

血清 S100 β 、A β 及 NSE 联合检测可提高急性脑梗死脑侧支循环建立的预测效能

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摘要 目的: 探讨血清钙结合蛋白 β (S100 β)、 β -淀粉样蛋白 (A β) 及神经元特异性烯醇化酶 (NSE) 水平联合检测在预测急性脑梗死 (ACI) 患者脑侧支循环建立中的价值。方法: 选取 132 例 ACI 患者为疾病组, 另选取同期 150 例健康体检者为对照组, 疾病组患者的侧支循环建立情况用脑血管数字减影血管造影 (DSA) 进行判断, 根据 DSA 检查结果, 将 0 级患者归为无侧支循环建立组 (51 例), 1~4 级患者归为侧支循环建立组 (81 例)。2 组血清 S100 β 、A β 及 NSE 水平用酶联免疫吸附法进行测定, 并采用受试者工作特征 (ROC) 曲线分析各项指标单项及联合检测对侧支循环建立的预测价值。结果: 疾病组血清 S100 β 、A β 及 NSE 水平高于对照组 (P 均 < 0.05); DSA 检查结果显示, 132 例患者中有 81 例 (61.36%) 患者侧支循环建立, 侧支循环建立组血清 S100 β 、A β 及 NSE 水平低于无侧支循环建立组 (P 均 < 0.05); ROC 结果显示, 血清 S100 β 、A β 及 NSE 水平联合检测判断 ACI 患者侧支循环建立的灵敏度及曲线下面积 (AUC) 高于三者单项检测 (P 均 < 0.05), 但特异性与三者单项检测比较, 差异无统计学意义 (P 均 > 0.05)。结论: ACI 患者血清 S100 β 、A β 及 NSE 水平较健康人群更高, 且与脑侧支循环的建立有关, 三者联合检测对 ACI 患者脑侧支循环建立预测效能更高。

关键词 急性脑梗死; 脑侧支循环; 钙结合蛋白 β ; β -淀粉样蛋白; 神经元特异性烯醇化酶

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Combined detection of serum S100 β , A β and NSE to improve the predictive efficacy of establishing cerebral collateral circulation in acute cerebral infarction ZHANG Chun-rui¹, WEI Jian-hui². ¹Department of Neurology, Hanzhong People's Hospital, Shaanxi Hanzhong, 723000, China; ²Department of Neurology, Baoji Central Hospital, Shaanxi Baoji, 721000, China

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Abstract Objective: To explore the value of combined detection of serum calcium binding protein β (S100 β), β -amyloid protein (A β) and neuron specific enolase (NSE) levels in predicting the establishment of cerebral collateral circulation in patients with acute cerebral infarction (ACI). Methods: A total of 132 patients with ACI were selected as the disease group, and 150 people receiving healthy physical examination were selected as the control group. The establishment of collateral circulation in the disease group was judged by digital subtraction angiography (DSA). According to the DSA examination results, the grade 0 patients were classified as non-collateral circulation establishment group (51 cases), and the grade 1-4 patients were classified as collateral circulation establishment group (81 cases). The levels of serum S100 β , A β and NSE in the two groups were measured by enzyme-linked immunosorbent assay, and the receiver operating characteristic (ROC) curve was used to analyze the predictive value of single and combined detection of each index for the establishment of collateral circulation. Results: The levels of serum S100 β , A β and NSE in the disease group were higher than those in the control group (all $P < 0.05$). The DSA results showed that 81 out of 132 patients (61.36%) had collateral circulation establishment, and the levels of serum S100 β , A β and NSE in the collateral circulation establishment group were lower than those in the non-collateral circulation establishment group (all $P < 0.05$). The ROC results showed that the sensitivity and area under the curve (AUC) of the combined detection of serum S100 β , A β and NSE levels in determining the establishment of collateral circulation in ACI patients were higher than those of the three separate tests (all $P < 0.05$), but there was no significant difference in specificity between combined detection and three separate tests (all $P > 0.05$). Conclusion: The levels of serum S100 β , A β and NSE in ACI patients are higher than those in healthy people, and they are related to the establishment of cerebral collateral circulation. The combined detection of the three is more effective in predicting the establishment of cerebral collateral circulation in ACI patients.

