·临床研究·

不同性别急性缺血性卒中后抑郁患者的临床异质性

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【摘 要】 目的 探讨不同性别卒中后抑郁(PSD)患者临床症状的异质性。**方法** 选取2020年12月至2022年2月于华北理工大学附属医院501例急性缺血性脑卒中患者为研究对象,收集其一般临床资料,入院24 h内进行美国国立卫生研究院脑卒中评分(NIHSS)、日常生活活动能力(ADL)评分,入院1周后采用24项汉密尔顿抑郁量表(HAMD-24)评估患者抑郁情绪。采用SPSS 26.0软件进行数据分析。根据数据类型,组间比较分别采用t检验、非参数检验及χ^2检验。**结果** 501例脑卒中患者中,PSD患者173例,其中男性96例,女性77例。男性PSD患者NIHSS评分显著高于女性[(5.44±4.25)和(3.97±5.63)分;$P<0.01$],男性PSD患者ADL评分显著低于女性[(68.07±20.10)和(79.35±21.69)分;$P<0.01$]。HAMD-24单项症状比较,男性PSD患者抑郁情绪得分低于女性PSD患者[1.00(0.00,2.00)和1.00(1.00,2.00)分;$P<0.05$],男性PSD患者的工作和兴趣[0.00(0.00,1.00)和0.00(0.00,0.00)分]、迟缓[0.00(0.00,1.00)和0.00(0.00,0.00)分]、激越[0.50(0.00,2.00)和0.00(0.00,1.00)分]、全身症状[2.00(1.00,3.00)和1.00(0.00,2.00)分]、体质量减轻[1.00(0.00,2.00)和0.00(0.00,1.00)分]、自知力[0.00(0.00,1.00)和0.00(0.00,0.00)分]得分均高于女性PSD患者(均$P<0.05$)。HAMD-24各因子比较,男性PSD患者体质量减轻[1.00(0.00,2.00)和0.00(0.00,1.00)分]、绝望感因子[1.00(0.00,2.00)和0.00(0.00,2.00)分]均高于女性PSD患者(均$P<0.05$)。不同性别PSD患者症状严重系数较高的因子均为焦虑/躯体化和睡眠障碍。**结论** 不同性别PSD患者临床症状存在异质性,临床工作中应针对不同性别脑卒中患者的临床症状予以鉴别。

【关键词】 性别;卒中后抑郁;临床异质性;汉密尔顿抑郁量表
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Clinical heterogeneity of depression after acute ischemic stroke between genders

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【Abstract】 Objective To explore the heterogeneity of clinical symptoms between genders in patients with post-stroke depression (PSD). **Methods** A total of 501 patients with acute ischemic stroke in Affiliated Hospital of North China University of Science and Technology from December 2020 to February 2022 were selected as the subjects. Their general clinical data were collected, and they were evaluated with National Institutes of Health Stroke Scale (NIHSS) and the activities of Daily Living (ADL) scale within 24 hours after admission. One week after admission, the depressive mood of patients was evaluated using the 24-item Hamilton Depression Scale (HAMD-24). SPSS 26.0 was used for statistical analysis. Depending on data type, comparison between groups was performed using t test, non-parametric test or χ^2 test. **Results** Among 501 patients with stroke, 173 (96 men and 77 women) had PSD. PSD men scored significantly higher than women [(5.44±4.25) *vs* (3.97±5.63) points; $P<0.01$] on NIHSS and significantly lower [(68.07±20.10) *vs* (79.35±21.69) points; $P<0.01$] on ADL scale. With the single symptom of HAMD-24, PSD men scored significantly lower than PSD women in depression [1.00(0.00,2.00) *vs* 1.00(1.00,2.00) points; $P<0.05$], but significantly higher in work and interest [0.00(0.00,1.00) *vs* 0.00(0.00,0.00) points], tardiness [0.00(0.00,1.00) *vs* 0.00(0.00,0.00) points], agitation [0.50(0.00,2.00) *vs* 0.00(0.00,1.00) points], systemic symptoms [2.00(1.00,3.00) *vs* 1.00(0.00,2.00) points], weight

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loss [1.00(0.00,2.00) *vs* 0.00(0.00,1.00) points] and self-awareness [0.00(0.00,1.00) *vs* 0.00(0.00,0.00) points] ($P<0.05$ for all). Among HAMD-24 symptoms, the scores for weight loss [1.00(0.00, 2.00) *vs* 0.00(0.00, 1.00) points] and for despair [1.00(0.00,2.00) *vs* 0.00(0.00,2.00) points] were higher in PSD men than in PSD women ($P<0.05$ for both). Anxiety, somatization, and sleep disorders were the factors with higher symptom severity coefficients in PSD patients of both genders. **Conclusion** The clinical symptoms of PSD patients are heterogeneous between genders. Attention should be paid to the gender differences in symptoms among stroke patients of in clinical practice.

