工具,从急性改变的精神状态、注意力不集中、意识水平、思维混乱等维度来评估患者,具有简便、快捷、有效的特点,而谵妄的评估是老年综合评估(comprehensive geriatric assessment, CGA)的主要内容之一<sup>[6]</sup>。因此,本研究重点关注 $\geq 80$ 岁的高龄老年住院患者,通过评估筛查出高危因素,以期为高龄老年住院患者谵妄的提早干预提供临床参考。

## 1 对象与方法

### 1.1 研究对象

选择2018年2月至2020年2月于徐州医科大学附属医院老年科住院的435例高龄患者为研究对象。纳入标准:(1)年龄 $\geq 80$ 岁的老年科住院患者;(2)符合谵妄的诊断标准;(3)患者及家属知情同意并签署知情同意书。排除标准:(1)有明确精神疾病史。(2)有认知功能障碍,无法沟通。(3)有严重心、肝、肾等脏器功能不全、急性心脑血管意外、肿瘤性疾病、感染性疾病、严重水电解质酸碱平衡紊乱。最终入组365例,根据意识模糊评估法将患者分为谵妄组(delirium group)与非谵妄组(non-delirium group)。

### 1.2 观察指标

1.2.1 老年综合评估 (1)生活能力:应用生活能力评估量表(activities of daily living, ADL)和工具日常生活能力量表(instrumental activity of daily living, IADL)评估;(2)躯体功能:应用3 m步行实验、5次起坐试验和平衡能力试验评估;(3)老年合并症:评估视力下降、听力下降、慢性疼痛、排尿及排便障碍、精神障碍(焦虑、抑郁)及跌倒风险;(4)营养:应用营养评定简表(mini-nutritional assessment short-form, MNA-SF)评估;(5)认知功能:应用简易智能状态检查量表(mini-mental state examination, MMSE)评估;(6)用药:记录多重用药情况;(7)衰弱:应用FRAIL量表,包括疲劳感、活动耐力、活动能力、疾病和体质量下降,每个条目1分,共计5分, $\geq 3$ 分为衰弱;(8)社会支持系统:患者居家环境、居住方式等。

1.2.2 血清中枢神经特异蛋白100 $\beta$ 检测 患者入院常规留取静脉血,4℃条件下离心留取上清液-80℃冰箱冻存。通过酶联免疫吸附法(enzyme linked immunosorbent assay, ELISA)测定血清中枢神经特异蛋白100 $\beta$ (serum central nervous system specific protein, S100 $\beta$ ),试剂盒购自南京建成生物科技有限公司。

1.2.3 谵妄评估 采用意识模糊评估表对患者进

行谵妄评估,包括4个核心症状:(1)急性起病且病情呈波动性;(2)注意力不够集中;(3)思维紊乱;(4)意识水平改变。其中1、2项为必须,3和4满足1条即可诊断。

### 1.3 统计学处理

采用SPSS 24.0统计软件进行数据分析。计量资料以均数 $\pm$ 标准差( $\bar{x}\pm s$ )表示,组间比较采用 $t$ 检验。计数资料以例数(百分率)表示,组间比较采用 $\chi^2$ 检验。采用logistic多因素回归方程分析谵妄发生的独立危险因素。 $P<0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 2组患者一般资料比较

记录患者性别、年龄、文化程度、婚姻情况、既往病史、入院7d内有无合并症(急性感染、水电解质紊乱、心脑血管意外等)。2组患者婚姻状况、文化程度、性别、民族及既往病史方面比较,差异无统计学意义( $P>0.05$ )。患者发生急性感染3例、水电解质紊乱8例、心脑血管意外1例,其中谵妄组10例,非谵妄组2例;年龄谵妄组 $>$ 非谵妄组,2组比较差异均有统计学意义( $P<0.05$ ;表1)。

### 2.2 患者CGA情况与S100 $\beta$ 蛋白结果比较

2组患者居家环境、居住方式、多重用药率、抑郁症、营养不良发生率、多病共存发生率、衰弱状态、MMSE评分及入院时S100 $\beta$ 蛋白水平比较,差异均有统计学意义( $P<0.05$ ;表2)。

### 2.3 2组患者老年综合征情况比较

非谵妄组发生老年综合征数目( $2.23\pm 0.12$ )低于谵妄组( $4.01\pm 0.49$ );谵妄组听力障碍、吞咽障碍、便秘或失禁、尿潴留或尿失禁、慢性疼痛、跌倒风险、焦虑及抑郁发生率均高于非谵妄组,差异均有统计学意义( $P<0.05$ ;表3)。

