

无症状脑梗死中西医临床研究进展

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摘要

近年来无症状脑梗死受到了广泛的关注, 成为了老年化社会的热门话题。无症状脑梗死(silent brain infarction, SBI), 或称为“静止性”或“隐匿性”脑梗死, 是指患者没有明确的脑卒中或TIA的既往病史, 但在头颅CT或MRI检查时发现与脑血管分布一致的脑梗死灶或脑软化灶, 而临床上没有与病灶相关的神经功能缺损的症状和体征。SBI在人群中患病率为8%~28%不等, 其危险因素与其他类型的脑梗死相同, 但有一些特殊因素值得重视, 在进展过程中可能有症状性脑梗死、认知功能减退、抑郁状态等。多项研究中SBI是否进行脑血管二级预防仍然存在争议。同时, 中医药历来重视“治未病”, 现就SBI的中西医临床研究进行阐述。

关键词

脑梗死, 无症状脑梗死, 危险因素, 综述

Progress of Clinical Research on Silent Brain Infarction in Traditional Chinese Medicine and Western Medicine

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Abstract

Asymptomatic silent brain infarction has received a lot of attention in recent years and has be-

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come a hot topic in an aging society. Silent brain infarction (SBI), or “silent” or “insidious” brain infarction, is a condition in which the patient does not have a clear past history of stroke or TIA, Foci of cerebral infarction or cerebral softening consistent with the distribution of cerebral blood vessels detected on cranial CT or MRI examination and there are no clinical signs and symptoms of neurologic deficits associated with the lesion. The prevalence of SBI in the population ranges from 8% to 28%, and its risk factors are the same as those for other types of cerebral infarction. However, there are some specific factors that deserve attention, and there may be symptomatic cerebral infarction, cognitive impairment, and depressive states during progression. Whether secondary cerebrovascular prevention is performed in SBI in several studies remains controversial. At the same time, traditional Chinese medicine has always emphasized the “treatment of future diseases”, and now we are going to elaborate on the traditional Chinese medicine and western clinical research on SBI.

Keywords

Cerebral Infarction, Silent Brain Infarction, Risk Factors, Review

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1. 引言

随着 MRI 的普及, 无症状性脑血管病成为临床常见病, 且与脑卒中和痴呆密切相关。无症状性脑梗死(silent brain infarcts, SBI)是指无短暂性脑缺血发作及脑卒中病史, 无明确的神经系统症状和定位体征, 但是在 CT、MRI 检查时发现脑梗死的病灶[1]。美国心脏协会(AHA)美国卒中协会(ASA)于 2017 年发布无症状性脑血管病患者预防脑卒中的科学声明, 对无症状性脑梗死进行阐述, 大多数无症状性脑梗死(大约 90%以上)位于基底节区或皮质下, 大小约 3~15 mm, 为楔形、卵圆形或不规则形; 且在 T2 层面上与脑脊液类似呈高信号, 在 T1 层面呈低信号[2]。

2. 无症状脑梗死流行病学调查

近年来, 无症状性脑梗死受到了广泛的关注, 关于其流行病学和影响的数据也在不断积累[3]。在没有已知卒中病史的人群研究中, 无症状性脑梗死是迄今为止 MRI 上最常见的偶然发现。SBI 在一般人群中的患病率高达 8%~28% [4]。患病率随年龄分布和研究人群的不同而有很大差异。每 5 名无卒中病似的老年人中就有人存在 SBI, 并且与将来发生卒中风险增加 2 倍[5]。(年龄 > 60 岁)的老年患者年发病率为 3%~4%, 大于 80 岁的老年患者年发病率高达 6.5% [6]。由于人们越来越关注将 SBI 作为一种标志物在神经损伤方面, 越来越多的研究对特定介入和外科手术中的发病率数据进行了分析, 研究表明, 经导管主动脉瓣置换术是 SBI 发生率最高的手术, 平均发生率达到 75%~93% [7]。

3. 造成无症状脑梗死的危险因素

SBI 危险因素与症状性脑梗死的危险因素相同。多数研究证明, 除年龄外, 高血压病与 SBI 关联的证据最强, 因此可以被认为是与缺血性卒中中相似的最重要的单一危险因素[8] [9] [10] [11]。虽然不同的脑血管事件有许多相同的危险因素, 并且这些危险因素往往共存, 但它们之间存在差异。无症状脑梗死的流行病学调查显示发病与年龄之间存在密切联系。高血压、颈动脉狭窄、慢性肾病和代谢综合征都与 SBI