【**Key words**】 gender; post-stroke depression; clinical heterogeneity; Hamilton Depression Scale

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脑卒中是成年人残疾的主要原因,脑卒中患者在短期或长期内可能出现精神障碍,脑卒中患者最常见的心理问题包括抑郁、焦虑和压力[1]。其中,卒中后抑郁(post-stroke depression, PSD)是严重影响脑卒中患者预后的精神障碍,PSD 患病率介于 22%~40%,大多数研究显示女性(5.9%~78.3%)的发生率较男性(4.7%~65.2%)高[2]。性别可能影响抑郁症的发生率及其临床特征[3],从而影响抑郁的早期识别、诊治及预后,重视不同性别 PSD 患者临床症状异质性具有重要意义。PSD 临床症状在不同性别患者之间是否存在差异、存在怎样的差异尚不明确[4],目前关于不同性别 PSD 患者临床症状异质性的相关研究较少。因此,本研究旨在探讨不同性别 PSD 患者临床症状的异质性,为 PSD 个性化诊疗提供理论依据。

1 对象与方法

1.1 研究对象

纳入 2020 年 12 月至 2022 年 2 月于华北理工大学附属医院收治的急性缺血性脑卒中患者 501 例。纳入标准:(1)符合《中国急性缺血性脑卒中诊治指南 2014》[5] 诊断标准,发病时间≤2 周;(2)年龄≥18 岁;(3)无语言表达障碍、意识障碍,可配合相关量表的评估;(4)已签署知情同意书。排除标准:(1)有语言表达、意识障碍以及一般状况差的患者;(2)合并或者既往有精神疾病,包括抑郁症及精神分裂症等;(3)合并重度感染、创伤及恶性肿瘤等严重器质性疾病。本研究通过华北理工大学附属医院医学伦理学委员会批准。

1.2 方法

入院 24 h 内收集患者一般临床资料,包括性别、年龄、体质量指数(body mass index, BMI)、婚姻状况、文化程度、既往史、吸烟史及饮酒史等。采用美国国立卫生研究院脑卒中评分(National Institutes of Health Stroke Scale, NIHSS)进行神经功能缺损程度评估,采用日常生活活动能力(activities of daily living, ADL)量表进行日常生活活动能力评估。入院 7 d 后采用 24 项汉密尔顿抑郁量表(24-item Hamilton depression scale, HAMD-24)评估患者抑郁情况。

1.3 研究工具

(1)HAMD-24:HAMD-24 是使用最普遍的抑郁评定量表,内部一致性良好,各条目与总分相关性好,分析各条目得分及因子构成,有助于判断抑郁严重程度[6]。因子分=每个因子各项得分的算术和,通过因子分析,可以反映靶症状群的临床特点[7]。症状严重系数=该项因子实际测得的分数之和/(n×该项因子的最高分)。症状严重系数越大,表示该症状群越突出。(2)NIHSS:采用 NIHSS 评估神经功能缺损程度,分值越高,神经功能缺损程度越重[8]。(3)ADL 量表:采用 ADL 量表评估日常生活活动能力,分值越高,日常生活活动能力越好[9]。

1.4 统计学处理

采用 SPSS 26.0 统计软件进行数据分析。符合正态分布的计量资料用均数±标准差($\bar{x}\pm s$)表示,采用 t 检验;非正态分布的计量资料,用中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,采用非参数检验。计数资料用例数(百分率)表示,采用 χ^2 检验。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 不同性别 PSD 患者一般临床资料比较

女性体质量指数(body mass index, BMI)水平高于男性,吸烟史、饮酒史比例低于男性组,差异均有统计学意义(均 $P<0.05$);其余指标比较,差异均无统计学意义(表 1)。