### 2.4 高龄老年住院患者谵妄发生的危险因素分析

logistic回归分析显示,年龄、营养状况、衰弱、认知功能减退、老年综合征数量、S100 $\beta$ 水平是高龄住院患者发生谵妄的独立危险因素( $P<0.05$ ;表4)。

## 3 讨论

谵妄在高龄老人中患病率高,延长了住院时间,增加了经济负担,同时导致治疗难度加大,且跌倒、压力性损伤、死亡风险增高<sup>[7]</sup>。国外有研究表明在多病共存的终末期老年患者中,谵妄的发生率高达42%~58%<sup>[8]</sup>。2019年,Shi等<sup>[9]</sup>前瞻性研究发现,男性、疲劳、听力受损、脑肿瘤等是住院患者发生谵妄的潜在危险因素。本研究通过CGA综合评估联合S100 $\beta$ 蛋白检测,筛选出年龄、营养状况、衰弱、认知功能减退、老年综合征数量及S100 $\beta$ 蛋白升高是高龄老年住院患者发生谵妄的独立危险因素。

表 1 2组患者一般资料比较

Table 1 Comparison of baseline data between two groups

Item	Non-delirium group( <i>n</i> =322)	Delirium group( <i>n</i> =43)	<i>t</i> / $\chi^2$	<i>P</i> value
Gender[ <i>n</i> (%) ]			1.281	>0.05
Male	158(49.1)	23(53.5)		
Female	164(50.9)	20(46.5)		
Age(years, $\bar{x}\pm s$ )	83.48±3.28	87.35±6.07	1.971	<0.05
Nationality[ <i>n</i> (%) ]			1.259	>0.05
Han nationality	318(98.8)	42(97.7)		
Others	4(1.2)	1(2.3)		
Education level[ <i>n</i> (%) ]			1.322	>0.05
Elementary school	271(84.2)	16(37.2)		
Junior high school	23(7.1)	14(32.6)		
Senior high school or above	28(8.7)	13(30.2)		
Marital status[ <i>n</i> (%) ]			0.364	>0.05
Married	260(80.7)	31(72.1)		
Widowed or divorced	62(19.3)	12(27.9)		
Diabetes mellitus[ <i>n</i> (%) ]	45(14.0)	7(16.3)	0.165	>0.05
Hypertension[ <i>n</i> (%) ]	103(32.0)	12(27.9)	0.293	>0.05
Coronary heart disease[ <i>n</i> (%) ]	165(51.2)	25(58.1)	0.723	>0.05
Hyperlipidemia[ <i>n</i> (%) ]	108(33.5)	18(41.8)	1.162	>0.05
Comorbidities[ <i>n</i> (%) ]	2(0.6)	10(23.3)	4.958	<0.05

表 2 2组患者 CGA 及 S100β 蛋白结果比较

Table 2 Comparison of CGA and S100β protein results between two groups

Item	Non-delirium group( <i>n</i> =322)	Delirium group( <i>n</i> =43)	<i>t</i> / $\chi^2$	<i>P</i> value
Home environment[ <i>n</i> (%) ]			5.761	<0.05
Safe	176(54.7)	13(30.2)		
Unsafe	146(45.3)	30(69.8)		
Economic status[ <i>n</i> (%) ]			3.192	>0.05
Better	215(66.8)	19(44.2)		
Poor	107(33.2)	24(55.8)		
Home style[ <i>n</i> (%) ]			9.474	<0.05
Living alone	30(9.3)	21(48.8)		
Living with spouse or children	259(80.4)	10(23.3)		
Pension agency	33(10.3)	12(27.9)		
Multi-drug ( $\geq 5$ ) [ <i>n</i> (%) ]	40(12.4)	32(74.4)	4.386	<0.05
Depression[ <i>n</i> (%) ]	21(6.5)	24(55.8)	6.724	<0.05
Malnutrition risk[ <i>n</i> (%) ]	39(12.1)	37(86.0)	5.280	<0.05
Multiple diseases coexistence[ <i>n</i> (%) ]	103(32.0)	39(90.7)	3.761	<0.05
Weak[ <i>n</i> (%) ]	24(7.5)	19(44.2)	4.666	<0.05
MMSE score(points, $\bar{x}\pm s$ )	26.24±0.76	20.33±0.57	2.451	<0.05
S100β( $\mu\text{g/L}$ , $\bar{x}\pm s$ )	0.167±0.12	0.355±0.19	2.922	<0.05

CGA: comprehensive geriatric assessment; MMSE: mini-mental state examination; S100β: serum central nervous system specific protein.

