

doi: 10.3978/j.issn.2095-6959.2020.12.036

View this article at: <http://dx.doi.org/10.3978/j.issn.2095-6959.2020.12.036>

口腔疾病与脑血管病的关系

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[摘要] 牙周炎、龋齿及无牙症是老年人普遍存在的口腔健康问题，不良的口腔预防性护理是口腔健康问题的危险因素之一。牙周炎、龋齿、无牙症及不良的口腔预防性护理均可能增加脑卒中的发病率。积极治疗口腔疾病、定期专业的口腔预防性护理、多进食膳食纤维及胆固醇低的食物等能减少脑血管病的发生。

[关键词] 牙周炎；龋齿；无牙症；口腔预防性护理；脑血管病

Relationship between oral diseases and cerebrovascular diseases

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Abstract Periodontitis, caries, edentulism are common oral health problems in the elderly, poor oral preventive care is one of the risk factors of oral health problems. Periodontitis, caries, edentulism and poor oral preventive care may increase the incidence of stroke. Therefore, active treatment of oral diseases, regularly professional oral preventive care, eating more dietary fiber and low cholesterol food can reduce the occurrence of cerebrovascular diseases.

Keywords periodontitis; caries; edentulism; oral preventive care; cerebrovascular diseases

口腔健康问题包括牙周炎、龋齿及无牙症，是老年人普遍存在的问题^[1]。牙周炎和龋齿被认为是导致牙齿脱落的两个主要原因，通常同时存在，且有共同的危险因素，如口腔卫生差、社会经济地位低及不良的口腔预防性护理等^[2]。不良的口腔预防性护理包括刷牙方法错误、未使用牙线或未寻求专业牙齿清洁等^[3]。无牙症是全球性的老年人健康问题，在一些欧洲国家的患病率高达78%^[4]。在口腔健康问题中，牙周炎常见，且其发生概率随着年龄的增长而增加^[5]。许多研究对口腔

健康问题与脑血管病的关系进行了探讨，发现两者之间存在联系。本文将分别对牙周炎、龋齿、无牙症及不良的口腔预防性护理与脑血管病的关系进行综述，阐述口腔疾病对脑血管病的影响。

1 牙周炎同脑血管病的关系

牙周炎可通过直接途径(血小板聚集、内皮细胞侵袭和损伤)或间接途径(细胞内黏附分子的合成，抗细菌LPS抗体的产生及免疫系统失衡)促进

动脉粥样硬化的形成，从而增加脑卒中发生的风险^[6]。流行病学证据发现牙周炎病原体血清抗体水平与卒中的发生及主动脉粥样硬化的发展相关，而特定牙周炎病原体水平可能会导致颈动脉内膜增厚^[7]。

牙周炎的病因多样，但主要与特定细菌有关，包括牙龈卟啉单胞菌和放线杆菌^[8]。这些细菌由于其病理特性而被广泛研究。这些病理特性包括：侵袭结缔组织、上皮和内皮细胞的能力；激活补体级联和免疫系统；刺激细胞因子和其他炎症介质的合成^[9]。牙龈卟啉单胞菌和放线杆菌可能在动脉粥样硬化的发展中发挥作用，从而增加脑卒中发生的风险，这些特定细菌可以刺激细胞因子和其他炎症介质的合成，包括白细胞介素-1(IL-1)、白细胞介素-6(IL-6)、C-反应蛋白(CRP)及TNF-α^[10]，能够引起全身性炎症反应，从而导致斑块不稳定，推动动脉粥样硬化的发展，增加脑卒中发生的可能^[2]。

循环系统中的细菌产物，如脂多糖(LPS)、外膜囊泡和菌毛，炎性细胞因子和趋化因子使细胞表面受体表达上调和黏附分子在血管内皮上表达^[11]。这些细菌蛋白的抗体作为自身抗体的过程加速了血管内皮的凋亡^[12]。载有低密度脂蛋白(LDL)的巨噬细胞凋亡导致脂质在内皮下积聚，形成动脉粥样斑块，其被纤维帽覆盖并促进血小板聚集。内皮细胞凋亡后，纤维帽的暴露和细胞外基质的酶促降解导致斑块破裂、血栓形成，从而导致血管闭塞，这与脑卒中的发生直接相关^[13]。