2.2 不同性别 PSD 患者神经功能缺损及病灶部位比较

男性 PSD 患者的 NIHSS 评分高于女性,ADL 评分低于女性,差异均有统计学意义(均 $P<0.05$);不同性别 PSD 患者病灶部位比较,差异无统计学意义(表 2)。

表1 不同性别PSD患者一般临床资料比较

Table 1 Comparison of general clinical data between PSD patients of different genders

Item	Male(n=96)	Female(n=77)	t/χ^2	P value
Age(years, $\bar{x}\pm s$)	63.6±10.7	65.0±10.6	−0.866	0.388
BMI(kg/m^2, $\bar{x}\pm s$)	24.8±2.8	26.3±3.4	−2.328	0.020
Marital status[n(%)]			2.718	0.437
Unmarried	1(1.0)	3(3.9)		
Married	86(89.6)	66(85.7)		
Divorced	3(3.1)	1(1.3)		
Death of a spouse	6(6.3)	7(9.1)		
Education level[n(%)]			−1.378	0.168
Elementary school or below	30(31.3)	33(42.9)		
Middle school	44(45.8)	31(40.3)		
High school	20(20.8)	6(7.8)		
College or above	2(2.1)	7(9.1)		
Hypertension[n(%)]	59(61.5)	52(67.5)	0.686	0.408
Diabetes mellitus[n(%)]	45(46.9)	42(54.5)	1.006	0.316
Heart disease[n(%)]	16(16.7)	18(23.4)	1.218	0.270
Hyperlipidemia[n(%)]	42(43.8)	40(51.9)	1.152	0.283
Smoking[n(%)]	50(52.1)	4(5.2)	43.752	<0.001
Drinking[n(%)]	43(44.8)	1(1.3)	42.619	<0.001

PSD: post-stroke depression; BMI: body mass index.

表2 不同性别PSD患者神经功能缺损及病灶部位比较

Table 2 Comparison of neurologic deficits and infarction area between PSD patients of different genders

Item	Male (n=96)	Female (n=77)	t/χ^2	P value
NIHSS(points, $\bar{x}\pm s$)	5.44±4.25	3.97±5.63	−3.621	<0.001
ADL(points, $\bar{x}\pm s$)	68.07±20.10	79.35±21.69	−3.785	<0.001
Infarction area [n(%)]			5.226	0.632
Frontal lobe	32(33.3)	32(41.6)		
Parietal lobe	28(29.2)	30(39.0)		
Temporal lobe	25(26.0)	27(35.1)		
Occipital lobe	17(17.7)	9(11.7)		
Basal ganglia region	45(46.9)	32(41.6)		
Brain stem	15(15.6)	11(14.3)		
Cerebellum	10(10.4)	13(16.9)		
Other areas	16(16.7)	18(23.4)		

PSD: post-stroke depression; NIHSS: National Institutes of Health Stroke Scale; ADL: activities of daily living.

2.3 不同性别PSD患者HAMD-24各项症状得分比较

不同性别PSD患者抑郁情绪、工作和兴趣、迟缓、激越、全身症状、体质量减轻及自知力比较,差异均有统计学意义(均P<0.05);2组患者HAMD-24总分、有罪感、自杀及睡眠等方面比较,差异均无统计学意义(表3)。

2.4 不同性别PSD患者HAMD-24各因子得分比较

2组PSD患者体质量因子、绝望感因子比较,差异均有统计学意义(均P<0.05);2组患者焦虑/躯体化、认知障碍、日夜变化、阻滞、睡眠障碍因子比较,差异均无统计学意义(表4)。

2.5 不同性别PSD患者症状严重系数比较

不同性别PSD患者症状严重系数较高的因子均为焦虑/躯体化和睡眠障碍,详见表5。

3 讨 论

世界卫生组织报告显示每年有1 500万脑卒中患者,脑卒中已被列为第三大致命疾病[10],PSD对脑卒中患者预后产生负面影响,持续的抑郁不仅加剧疾病恶化,还会导致社会功能缺陷,增加自杀风险。PSD在男性、女性中都非常普遍,但在PSD的急性期和慢性期女性发生率普遍高于男性[11]。在脑卒中特定人群的研究中,性别对抑郁异质性的影响远比其他人群更为显著,PSD存在的临床异质性影响疾病的早期识别、诊治及预后。例如,肿瘤异质性是肿瘤演进过程中分子生物学或基因方面发生改变,使不同肿瘤细胞生长速度、侵袭能力及药物敏感性等产生差异。肿瘤异质性不仅影响治疗,在肿瘤发展和患者预后评估中至关重要,肿瘤异质性为实现临床精准诊治、克服耐药问题带来重大挑战[12]。

