

急性重症脑卒中患者脑心交互现象的临床特点与预后分析

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【摘要】 目的 分析急性重症脑卒中患者脑心交互现象(BHI)的临床特点和预后。方法 选择2015年1月1日至2017年12月31日首都医科大学宣武医院神经内科重症病房收治的急性重症脑卒中患者,收集其一般资料、BHI相关指标、预后结局。按照是否出现BHI将患者分为BHI组和非BHI组,比较两组患者各指标的差异,并使用多因素Logistic回归分析发生BHI的独立危险因素。此外,再根据是否存在Takotsubo综合征(TTS)将BHI组患者进行亚组分析,采用多因素Logistic回归分析发生TTS的独立危险因素。结果 共纳入119例急性重症脑卒中患者,有91例(76.5%)并发BHI(BHI组),其中有17例(14.3%)患者发生TTS。与非BHI组比较,BHI组脑血管疾病史比例低(20.9%比42.9%, $P=0.020$),吸烟史比例低(25.3%比50.0%, $P=0.013$),他汀类药物使用比例低(16.5%比50.0%, $P=0.000$),总胆固醇(TC)水平低(mmol/L : 3.97 ± 1.05 比 4.43 ± 0.88 , $P=0.039$),低密度脂蛋白(LDL)水平低(mmol/L : 2.30 ± 0.76 比 3.00 ± 0.84 , $P=0.000$);多因素Logistic回归分析显示,他汀类药物使用[优势比(OR)=0.222,95%可信区间(95% CI)=0.075~0.658, $P=0.007$]和脑血管疾病史($OR=0.321$,95% $CI=0.113 \sim 0.912$, $P=0.033$)是BHI的保护性因素。与非TTS亚组比较,TTS亚组糖尿病史比例更低(0%比37.8%, $P=0.002$),糖化血红蛋白(HbA1c)水平更低[0.055(0.050,0.056)比0.064(0.056,0.075), $P=0.000$],TC水平更高(mmol/L : 4.70 ± 1.16 比 3.80 ± 0.95 , $P=0.001$),入院第1天平均动脉压[MAP(mmHg , $1 \text{ mmHg}=0.133 \text{ kPa}$):114(98,122)比103(94,108), $P=0.042$],第3天舒张压[DBP(mmHg):82(77,94)比67(59,86), $P=0.002$]和第3天MAP[mmHg :106(95,114)比94(80,106), $P=0.015$]更高;多因素Logistic回归分析显示,入院第3天MAP升高是TTS的独立危险因素($OR=11.833$,95% $CI=1.113 \sim 125.779$, $P=0.040$),HbA1c增高是TTS的保护性因素($OR=0.022$,95% $CI=0.001 \sim 0.345$, $P=0.006$)。合并BHI的急性重症脑卒中患者预后不良率比未合并BHI者更高(34.1%比14.3%, $P=0.045$)。结论 急性重症脑卒中患者BHI发生率较高,且预示预后不良;可能可以通过应用他汀类降脂药和缺血预适应以及管控血压来减少BHI的发生。

【关键词】 重症脑卒中; 脑心交互; Takotsubo综合征

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Clinical characteristics and prognosis of brain-heart interaction in patients with acute severe stroke