表 3 2组患者老年综合征发生情况比较

Table 3 Comparison of occurrence of senile syndrome between two groups

Item	Non-delirium group( <i>n</i> =322)	Delirium group( <i>n</i> =43)	$\chi^2$	<i>P</i> value
Hearing impairment	56(17.4)	31(72.1)	6.755	<0.05
Vision impairment	78(24.2)	29(67.4)	4.912	<0.05
Swallowing impairment	41(12.7)	24(55.8)	7.086	<0.05
Constipation or incontinence	9(2.8)	17(39.5)	22.006	<0.05
Urinary retention or incontinence	16(5.0)	22(51.2)	15.181	<0.05
Chronic pain	29(9.0)	27(62.8)	9.381	<0.05
Risk of falling	22(6.8)	20(46.5)	10.907	<0.05
Depression	21(6.5)	24(55.8)	14.523	<0.05
Anxiety	40(12.4)	28(65.1)	8.078	<0.05

表 4 logistic 回归分析谵妄发生的危险因素

Table 4 Logistic regression analysis of risk factors for delirium

Factor	B	SE	Wald	OR	95%CI	P value
Age	0.987	0.444	4.942	2.683	1.005-4.019	<0.05
Nutritional status	0.794	0.342	5.390	2.212	1.101-5.212	<0.05
Weak	1.134	0.657	2.979	3.108	1.005-5.015	<0.05
Multi-drug	-0.078	0.333	0.055	0.925	0.444-2.113	>0.05
MMSE score	0.991	0.557	3.165	2.694	0.705-3.117	<0.05
Number of geriatric syndrome	0.345	0.111	9.660	1.412	1.025-4.041	<0.05
S100β	0.652	0.267	5.963	1.919	1.789-4.664	<0.05

MMSE: mini-mental state examination; S100β: serum central nervous system specific protein.

高龄是老年住院患者发生谵妄的独立危险因素,其发生机制可能与老年人随年龄增长,神经细胞凋亡增多,脑萎缩与功能退化,神经突触间的递质减少等因素有关<sup>[10]</sup>。而衰弱是老年人多种不良预后重要的预测因子,有研究表明衰弱患者术后发生谵妄的风险是非衰弱患者的 3.63 倍<sup>[11]</sup>。本研究发现谵妄患者的衰弱发生率显著高于非谵妄组。营养状况是衰弱的一个重要影响因素,两者相互影响,互为因果<sup>[12]</sup>。MMSE 评分主要用于早期识别老年人群中的认知功能障碍,研究表明认知功能受损是老年住院患者发生谵妄的独立危险因素<sup>[13]</sup>。本研究中非谵妄组 MMSE 评分明显高于谵妄组,logistic 回归分析显示低 MMSE 评分是高龄老年住院患者发生谵妄的独立危险因素。

在老年共病患者中,老年综合征的发生率竟达 100%<sup>[14]</sup>。本研究结果显示,高龄老年人的老年综合征发病率与住院期间谵妄的发生有相关性,而高龄老年患者入院后因多种因素诱发感染、水电解质紊乱容易导致患者发生谵妄,临床上对于此类患者需加强临床观察,及时处理急性并发症,以改善患者预后和减少住院期间谵妄发生的可能。

S100β 蛋白是目前公认的可以反映脑损伤的指标之一,作为评估脑损伤程度和预后的指标具有较高的灵敏性和特异性。本研究发现,在高龄老年谵妄患者中 S100β 的水平显著高于非谵妄患者,但在患者入院时就已经升高,可能与高龄、样本量较少、检验误差有关,但也可能与患者入院时合并脑组织缺血缺氧等因素有关,尚需进一步研究以证实。

本研究的局限性在于没有动态观察干预后谵妄的改善情况,S100β 蛋白和其他反映脑组织损伤蛋白如脑源性神经营养因子、神经元特异性烯醇化酶等在患者发生谵妄前后的变化,这些不足将在下一步的临床研究中加以完善。

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