密切相关。心力衰竭、冠状动脉疾病、高同型半胱氨酸血症和阻塞性睡眠呼吸暂停也可能具有重要意义。

1) 氧化应激

导致血管氧化应激的各种有害刺激与中风等多种疾病的发病机制有关[12]。事实上,大多数已确定的 SBI 危险因素可促进活性氧和丙烯醛(缺血时多胺降解的产物)的生成和积累或导致慢性炎症。许多研究人员利用缺血时血脑屏障特性的改变来确定进入全身循环的各种分子与 SBI 之间的关联。日本研究员吉田等报道,当联合丙烯醛时,高水平的血管炎性标志物预测 SBI 具有较高的敏感性和特异性[13]。另一项研究发现, SBI 患者的超敏 C 反应蛋白和白细胞介素-6 水平显著高于无 SBI 患者[14]。然而,通过这些研究,我们尚未确定这种炎症反应是缺血的原因,还是继发于缺血后才出现。

2) 内皮功能障碍

有研究假设 SBI 的发病机制涉及脑小血管内皮功能障碍,血浆成分外渗到血管壁和周围脑组织,造成血管周围损伤和炎症[15]。在一项研究腔隙性脑梗死循环血液标志物的研究中,学者认为内皮功能障碍是无症状脑梗死而非症状性脑梗死的重要疾病机制[16]。

3) 同型半胱氨酸

同型半胱氨酸升高已被确定为 SBI 的重要危险因素[17][18][19]。研究者提出可几种机制,包括对血管内皮的氧化,导致氧化亚氮生成减少,血小板与内皮细胞的粘附增加,以及血栓前因子水平的增加等。研究表明,与大血管的病变相比,同型半胱氨酸升高与脑小血管病变之间的关系可能更紧密[20]。

4) 遗传因素

遗传是症状性脑梗死的确定危险因素,在 SBI 的发生中也可能有重大意义。虽然遗传因素与 SBI 之间的关系研究量非常少,但遗传易感性被认为有病史的父母的后代中确定的 SBI 的独立危险因素[21][22]。

5) 高血压

研究者认为,动脉高血压(包括血压变异性和非稍型高血压) SBI 关联的证据最强,因此可以被认为是与急性脑梗死相似的最重要的单一危险因素[2][8][10][11]。

6) 心房颤动

SBI 在约 30%的心房颤动(房颤)患者中被发现,与其他心脏病相比,房颤患者的栓塞更常见[23]。Cha 等人报告称,与没有 SBI 的房颤患者相比,有房颤且有 SBI 的患者在随访 10 年后死亡率增加[24]。无症状脑梗死患者的心房颤动也与发生症状脑梗死有关,而发生症状脑梗死但没有已知心房颤动的患者的心房颤动也与发生症状性脑梗死有关[24][25][26]。

7) 动脉粥样硬化

有可靠证据表明颈动脉狭窄和无症状脑梗死有关,尽管病灶的位置并不总是在动脉病变的同侧[10][2][5][27][28]。在亚洲患者中,颅内血管狭窄证明与 SBI 相关[29]。

8) 其他危险因素

除常见无症状脑梗死的危险因素外,25-羟维生素 D3、Hcy、LDL 也是无症状脑梗死的高危因素 25 羟维生素 D3 水平、Hcy、LDL 可作为无症状脑梗死患者临床初筛易损斑块的血清生物学标志物[30]。超重、肥胖及腹型肥胖也是无症状脑梗死患者的危险因素之一[31]。心脏手术后,约 25%的冠状动脉搭桥术患者和约 70%的经导管主动脉瓣植入术患者在头颅 MRI 上表现为急性、无症状性脑梗死[32]。同样,对接受非心脏手术的患者进行的一项大型前瞻性研究显示,其中 7%的患者在头颅 MRI 上显示脑梗死[33]。

4. 无症状脑梗死的预后

对无症状脑梗死患者进行全面的病史采集和神经系统查体会发现很多细微的症状[34],这些可能包括

视野缺损、精细运动障碍、吞咽困难、头晕、麻木或瘫痪。已经有大量研究对 SBI 患者与健康患者的健康结果进行了比较。大量证据表明, 无症状脑梗死会增加症状性脑梗死发生的概率, 对认知功能产生不利影响, 甚至可能会造成死亡。此外, 在多个 SBI 病灶存在的情况下, 显性 AIS 可能更严重, 并且在 SBI 病灶存在的情况下, 发生症状性脑梗死, 残疾风险较无 SBI 者增加[35] [36]。

1) 症状性脑梗死: 研究表明, SBI 患者首次中风的风险增加, 每年高达 10%, 是健康患者的 5 倍[37]。SBI 是脑梗死的特殊类型, 是因血液供应障碍, 缺血缺氧所致的局限性脑组织的缺血性坏死或软化灶, 也有专家认为在首次卒中的患者中, SBI 也与复发性卒中的发生有关[38]。