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【Abstract】 **Objective** To investigate and analyze the clinical characteristics and prognosis of brain-heart interaction (BHI) in patients with acute severe stroke. **Methods** The patients with acute severe stroke admitted to Neurointensive Care Unit of Xuanwu Hospital, Capital Medical University from January 1st, 2015 to December 31st, 2017 were enrolled. The clinical data, indicators related to BHI and prognosis were collected. Patients were divided into BHI group and non-BHI group according to the presence or absence of BHI. The differences of each index were compared between two groups. The independent risk factors of BHI were analyzed using multivariate Logistic regression analysis. In addition, subgroup analysis was performed for patients in the BHI group based on the presence or absence of Takotsubo syndrome (TTS), and multivariate Logistic regression was used to analyze independent risk factors for TTS. **Results** 119 patients with acute severe stroke were analyzed, BHI occurred in 91 cases (76.5%), and 17 cases (14.3%) TTS were included in the BHI group. Compared with non-BHI group, BHI group had lower rates of cerebrovascular disease history (20.9% vs. 42.9%, $P=0.020$), lower smoking history (25.3% vs. 50.0%, $P=0.013$), lower statin use (16.5% vs. 50.0%, $P=0.000$), lower total cholesterol [TC (mmol/L): 3.97 ± 1.05 vs. 4.43 ± 0.88 , $P=0.039$], and lower low density lipoprotein [LDL (mmol/L): 2.30 ± 0.76 vs. 3.00 ± 0.84 , $P=0.000$]. Multivariate Logistic regression showed that the use of statins [odds ratio (OR) = 0.222, 95% confidence interval (95% CI) = 0.075–0.658, $P=0.007$] and the history of cerebrovascular diseases ($OR=0.321$, 95% $CI=0.113 \sim 0.912$, $P=0.033$) were protective factors

of BHI. Compared with non-TTS subgroup, TTS subgroup had a lower percentage of diabetes history (0% vs. 37.8%, $P = 0.002$), lower glycated hemoglobin [HbA1c: 0.055 (0.050, 0.056) vs. 0.064 (0.056, 0.075), $P = 0.000$], higher TC (mmol/L: 4.70 ± 1.16 vs. 3.80 ± 0.95 , $P = 0.001$), first day mean arterial pressure [MAP (mmHg, 1 mmHg = 0.133 kPa): 114 (98, 122) vs. 103 (94, 108), $P = 0.042$], third day diastolic blood pressure [DBP (mmHg): 82 (77, 94) vs. 67 (59, 86), $P = 0.002$], and third day MAP [mmHg: 106 (95, 114) vs. 94 (80, 106), $P = 0.015$]. Multivariate Logistic regression analysis showed that increased MAP on the third day of admission was an independent risk factor for TTS ($OR = 11.833$, $95\%CI = 1.113-125.779$, $P = 0.040$), increased HbA1c was protective factor of TTS ($OR = 0.022$, $95\%CI = 0.001-0.345$, $P = 0.006$). The rate of poor outcome at discharge of all the BHI patients were higher than those of the non-BHI patients (34.1% vs. 14.3%, $P = 0.045$).

Conclusions Acute severe stroke patients with high incidence of acquiring BHI and having BHI is associated with poor outcome after discharge. Using statins, ischemic preconditioning and control blood pressure, the occurrence of BHI can be reduced and might be beneficial to patients.

【Key words】 Severe stroke; Brain-heart interaction; Takotsubo syndrome

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1947年, Byer等^[1]首次报道脑血管疾病可导致心肌损伤和心律失常。脑卒中发生后,脑心交互现象(BHI)可能会继发心肌损伤、缺血样心电图改变、心律失常、心功能不全等情况^[2-4],并包括一种特殊类型,即Takotsubo综合征(TTS)^[2],且缺血性脑血管病患者脑梗死面积与心脏并发症的严重程度呈正相关^[5]。急性重症脑卒中对神经系统造成严重损害后,合并出现心脏并发症会进一步导致患者预后不良,全因病死率、心因病死率明显增高^[2-3,6]。然而目前对重症脑卒中后BHI仍缺乏足够的认识,缺乏有效的预防和治疗手段。本研究通过回顾性分析急性重症脑卒中患者BHI的临床特点和预后,并筛选BHI、TTS的危险因素,以期早期识别BHI,进行个体化的监测和干预,以有效改善患者预后。

1 对象和方法

1.1 研究对象:选择2015年1月1日至2017年12月31日本院神经内科重症病房收治的急性重症脑卒中患者。

1.1.1 纳入标准:①年龄 ≥ 18 岁;②头颅磁共振成像(MRI)或CT证实脑出血或脑梗死;③发病1周内;④格拉斯哥昏迷评分(GCS) ≤ 8 分或美国国立卫生研究院卒中量表(NIHSS) ≥ 16 分。