2 龋齿与脑血管病的关系

龋齿是牙齿脱落最常见的原因，是口腔卫生不良与经常摄入富含糖食品的个体，在长期不重视牙齿卫生的情况下，由口腔微生物群产生的酸性物质引起的。与牙周炎相反，龋齿通常不会引起全身炎症反应^[14]。

有研究报道了龋齿与脑血管病的关系。Glodny等^[15]分析了巴西293名患者的计算机断层扫描数据，发现龋齿与动脉粥样硬化的发展情况呈正相关。采用患者牙齿的腐烂表面数量评估龋齿情况，动脉钙化评分评估动脉粥样硬化程度，发现龋齿/牙齿<1的患者动脉粥样硬化的概率低于龋齿/牙齿≥1的患者^[16]。变形链球菌是引起龋齿的主要病原体之一。研究^[17]发现：使用PCR技术可在动脉粥样硬化斑块样品中检测到变形链球菌。预防和控制龋齿可能值得在临床实践中推广，以

预防动脉粥样硬化。

3 无牙症与脑血管病的关系

研究^[18]表明：牙齿的数量可能影响卒中发生，患者的牙齿数量越少，卒中风险越高。Grau等^[19]对卒中患者进行研究，结果显示：与人群对照组相比，患者的牙齿数量明显减少。Grau等^[20]用总牙齿指数表明牙齿状况与脑血管疾病的关系。Leira等^[21]发现：腔隙性脑梗死患者的缺牙数明显高于对照组。Del Brutto等^[22]发现：重度无牙症是脑卒中发病率的独立危险因素。

在亚洲地区，牙齿脱落与脑卒中存在明显相关性及显著的剂量反应关系。每增加2颗牙齿脱落，患脑卒中的风险增加3%^[23]。义齿或缺齿咀嚼效率低，患者不得不适应低纤维、低必需微量营养素、高饱和脂肪酸及高胆固醇饮食，这样的饮食变化，可能会增加患高脂血症的风险^[24]。

研究^[25]证明：高脂血症患者血脂水平下降1%，心脑血管疾病的病死率可下降2%；低密度脂蛋白胆固醇降低1 mmol/L，脑卒中和冠心病的风险可降低约20%。膳食纤维的摄入与脑血管疾病的风险降低有关。现有如下在动物模型中进行的研究，Lo等^[26]表明：从大豆中分离出的膳食纤维可有效预防兔的动脉粥样硬化；Baekey等^[27]报道：葡萄柚果胶可减少小型猪的动脉粥样硬化；可溶性纤维和不溶性纤维在降低血液胆固醇，减轻动脉粥样硬化的过程中具有显著作用。因此，无牙症会增加患脑血管病的风险^[28]。

4 不良的口腔预防性护理与脑血管病的关系

在不良的口腔预防性护理过程中，口腔细菌能够通过牙龈组织中的细微结构进入血液中，导致低水平的瞬时菌血症^[29]。由不良的口腔预防性护理引起的反复短暂菌血症，可能会使病原体滞留在动脉粥样硬化斑块中，并促进斑块破裂^[30]。研究^[31]表明：口腔病原体可刺激内皮细胞产生各种促炎细胞因子，如IL-6和干扰素-γ，这些细胞因子参与动脉粥样硬化的发病，且可促进斑块破裂。口腔病原体可以激活Toll样受体，Toll样受体介导对病原体的炎症反应并引起内皮功能障碍，是动脉粥样斑块形成的重要原因，同时也增加了脑卒中的风险及可能^[32]。