表 3 不同性别 PSD 患者 HAMD-24 各项症状得分比较

Table 3 Comparison of HAMD-24 between PSD patients of different genders [points, $M(Q_1, Q_3)$]

Items	Male(n=96)	Female(n=77)	Z	P value
HAMD-24	17.00(12.00,25.75)	14.00(9.50,21.00)	−1.833	0.067
Depressed mood	1.00(0.00,2.00)	1.00(1.00,2.00)	−2.053	0.040
Feeling of guilt	1.00(0.00,2.00)	1.00(1.00,2.00)	−0.815	0.415
Suicide	1.00(0.00,1.75)	1.00(0.00,1.00)	−0.343	0.732
Insomnia-early	1.00(0.00,2.00)	1.00(1.00,2.00)	−0.233	0.816
Insomnia-middle	1.00(0.00,2.00)	0.00(0.00,1.50)	−0.820	0.412
Insomnia-late	1.00(0.00,1.00)	1.00(0.00,1.50)	−0.861	0.389
Work and interests	0.00(0.00,1.00)	0.00(0.00,0.00)	−2.161	0.031
Retardation	0.00(0.00,1.00)	0.00(0.00,0.00)	−2.244	0.025
Agitation	0.50(0.00,2.00)	0.00(0.00,1.00)	−2.612	0.009
Psychic anxiety	0.00(0.00,1.00)	0.00(0.00,1.00)	−1.292	0.196
Somatic anxiety	1.50(0.25,3.00)	2.00(1.00,3.00)	−0.031	0.975
Gastro-intestinal	2.00(1.00,3.00)	2.00(1.00,3.00)	−0.084	0.933
General somatic symptoms	2.00(1.00,3.00)	1.00(0.00,2.00)	−3.443	0.001
Genital symptoms	0.00(0.00,1.00)	0.00(0.00,0.00)	−1.856	0.063
Hypochondriasis	1.00(0.00,2.00)	1.00(0.00,2.00)	−1.274	0.203
Loss of weight	1.00(0.00,2.00)	0.00(0.00,1.00)	−2.682	0.007
Insight	0.00(0.00,1.00)	0.00(0.00,0.00)	−2.562	0.010
Diurnal variation	0.00(0.00,0.00)	0.00(0.00,0.00)	−0.709	0.478
Depersonalization/derealization	0.00(0.00,0.00)	0.00(0.00,0.00)	−1.545	0.122
Paranoid symptoms	0.00(0.00,0.00)	0.00(0.00,0.00)	−1.578	0.114
Paranoid symptoms	0.00(0.00,0.00)	0.00(0.00,0.00)	−0.180	0.857
Helplessness	0.00(0.00,0.00)	0.00(0.00,0.00)	−0.987	0.324
Hopelessness	1.00(0.00,2.00)	0.00(0.00,1.00)	−1.666	0.096
Worthlessness	0.00(0.00,1.00)	0.00(0.00,1.00)	−1.039	0.299

PSD: post-stroke depression; HAMD-24: Hamilton depression scale.

表 4 不同性别 PSD 患者 HAMD-24 各因子得分比较

Table 4 Comparison of HAMD-24 factor scores between PSD patients of different genders [points, $M(Q_1, Q_3)$]

Factor	Male(n=96)	Female(n=77)	Z	P value
Anxiety/somatization	5.00(4.00,8.00)	5.00(4.00,8.00)	−0.406	0.685
Body weight	1.00(0.00,2.00)	0.00(0.00,1.00)	−2.682	0.007
Cognitive disturbance	3.00(1.00,6.00)	2.00(1.00,5.00)	−0.956	0.339
Diurnal-variation	0.00(0.00,0.00)	0.00(0.00,0.00)	−0.709	0.478
Retardation	2.00(1.00,4.00)	2.00(1.00,4.00)	−0.758	0.449
Sleep disturbance	3.00(2.00,5.00)	3.00(2.00,4.50)	−0.513	0.608
Hopelessness	1.00(0.00,2.00)	0.00(0.00,2.00)	−2.022	0.043

PSD: post-stroke depression; HAMD-24: 24-item Hamilton Depression Scale.