1.1.2 排除标准:既往有心脏病史;临床资料不全。

1.2 伦理学:本研究符合医学伦理学标准,经医院伦理委员会审批通过(审批号:2019009),所有治疗及临床检查均获得过患者亲属的知情同意。

1.3 观察指标:收集患者性别、年龄、既往病史、脑卒中类型、脑卒中部位,入院时GCS和NIHSS评分,入院后连续3d的血压,入院后首次心电图、心脏彩超、血浆N末端脑钠肽前体(NT-proBNP)、肌酸激酶同工酶(CK-MB)、肌红蛋白(MYO)、心肌肌钙蛋白I(cTnI)、空腹血糖、糖化血红蛋白(HbA1c)、甘油三

酯(TG)、总胆固醇(TC)和低密度脂蛋白(LDL)水平,出院时生存、死亡及预后不良情况。改良Rankin评分(mRS) ≥ 5 分为预后不良^[7]。

1.4 分组:根据是否存在BHI现象^[2]将患者分为BHI组和非BHI组。再根据是否存在TTS^[8]将BHI患者分为TTS亚组和非TTS亚组。

1.5 统计学方法:应用SPSS 20.0统计软件分析数据。正态分布的计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,组间比较采用两独立样本 t 检验;非正态分布的计量资料以中位数(四分位数)[$M(Q_L, Q_U)$]表示,组间比较采用Mann-Whitney U 检验;计数资料以频数和百分比表示,组间比较采用 χ^2 检验或Fisher精确检验。使用多因素Logistic回归分析BHI和TTS的独立危险因素。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者一般资料:共纳入119例患者,男性71例(59.7%),女性48例(40.3%);年龄(64.4 ± 12.5)岁。119例患者中91例并发BHI,发生率为76.5%;BHI患者中有17例(14.3%)存在TTS。

2.2 急性重症脑卒中患者发生BHI的危险因素(表1~2):与非BHI组比较,BHI组脑血管疾病史、吸烟史、他汀类药物使用比例以及TC、LDL水平更低(均 $P < 0.05$)。多因素Logistic回归分析显示,他汀类药物使用和脑血管疾病史是BHI的保护性因素(均 $P < 0.05$)。

2.3 急性重症脑卒中患者发生TTS的危险因素(表1,表3):与非TTS亚组比较,TTS亚组糖尿病史比例、HbA1c水平更低,TC、入院第1天平均动脉压(MAP)、入院第3天DBP和MAP更高(均 $P < 0.05$)。多因素Logistic回归分析显示,入院第3天MAP升高是TTS的独立危险因素,HbA1c水平增高是TTS的保护因素(均 $P < 0.05$)。