Key words Acute cerebral infarction; Cerebral collateral circulation; Calcium binding protein β ; β -amyloid protein; Neuron specific enolase

急性脑梗死(acute cerebral infarction, ACI)是指脑组织缺血而导致的脑组织坏死,造成神经功能障碍,是临床最常见的脑卒中类型^[1,2]。脑侧支循环是指当供血动脉出现严重狭窄时,能够从旁边出现或生成小的毛细血管,供给供血动脉所支配的区域,对维持脑局部血流、减少脑组织损伤有重要作用^[3]。血清钙结合蛋白 β (S100 β calcium binding protein, S100 β)、 β -淀粉样蛋白 (β -amyloid protein, A β)及神经元特异性烯醇化酶(neuron-specific enolase, NSE)在临床诊断及判断脑神经损伤的严重程度方面具有一定作用。研究表明,神经功能缺损程度与脑侧支循环的建立密切相关^[4~6]。本研究探讨 ACI 患者血清 S100 β 、A β 及 NSE 水平的变化,分析其与侧支循环建立的关系。

资料与方法

1. 研究对象:选取 2019 年 6 月-2021 年 6 月汉中市人民医院收治的 132 例 ACI 患者,其中男 79 例,女 53 例;年龄 45~85 岁,平均(62.3 ± 10.2)岁;体重指数(body mass index, BMI)20~26 kg/m²,平均(22.78 ± 2.57)kg/m²;另选取同期 150 例健康体检者为对照组,其中男 90 例,女 60 例;年龄 45~85 岁,平均(63.1 ± 9.9)岁;BMI 为 20~26 kg/m²,平均(22.53 ± 2.33)kg/m²,2 组性别、年龄及 BMI 比较,差异无统计学意义(P 均 >0.05)。

纳入标准:①ACI 患者诊断均符合中华医学会发布的中国急性缺血性脑卒中诊治指南 2018 诊断标准^[7];②ACI 发病 24 h 内入院;③对照组经头颅 CT 或磁共振(MRI)检查均无脑血管狭窄或闭塞,无侧支循环建立。排除标准:①合并严重脏器功能障碍、恶性肿瘤;②合并血液疾病、免疫性疾病;③既往脑部疾病史,如脑出血、脑梗死等;④合并颅内动脉瘤、动脉畸形等。本研究经医院伦理委员会批准[批号:院准字(2019 年 021 号)],受试者或家属均知情并签署同意书。

2. 脑血管数字减影血管造影(digital subtraction angiography, DSA):患者在入院 5 d 时进行脑血管 DSA 检查,患者取仰卧位,常规消毒铺巾,局部麻醉后, Seldinger 技术进行穿刺,使用 5F 的 Pigtail 导管进行造影,观察血管开口状态,用单弯导管对患者进行脑血管造影。造影剂选择用 62.34 g/100 mL 的碘普罗胺,采用高压注射器对造影剂进行注射。采用超声参数法评估脑血管狭窄率^[8],狭窄程度分为 4 级:轻度:动脉直径狭窄 $<50\%$;中度: $50\% \leq$ 动脉直径狭窄 $<70\%$;重度: $70\% \leq$ 动脉直径狭窄 $<$

100%;完全闭塞:动脉直径狭窄为 100%。另根据侧支循环分级标准^[9]将侧支循环分为 5 级。根据 DSA 检查结果,将 0 级患者归为无侧支循环建立组(51 例),1~4 级患者归为侧支循环建立组(81 例)。

3. 观察指标:

(1)比较疾病组与对照组血清 S100 β 、A β 及 NSE 水平,所有受试者均于入院 24 h 内抽取静脉血 5 mL,以 3 000 转/min 离心 10 min,取上层血清,18℃保存待检。使用美国 R&D Systems 公司的酶联免疫吸附法(enzyme linked immunosorbent assay, ELISA)试剂盒检测 2 组血清 S100 β 、A β 及 NSE 水平。