表 5 不同性别 PSD 患者症状严重系数比较

Table 5 Comparison of symptom severity coefficients in PSD patients by different genders

Factor	Male(n=96)			Female(n=77)		
	Actual score (points)	Top score (points)	Symptom severity coefficient	Actual score (points)	Top score (points)	Symptom severity coefficient
Anxiety/somatization	574	1344	0.43	440	1078	0.41
Body weight	93	384	0.24	42	308	0.14
Cognitive disturbance	370	1440	0.26	268	1155	0.23
Diurnal-variation	26	384	0.07	21	308	0.07
Retardation	261	960	0.27	184	770	0.24
Sleep disturbance	311	864	0.36	241	693	0.35
Hopelessness	164	864	0.19	106	693	0.15

Symptom severity coefficient = actual score/top score, the greater the symptom severity coefficient, the more severe the symptom cluster. PSD: post-stroke depression.

本研究结果显示,PSD发生率34.5%(173/501),其中男性30.6%(96/314)、女性41.2%(77/187),与国外的研究结果类似[2]。女性PSD患者BMI指数较男性大,婚姻状况、文化程度等无明显差异。女性PSD的吸烟史、饮酒史较男性少,但高血压病、糖尿病、冠心病及高脂血症等既往病史与男性相比无差异,既往病史等方面未表现出异质性,提示脑卒中常见危险因素可能并不是女性PSD的危险因素[13],不同性别PSD患者的危险因素可能存在异质性,且不同性别PSD患者神经功能缺损、日常生活活动能力存在异质性。提示需要积极关注不同性别PSD患者的BMI指数、NIHSS评分及ADL评分等存在异质性的指标,有利于PSD的早期识别。

本研究结果显示,女性PSD患者的抑郁情绪较男性突出,工作和兴趣、迟缓、激越、全身症状、体质量减轻、自知力方面与男性比较均存在差异。而在精神性焦虑、躯体性焦虑、胃肠道症状方面与男性比较无差异,说明女性在脑卒中急性期的情感障碍以抑郁情绪为主,而这种抑郁情绪可能影响女性脑卒中患者的预后。在因子结构方面,不同性别PSD患者均以体质量减轻、绝望感为主要表现,女性PSD患者体质量减轻、绝望感因子分均低于男性,可能是因为该研究中女性的BMI基数大,女性在遭受应激时,擅于通过积极应对方式发泄情绪,不容易产生绝望感[14]。有研究表明女性PSD的诊治率低于男性[15],PSD诊治严重不足可能与PSD的上述症状具有一定的隐蔽性、异质性有关,早期不易被发现[16],提示需要对脑卒中患者临床症状进行积极细致的筛查[17]。男性PSD患者神经功能缺损程度较重、日常生活活动能力较差,针对男性神经功能缺损程度重的脑卒中患者应更加警惕PSD的发生。男性PSD患者以全身症状、睡眠障碍等症状更加突出,要积极关注男性患者躯体不适、睡眠情况等。女性PSD患者临床症状以抑郁情绪更加突出,针对女性患者,临床工作中应注意观察患者情绪变化。在不同性别脑卒中患者出现上述症状时,应考虑患者是否伴发抑郁。

性别对PSD的影响机制尚未明确,不同性别PSD患者存在临床症状异质性的可能机制:(1)人格特征,易受压力和感觉负面情绪倾向有关的人格特征易卒中后抑郁[18],如较高的神经质评分与较高的MDD发生率、更高的MDD复发率、较严重的抑郁症状的关系;(2)生物学因素,如性腺激素和遗传的差异[19];(3)心理因素,如性别特异性症状概况;(4)社会因素,如对压力源的性别特异性暴露[20]。

综上,女性PSD发生率高于男性,不同性别PSD患者的神经功能缺损程度、日常生活活动能力、抑郁症状存在异质性。因此,临床医师应根据患者的性别、临床症状特征等判断患者病情,制定个性化的诊治策略。

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