表1 各组急性重症脑卒中患者基线资料、实验室指标及预后指标比较

| 变量 | BHI组 (n=91) | 非BHI组 (n=28) | $\chi^2/t/Z$ 值 | P值 | TTS亚组 (n=17) | 非TTS亚组 (n=74) | $\chi^2/t/Z$ 值 | P值 |
|----------------------------------|---------------------|---------------------|----------------|-------|---------------------|---------------------|----------------|-------|
| 男性[例(%)] | 51(56.0) | 20(71.4) | 2.106 | 0.147 | 13(76.5) | 38(51.4) | 3.541 | 0.060 |
| 年龄(岁, $\bar{x} \pm s$) | 65.4 ± 13.3 | 61.3 ± 9.0 | 1.520 | 0.131 | 63.9 ± 14.0 | 65.7 ± 13.3 | -0.513 | 0.609 |
| 既往史[例(%)] | | | | | | | | |
| 高血压史 | 69(75.8) | 18(64.3) | 1.450 | 0.229 | 15(88.2) | 54(73.0) | 1.023 | 0.312 |
| 糖尿病史 | 28(30.8) | 12(42.9) | 1.402 | 0.236 | 0(0) | 28(37.8) | 9.291 | 0.002 |
| 脑血管疾病史 | 19(20.9) | 12(42.9) | 5.369 | 0.020 | 1(5.9) | 18(24.3) | 1.839 | 0.175 |
| 吸烟史 | 23(25.3) | 14(50.0) | 6.110 | 0.013 | 5(29.4) | 18(24.3) | 0.016 | 0.900 |
| 饮酒史 | 12(13.2) | 2(7.1) | 0.284 | 0.594 | 2(11.8) | 10(13.5) | 0.000 | 1.000 |
| GCS[分, $M(Q_L, Q_U)$] | 7(5, 9) | 8(5, 9) | -0.297 | 0.766 | 7(4, 11) | 7(6, 9) | -0.474 | 0.635 |
| NIHSS[分, $M(Q_L, Q_U)$] | 22(18, 31) | 20(17, 32) | -1.107 | 0.268 | 21(18, 32) | 22(18, 31) | -0.276 | 0.782 |
| 血脂(mmol/L, $\bar{x} \pm s$) | | | | | | | | |
| TC | 3.97 ± 1.05 | 4.43 ± 0.88 | -2.085 | 0.039 | 4.70 ± 1.16 | 3.80 ± 0.95 | 3.396 | 0.001 |
| TG | 1.52 ± 2.26 | 1.20 ± 0.55 | 0.749 | 0.455 | 2.92 ± 4.96 | 1.21 ± 0.58 | 1.422 | 0.174 |
| LDL | 2.30 ± 0.76 | 3.00 ± 0.84 | -4.058 | 0.000 | 2.37 ± 0.70 | 2.29 ± 0.78 | 0.415 | 0.679 |
| 空腹血糖 [mmol/L, $M(Q_L, Q_U)$] | 9.13(6.90, 13.09) | 7.90(6.12, 12.43) | -1.504 | 0.133 | 7.90(6.65, 10.94) | 9.93(7.22, 13.74) | -1.375 | 0.169 |
| HbA1c [$M(Q_L, Q_U)$] | 0.062(0.055, 0.073) | 0.061(0.058, 0.078) | -0.376 | 0.707 | 0.055(0.050, 0.056) | 0.064(0.056, 0.075) | -3.546 | 0.000 |
| 血压[mmHg, $M(Q_L, Q_U)$] | | | | | | | | |
| 第1天SBP | 150(126, 166) | 154(126, 165) | -0.646 | 0.518 | 160(137, 180) | 147(126, 159) | -1.905 | 0.057 |
| 第1天DBP | 81(68, 90) | 81(74, 88) | -0.025 | 0.980 | 88(78, 100) | 79(66, 88) | -1.905 | 0.057 |
| 第1天MAP | 104(94, 115) | 103(98, 111) | -0.069 | 0.945 | 114(98, 122) | 103(94, 108) | -2.038 | 0.042 |