(2)疾病组患者侧支循环建立情况及有无侧支循环建立患者血清 S100 β 、A β 及 NSE 水平比较。

(3)分析血清 S100 β 、A β 及 NSE 水平单项及联合检测对脑侧支循环建立的预测价值,统计最佳截断值、灵敏度、特异性、曲线下面积(area under curve, AUC)和置信区间(95% CI)。

4. 统计学分析:采用 SPSS 25.0 统计学软件。经检验符合正态分布的计量资料以($\bar{x} \pm s$)表示,采用 t 检验;不符合正态分布的计量资料以 $M(Q1, Q3)$ 表示,采用 Mann-Whitney U 检验;计数资料以百分数(%)表示,用 χ^2 检验;绘制受试者工作特征(receiver operating characteristic, ROC)曲线,预测血清 S100 β 、A β 及 NSE 水平对 ACI 患者脑侧支循环建立的价值。以 $P < 0.05$ 为差异有统计学意义。

结果

1. 血清 S100 β 、A β 、NSE 水平:疾病组血清 S100 β 、A β 及 NSE 水平高于对照组(P 均 <0.05),见表 1。

2. 疾病组患者脑血管狭窄情况、狭窄部位、侧支循环建立情况及有无侧支循环建立患者血清 S100 β 、A β 及 NSE 水平:DSA 检查结果显示,132 例患者中轻度脑血管狭窄 24 例,中度 49 例,重度 40 例,完全闭塞 19 例;颈内动脉主干狭窄 63 例,大脑中动脉狭窄 40 例,椎动脉狭窄 12 例,基底动脉狭窄 11 例,锁骨下动脉狭窄、大脑前动脉狭窄、大脑后动脉狭窄各 2 例;132 例患者中有 51 例为 0 级,17 例为 1 级,23 例为 2 级,20 例为 3 级,21 例为 4 级,共 81 例(61.36%)患者侧支循环建立,侧支循环建立组血清 S100 β 、A β 及 NSE 水平低于无侧支循环建立组(P 均 <0.05),见表 2。

3. 血清 S100 β 、A β 、NSE 水平对 ACI 患者脑侧支循环建立的预测价值:血清 S100 β 、A β 及 NSE 水平联合检测 ACI 患者脑侧支循环建立的灵敏度高

于单项检测($\chi^2 = 8.976, P = 0.003; \chi^2 = 23.080, P < 0.001; \chi^2 = 14.286, P < 0.001$), AUC 高于单项检测($Z = 4.083, P < 0.001; Z = 3.667, P < 0.001; Z = 2.552, P = 0.007$), 特异性与单项检测比较差异无统计学意义($\chi^2 = 0.078, P = 0.780; \chi^2 = 0.793, P = 0.373; \chi^2 = 0.331, P = 0.565$), 见表 4、图 1。

表 1 2 组血清 S100β、Aβ 及 NSE 水平比较[μg/L, M(Q1, Q3)]

组别	例	S100β	Aβ	NSE
疾病组	132	1.55(1.24, 1.89)	1.61(1.30, 1.95)	27.55(23.23, 30.99)
对照组	150	0.75(0.53, 0.99)	0.92(0.63, 1.12)	8.33(6.21, 10.57)
U 值		8.712	7.733	15.631
P 值		<0.001	<0.001	<0.001

表 2 2 组血清 S100β、Aβ、NSE 水平比较[μg/L, M(Q1, Q3)]

组别	例	S100β	Aβ	NSE
侧支循环建立组	81	1.34(1.18, 1.67)	1.38(1.22, 1.78)	24.65(22.65, 28.25)
无侧支循环建立组	51	1.78(1.65, 1.94)	1.85(1.62, 2.07)	30.37(27.92, 34.32)
U 值		11.268	12.904	10.801
P 值		<0.001	<0.001	<0.001