2) 认知功能障碍: SBI 的存在与痴呆的概率增高有关, 他们推测是由于反复的脑梗死造成痴呆[39] [40]。此外, 在痴呆人群中, 有 SBI 的人群在语言功能、延迟回忆和语义流畅性等几个认知领域的下降比健康人群更严重[41]。在 SBI 人群中, 已经注意到了多种神经认知联系, 从认知功能的整体恶化到与记忆、语言等更具体的能力有所下降[42]。

3) 精神类疾病: SBI 在多种精神疾病患者中被发现。有研究发现, SBI 在患有抑郁症的老年人(平均年龄 > 60 岁)中的患病率高达 40%~50% [43] [44]。

4) 其他不良预后: Willey 等人对北曼哈顿人群(平均年龄 70 ± 9 岁)中招募的 1238 名临床无卒中病史的成年人的活动总体水平进行了研究, 发现有 SBI 的成年人的活动水平比没有 SBI 的成年人差, 但不能推断 SBI 是否会导致活动减少[45]。患有 SBI (平均年龄 79 岁)的老年人患肺炎的几率几乎是健康老年人的 5 倍[46]。

5) 死亡: 在所有关于 SBI 的研究中都发现了死亡率的增加。特别值得注意的是 2 项大型纵向社区研究中死亡率在有 SBI 的人群中增加了 3~4 倍[6] [39]。

5. 无症状脑梗死治疗

科学声明宣称, 由于无症状脑梗死和急性脑梗死的病理生理及发病机制相似, 都成为脑梗死, 因此对 SBI 的诊断方法应与对 AIS 的诊断方法相同[2]。有共识认为, 在 AIS 的一级预防中, 需评估 SBI 患者的心血管危险因素, 包括高血压、糖尿病、血脂异常、吸烟、饮食和身体活动不足[47]。

主要的 ASPREE 试验(阿司匹林在减少老年人事件中的应用)并未显示对健康老年人群的一级预防有任何益处[48] [49] [50] [51]。有意思的是, 他汀类药物最近被证明可以减少 SBI 的发生[52]。然而, 目前有几项针对 SBI 患者的试验正在进行中, 包括药物和生活方式干预[53]。

6. 中西医诊疗展望

中医学未发现有无症状脑梗死的记载, 辨证论治应该先从基本病机入手, 依据中医学对中风病的观点, 无症状脑梗死属于中风, 为正虚邪实, 脑脉被阻。中风病在老年群体中发生比率高, 《内经》云“年四十而阴气自半, 起居衰矣”。主要是因为身体衰弱, 正气亏损, 气血亏虚, 与心、肝、脾、肾等诸脏密切相关。由于诸脏阴阳失调, 加之忧思恼怒, 或恣食肥甘厚腻, 或房劳过度, 精血亏耗, 导致阴亏于下, 肝阳上亢, 气血逆乱, 夹痰夹瘀, 上蒙清窍, 阻滞经络, 故痰、火、瘀上犯于脑, 而致脑脉被阻。瘀血阻络及肝阳上亢是无症状脑梗死最根本的病理改变[54]。

治疗疾病的关键在于正确认识疾病的本质, 中医学的最大优点在于以整体的观点, 通过各种临床症状的变化规律来认识机体的病理改变, 最后确立治疗方案。无症状脑梗死的特点是“无症状”, 故在治疗过程中, 应该遵循中医辨证论治的原则, 以辨病为主导, 以脑卒中病的基本病机为基础, 根据不同病因和体质进行辨证论治, 分清阴阳属性、虚实变化、脏腑盛衰, 进而找出相应的治疗方法, 确立对应的方剂和药物[55]。

“不治己病治未病”是早在《黄帝内经》中就提出来的防病养生谋略,是至今为止我国卫生界所遵守的“预防为主”策略的最早思想,这一治疗思想在无症状脑梗死的防治中尤为重要。由于有无症状性脑梗死病史的患者发生急性脑梗死的风险较高,因此有效预防和治疗无症状性脑梗死的危险因素可有效控制急性脑梗死的发生。吸烟、饮酒、肥胖、缺乏运动、高血压、高脂血症、糖尿病和心房颤动等疾病是脑梗死的主要危险因素,而且具备这些高危因素的人随着年龄增加脑卒中风险也增加,因此我们应积极治疗这些基础疾病,控制血压、血糖和血脂水平,而且要注意控制体重、增加运动、戒烟酒,保持良好的心情,避免不良生活习惯,阻止疾病的发展。

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