| 第2天SBP | 149(135, 160) | 143(140, 154) | -0.451 | 0.652 | 158(130, 163) | 148(135, 159) | -1.263 | 0.206 |
| 第2天DBP | 76(67, 86) | 74(69, 89) | -0.602 | 0.547 | 83(73, 101) | 76(67, 85) | -1.947 | 0.052 |
| 第2天MAP | 99(93, 113) | 101(94, 109) | -0.094 | 0.925 | 109(92, 120) | 98(93, 108) | -1.580 | 0.114 |
| 第3天SBP | 140(125, 159) | 144(133, 158) | -0.952 | 0.341 | 152(130, 157) | 139(124, 159) | -0.782 | 0.434 |
| 第3天DBP | 73(60, 88) | 76(67, 83) | -0.313 | 0.754 | 82(77, 94) | 67(59, 86) | -3.097 | 0.002 |
| 第3天MAP | 95(82, 107) | 98(92, 104) | -0.878 | 0.380 | 106(95, 114) | 94(80, 106) | -2.432 | 0.015 |
| 脑卒中类型[例(%)] | | | | | | | | |
| 脑梗死 | 73(80.2) | 18(64.3) | 3.021 | 0.082 | 13(76.5) | 60(81.1) | 0.009 | 0.926 |
| 脑出血 | 12(13.2) | 6(21.4) | 0.582 | 0.446 | 4(23.5) | 8(10.8) | 1.000 | 0.317 |
| 梗死伴出血 | 6(6.6) | 4(14.3) | 0.798 | 0.372 | 0(0) | 6(8.1) | 0.453 | 0.501 |
| 脑卒中部位[例(%)] | | | | | | | | |
| 额叶 | 48(52.7) | 16(57.1) | 0.166 | 0.683 | 8(47.1) | 40(54.1) | 0.271 | 0.602 |
| 顶叶 | 36(39.6) | 10(35.7) | 0.134 | 0.715 | 8(47.1) | 28(37.8) | 0.492 | 0.483 |
| 颞叶 | 42(46.2) | 18(64.3) | 2.816 | 0.093 | 8(47.1) | 34(45.9) | 0.007 | 0.934 |
| 枕叶 | 19(20.9) | 8(28.6) | 0.722 | 0.395 | 3(17.6) | 16(21.6) | 0.001 | 0.974 |
| 岛叶 | 26(28.6) | 8(28.6) | 0.000 | 1.000 | 8(47.1) | 18(24.3) | 2.476 | 0.116 |
| 丘脑 | 14(15.4) | 4(14.3) | 0.000 | 1.000 | 4(23.5) | 10(13.5) | 0.435 | 0.510 |
| 基底节 | 33(36.3) | 12(42.9) | 0.369 | 0.529 | 7(41.2) | 26(35.1) | 0.218 | 0.640 |
| 小脑 | 16(17.6) | 2(7.1) | 1.095 | 0.295 | 4(23.5) | 12(16.2) | 0.130 | 0.718 |
| 桥脑 | 21(23.1) | 10(35.7) | 1.775 | 0.183 | 5(29.4) | 16(21.6) | 0.136 | 0.713 |
| 中脑 | 5(5.5) | 4(14.3) | 1.277 | 0.259 | 3(17.6) | 2(2.7) | 3.416 | 0.078 |
| 延髓 | 6(6.6) | 2(7.1) | 0.000 | 1.000 | 2(11.8) | 4(5.4) | 0.169 | 0.681 |
| 他汀类药物[例(%)] | 15(16.5) | 14(50.0) | 13.050 | 0.000 | 3(17.6) | 12(16.2) | 0.000 | 1.000 |
| 死亡[例(%)] | 18(19.8) | 2(7.1) | 1.625 | 0.202 | 2(11.8) | 16(21.6) | 0.339 | 0.560 |
| 预后不良[例(%)] | 31(34.1) | 4(14.3) | 4.035 | 0.045 | 7(41.2) | 24(32.4) | 0.471 | 0.493 |