除了常规的炎症反应途径，口腔细菌可以直接与血小板相互作用，导致其活化^[33]，如牙源性

细菌可分泌牙龈蛋白酶, 使细胞内 Ca^{2+} 增加, 导致血小板活化与聚集^[34], 活化血小板可诱导动脉粥样硬化前细胞的募集, 加速动脉粥样硬化的发展, 从而增加脑卒中的风险^[35]。链球菌表面蛋白可直接与多种血小板受体结合, 也可通过血浆免疫球蛋白G间接活化^[36]。因此, 定期的口腔护理可以降低缺血性卒中的风险。

5 结语

综上所述, 口腔疾病与脑血管病存在明显的相关性。积极治疗口腔疾病、定期专业的口腔预防性护理、多进食膳食纤维及胆固醇低的食物等能够降低脑血管病的发生与发展。

参考文献

- Beck JD, Koch GG, Rozier RG, et al. Prevalence and risk indicators for periodontal attachment loss in a population of older community-dwelling blacks and whites[J]. *J Periodontol*, 1990, 61(8): 521-528.
- Noble JM, Scarmeas N, Papapanou PN. Poor oral health as a chronic, potentially modifiable dementia risk factor: review of the literature[J]. *Curr Neurol Neurosci Rep*, 2013, 13(10): 384.
- Pillai RS, Iyer K, Spin-Neto R, et al. Oral health and brain injury: causal or casual relation? [J]. *Cerebrovasc Dis Extra*, 2018, 8(1): 1-15.
- Petersen PE, Yamamoto T. Improving the oral health of older people: the approach of the WHO Global Oral Health Programme[J]. *Community Dent Oral Epidemiol*, 2005, 33(2): 81-92.
- Rosling B, Serino G, Hellstrom MK, et al. Longitudinal periodontal tissue alterations during supportive therapy. Findings from subjects with normal and high susceptibility to periodontal disease[J]. *J Clin Periodontol*, 2001, 28(3): 241-249.
- Armitage GC. Periodontal infections and cardiovascular disease how strong is the association[J]. *Oral Dis*, 2000, 6(6): 335-350.
- Ghizoni JS, Taveira LA, Garlet GP, et al. Increased levels of *Porphyromonas gingivalis* are associated with ischemic and hemorrhagic cerebrovascular disease in humans: an in vivo study[J]. *J Appl Oral Sci*, 2012, 20(1): 104-112.
- Page RC, Offenbacher S, Schroeder HE, et al. Advances in the pathogenesis of periodontitis: summary of developments, clinical implications and future directions[J]. *Periodontol 2000*, 1997, 14: 216-248.
- Lamont RJ, Yilmaz O. In or out: the invasiveness of oral bacteria[J]. *Periodontol 2000*, 2002, 30: 61-69.
- Bodet C, Chandad F, Grenier D. *Porphyromonas gingivalis*-induced inflammatory mediator profile in an ex vivo human whole blood model[J]. *Clin Exp Immunol*, 2006, 143(1): 50-57.
- Kebusch M, Demmer RT, Papapanou PN. "Gum bug, leave my heart alone!" --epidemiologic and mechanistic evidence linking periodontal infections and atherosclerosis[J]. *J Dent Res*, 2010, 89(9): 879-902.
- Epstein SE, Zhu J, Burnett MS, et al. Infection and atherosclerosis: potential roles of pathogen burden and molecular mimicry[J]. *Arterioscler Thromb Vasc Biol*, 2000, 20(6): 1417-1420.
- Papapanou, Panos N. Systemic effects of periodontitis: lessons learned from research on atherosclerotic vascular disease and adverse pregnancy outcomes[J]. *Int Dent J*, 2015, 65(6): 283-291.
- Takahashi N, Nyvad B. The role of bacteria in the caries process: ecological perspectives[J]. *J Dent Res*, 2011, 90(3): 294-303.
- Glodny B, Nasseri P, Crismani A, et al. The occurrence of dental caries is associated with atherosclerosis[J]. *Clinics*, 2013, 68(7): 946-953.
- Kim K, Choi S, Chang J, et al. Severity of dental caries and risk of coronary heart disease in middle-aged men and women: a population-based cohort study of Korean adults, 2002-2013[J]. *Sci Rep*, 2019, 9(1): 10491.
- Nakano K, Inaba H, Nomura R, et al. Detection of Cariogenic *Streptococcus mutans* in Extricated Heart Valve and Atheromatous Plaque Specimens[J]. *J Clin Microbiol*, 2006, 44(9): 3313-3317.
- Haraszthy VI, Zambon JJ, Trevisan M, et al. Identification of periodontal pathogens in atherosomatous plaques[J]. *J Periodontol*, 2000, 71(10): 1554-1560.
- Grau AJ, Becher H, Ziegler CM, et al. Periodontal disease as a risk factor for ischemic stroke[J]. *Stroke*, 2004, 35(2): 496-501.
- Grau AJ, Buggle F, Ziegler C, et al. Association between acute cerebrovascular ischemia and chronic and recurrent infection[J]. *Stroke*, 1997, 28(9): 1724-1729.
- Leira Y, López-Dequidt I, Arias S, et al. Chronic periodontitis is associated with lacunar infarct: a case-control study[J]. *Eur J Neurol*, 2016, 23(10): 1572-1579.
- Del Brutto OH, Mera RM, Zambrano M, et al. Severe edentulism is a major risk factor influencing stroke incidence in rural Ecuador (The Atahualpa Project)[J]. *Int J Stroke*, 2017, 12(2): 201-204.
- Cheng F, Zhang M, Wang Q, et al. Tooth loss and risk of cardiovascular disease and stroke: a dose-response meta analysis of prospective cohort studies[J]. *PLoS One*, 2018, 13(3): e0194563.
- Sheiham A, Steele J. Does the condition of the mouth and teeth affect the ability to eat certain foods, nutrient and dietary intake and nutritional status amongst older people?[J]. *Public Health Nutr*, 2001, 4(3): 797-803.
- Valdes-Marquez E, Parish S, Clarke R, et al. Relative effects of LDL-C on ischemic stroke and coronary disease:a Mendelian randomization study[J]. *Neurology*, 2019, 92(11): e1176-e1187.
- Lo GS, Evans RH, Phillips KS, et al. Effect of soy fiber and soy