表 4 各指标单项及联合对 ACI 患者脑侧支循环建立的预测价值

指标	截断值	灵敏度	特异性	AUC	95% CI
血清 S100β 水平	1.52μg/L	71.60(58/81)	86.27(44/51)	0.714	0.628 ~ 0.789
血清 Aβ 水平	1.44μg/L	56.79(46/81)	90.19(46/51)	0.747	0.664 ~ 0.819
血清 NSE 水平	26.62μg/L	65.43(53/81)	88.23(45/51)	0.811	0.733 ~ 0.874
三项联合	—	90.12(73/81)	84.31(43/51)	0.924	0.865 ~ 0.963

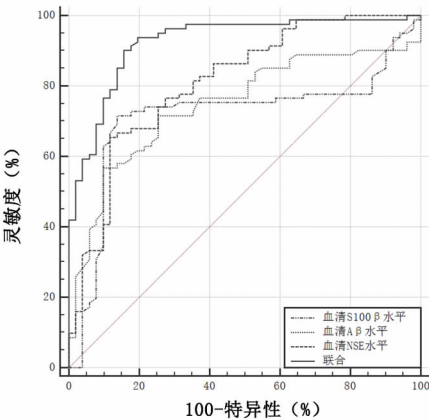


图 1 各指标单项及联合评估 ACI 患者脑侧支循环建立的 ROC 曲线

讨论

当患者发生 ACI 时, 脑细胞和血脑屏障被破坏, 致使 S100β 和 NSE 在脑脊液中大量释放, 继而透过血脑屏障释放于血液中, 使血液中的浓度迅速提高^[10, 11]。本研究显示, 疾病组血清 S100β、Aβ 及 NSE 水平高于对照组, 与朱晓峰^[12]研究结果一致, 表明血清 S100β、Aβ 及 NSE 水平与患者发生 ACI 密切相关。ACI 患者因脑组织缺血缺氧导致大量自由基产生, 触发 β 肽分泌, 导致淀粉样蛋白前体形成, 使大量 Aβ 生成并沉淀于神经细胞和血管^[13]。

本研究经 DSA 检查发现 132 例 ACI 患者中 81 例患者脑侧支循环建立, 发生率为 61.36%, 与既往孙光明^[14]报道的 63.04% 相近, 表明多数 ACI 患者会建立脑侧支循环, 另侧支循环建立组的血清 S100β、Aβ 及 NSE 水平低于无侧支循环建立组, 表明血清 S100β、Aβ 及 NSE 水平变化与 ACI 患者脑侧支循环建立有关。可能因为随着 ACI 患者神经功能缺损加重, 血清 S100β 及 NSE 含量也随之增加, 且血清 Aβ 水平上升是神经细胞损伤或凋亡的信号^[15, 16]。S100β、Aβ 及 NSE 水平越高, ACI 患者神经功能缺损越严重, 梗死部位脑血流灌注越差, 远端脑组织供血无法到达缺血区, 导致 ACI 患者脑中的缺血区域无法得到良好的灌注, 提示侧支循环对缺血组织的代偿不良。不仅如此, S100β 有利于促进单核细胞和中性粒细胞转移, 进一步引导内皮细胞和巨噬细胞分泌促炎症因子, 从而对血管动脉粥样硬化的发展产生促进作用, 最终影响侧支循环的建立^[17], 而过多的 Aβ 在血管壁内和血管周围沉积均会影响血管的粥样硬化, 也会影响侧支循环的建立^[18]。因此, 血清 S100β、Aβ 及 NSE 水平越高, 反映脑神经功能损伤越严重, 也提示了脑侧支循环代偿缺乏或代偿较差。本研究 ROC 结果显示: 血清

(下转第 564 页)

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(上接第 544 页)

S100β、Aβ 及 NSE 水平对 ACI 患者脑侧支循环建立有一定预测价值,单独预测的灵敏度较低,但三者联合预测可提高灵敏度和诊断效能。建议临床可早期检测 ACI 患者的血清 S100β、NSE 及 Aβ 水平,以辅助评估脑侧支循环建立情况,从而有助于为 ACI 患者制定个性化的措施干预,并为预后提供依据。

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