注: BHI为脑心交互现象, TTS为Takotsubo综合征, GCS为格拉斯哥昏迷评分, NIHSS为美国国立卫生研究院卒中量表, TC为总胆固醇, TG为甘油三酯, LDL为低密度脂蛋白, HbA1c为糖化血红蛋白, SBP为收缩压, DBP为舒张压, MAP为平均动脉压; 1mmHg=0.133kPa

表2 急性重症脑卒中患者BHI危险因素的多因素Logistic回归分析

| 变量 | OR值 | 95%CI | P值 |
|--------|-------|---------------|-------|
| 他汀类药物 | 0.222 | 0.075 ~ 0.658 | 0.007 |
| 脑血管疾病史 | 0.321 | 0.113 ~ 0.912 | 0.033 |

注: BHI为脑心交互现象, OR为优势比, 95%CI为95%可信区间

表3 急性重症脑卒中患者TTS危险因素的多因素Logistic回归分析

| 变量 | OR值 | 95%CI | P值 |
|--------|--------|-----------------|-------|
| 第3天MAP | 11.833 | 1.113 ~ 125.779 | 0.040 |
| HbA1c | 0.022 | 0.001 ~ 0.345 | 0.006 |

注: TTS为Takotsubo综合征, MAP为平均动脉压, HbA1c为糖化血红蛋白, OR为优势比, 95%CI为95%可信区间

2.4 BHI患者心脏异常表现(表4):

BHI患者心电图表现以T波倒置为主,其次是窦性心动过速、Q-T间期延长、心房颤动(房颤);而在TTS亚组中,T波倒置比例更高,其次是窦性心动过速。NT-proBNP在BHI组和TTS亚组中均有增高,而左室射血分数(LVEF)并未出现显著降低。

2.5 TTS患者心室壁运动异常情况:

17例TTS患者中心室壁运动普遍异常1例(5.9%),基底部异常13例(76.5%),中部异常4例(23.5%),心尖部异常6例(35.3%)。

2.6 预后情况(表1):BHI组预后不良率明显高于非BHI组($P < 0.05$)。

TTS亚组与非TTS亚组预后不良率差异无统计学意义($P > 0.05$)。

3 讨论

急性重症脑卒中患者BHI发生率较高,在本研究中高达76.5%,且与不良预后相关,提醒我们在临床工作中应予以高度关注。

BHI的主要病理生理机制:①支配心脏活动的高级神经中枢位于下丘脑、脑干以及包括岛叶在内的大脑边缘系统,这些部位病变会造成心律失常、心肌损伤等一系列的心脏问题^[9]。②急性脑卒中发病后机体进入应激状态,激活下丘脑-垂体-肾上腺皮质轴和交感神经-肾上腺髓质轴,交感神经过度兴奋,儿茶酚胺、肾上腺素、去甲肾上腺素水平明显升高。心脏神经附近的心肌细胞死亡于高收缩状态并形成收缩带,且有早期钙化和肌原纤维损伤,不沿血管供血区域分布的可逆性室壁运动异常^[3]。③脑卒中后内皮细胞损伤,血中内皮素、血栓素A₂、前列环素等炎性因子明显增加,造成炎症和免疫反应,影响心肌代谢,并对心肌有直接毒性作用^[3-4]。

本研究结果提示,他汀类药物的使用是BHI的保护性因素。一项随机对照研究显示,大动脉粥样硬化型缺血性脑卒中患者早期应用大剂量阿托伐他汀(80 mg/d)治疗比未进行他汀类药物治疗者,有效降低了血浆肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)、血管细胞黏附分子-1(VCAM-1)水平,提示脑卒中急性期使用他汀类药物治疗能降低免疫炎症激活^[10]。亦有研究显示,他汀类药物可以减轻急性脑卒中后的炎症反应^[11],保护血管内皮^[12],抗

表4 急性重症脑卒中合并BHI患者心功能情况

| 变量 | BHI患者 | | |
|--|---------------------|---------------------|---------------------|
| | 全体(n=91) | TTS亚组(n=17) | 非TTS亚组(n=74) |
| 心电图表现[例(%)] | | | |
| 房颤 | 16(17.6) | 4(23.5) | 14(18.9) |
| 窦性心动过速 | 19(20.9) | 7(41.2) | 12(16.2) |
| 窦性心动过缓 | 1(1.1) | 0(0) | 1(1.4) |
| 房性期前收缩 | 2(2.2) | 2(11.8) | 0(0) |
| 室性期前收缩 | 6(6.6) | 0(0) | 6(8.1) |
| ST-T段压低 | 2(2.2) | 0(0) | 2(2.7) |
| ST-T段抬高 | 11(12.1) | 5(29.4) | 6(8.1) |
| T波倒置 | 49(53.8) | 13(76.5) | 36(48.6) |
| Q-T间期延长 | 17(18.7) | 1(5.9) | 16(21.6) |
| 实验室指标[M(Q _L , Q _U)] | | | |
| NT-proBNP(μ g/L) | 1293(844, 3145) | 1173(317, 3430) | 1295(930, 3145) |
| CK-MB(μ g/L) | 2.48(1.44, 4.30) | 1.44(0.82, 8.54) | 2.51(1.90, 4.28) |
| MYO(μ g/L) | 127.0(47.8, 291.0) | 76.4(43.9, 376.0) | 134.0(50.4, 264.8) |
| cTnI(μ g/L) | 0.014(0.005, 0.091) | 0.005(0.004, 0.030) | 0.031(0.006, 0.097) |
| LVEF | 0.630(0.590, 0.670) | 0.580(0.530, 0.640) | 0.635(0.600, 0.705) |

注:BHI为脑心交互现象,TTS为Takotsubo综合征,NT-proBNP为N末端脑钠肽前体,CK-MB为肌酸激酶同工酶,MYO为肌红蛋白,cTnI为心肌肌钙蛋白I,LVEF为左室射血分数

氧化^[13],减轻脑水肿^[14]。这些作用可以解释他汀类药物存在多重机制减少BHI的发生。

本研究显示,既往有脑卒中病史患者BHI发生率较低,而这一现象可以用缺血预适应的理论来解释,其作用机制为:通过对细胞离子及pH稳态和细胞能量代谢稳态的保护^[15];线粒体代谢的调节^[16];防护兴奋性毒性损伤及缺氧/缺血去极化^[17];抑制凋亡^[18];减轻炎症反应^[19];调节缺血/再灌注阶段的血流及血管重构^[20]。可见其中多个机制对BHI的发生可以起到作用。缺血预适应训练已使很多心脑血管疾病高危患者受益,但这种训练能否明显减少BHI仍需进一步的前瞻性随机对照研究来证实。

已有研究证实,支配心脏活动的高级神经中枢位于下丘脑、脑干以及包括岛叶在内的大脑边缘系统,这些部位病变更易导致BHI的发生^[9]。但本研究并未显示BHI的发生与脑内病变部位相关,可能因为重症脑卒中病变范围比较广泛,且大面积脑梗死或大容积脑出血后颅内压升高明显,使邻近部位受到压迫,进一步扩大了病变影响范围,所以在重症脑卒中患者中BHI发生率高,却难以明确某个脑区病变更易发生BHI。

TTS是BHI值得关注的特殊类型。在急性重症脑卒中继发TTS患者中,基底部室壁运动异常比例最高,其次是心尖部异常和中部异常,与以往研究显示心尖部运动异常比例最高的结果不一致^[21],可能原因:以往研究采用的是2008年梅奥诊所的

诊断标准^[22],很多学者认为心脏基底或中部运动异常属于神经源性心肌顿抑(NSM)^[2,23];而本研究采用的是2018年TTS国际专家共识的新诊断标准,认为这3个部位的运动异常均归属于TTS的不同表现形式^[8]。另外,以往研究纳入患者多数由情绪因素继发;而本研究TTS均发生在严重脑卒中之后。有研究者认为情绪因素造成的TTS女性发生率高,而器质性疾病继发的TTS则男性发生率高^[21],这与本研究结果一致(男性占76.5%)。现在越来越多的研究表明TTS并不是一种预后良好的疾病^[21],且男性和由器质性疾病继发者病死率更高^[24];本研究中重症脑卒中合并TTS患者不良预后率达41.2%,所以对TTS决不能轻视,需要尽快明确诊断和管控。本研究显示,血压升高是TTS的独立危险因素,同时也是交感神经过度兴奋的一个信号,提示我们应精细管理急性重症脑卒中患者的高血压。

有研究显示,糖尿病患者TTS发生率低、预后好^[25]。本研究显示,HbA1c升高者TTS发生率低,这可能与TTS的机制是交感神经过度兴奋有关。如果糖尿病患者长期血糖控制不好会出现广泛的神经病变,这些神经病变使心脏对于交感神经的敏感度下降;此外,高血糖还可抑制儿茶酚胺水平^[26]。

综上所述,急性重症脑卒中患者BHI发生率高,且预示预后不良,我们可能可以通过应用他汀类降脂药和缺血预适应以及管控血压来减少TTS的发生。但本研究存在一定局限性,如病例数较少且属于单中心回顾性研究,对BHI患者的观察指标缺乏动态评估。所以未来仍需多中心前瞻性随机对照研究来进一步了解BHI。

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