- protein on cholesterol metabolism and atherosclerosis in rabbits[J]. Atherosclerosis, 1987, 64(1): 47-54.
27. Baekey PA, Cerdá JJ, Burgin CW, et al. Grapefruit pectin inhibits hypercholesterolemia and atherosclerosis in miniature swine[J]. Clin Cardiol 1988, 11(9): 597-600.
28. Soliman GA. Dietary fiber, atherosclerosis, and cardiovascular disease[J]. Nutrients, 2019, 11(5): 1155.
29. Velsko IM, Chukkapalli SS, Rivera MF, et al. Active invasion of oral and aortic tissues by *Porphyromonas gingivalis* in mice causally links periodontitis and atherosclerosis[J]. PLoS One, 2014, 9(5): e97811.
30. Patrakka O, Pienimäki JP, Tuomisto S, et al. Oral bacterial signatures in cerebral thrombi of patients with acute ischemic stroke treated with thrombectomy[J]. J Am Heart Assoc, 2019, 8(11): e012330.
31. Chia JS, Lien HT, Hsueh PR, et al. Induction of cytokines by glucosyltransferases of *Streptococcus mutans*[J]. Clin Diagn Lab Immunol, 2002, 9(4): 892-897.
32. Ramji DP, Davies TS. Cytokines in atherosclerosis: key players in all stages of disease and promising therapeutic targets[J]. Cytokine Growth Factor Rev, 2015, 26(6): 673-685.
33. Arman M, Krauel K, Tilley DO, et al. Amplification of bacteria-induced platelet activation is triggered by Fc γ RIIA, integrin α IIb β 3, and platelet factor 4[J]. Blood, 2014, 123(20): 3166-3174.
34. Klarström Engström K, Khalaf H, Kälvegren H, et al. The role of *Porphyromonas gingivalis* gingipains in platelet activation and innate immune modulation[J]. Mol Oral Microbiol, 2015, 30(1): 62-73.
35. Langer HF, Gawaz M. Platelet-vessel wall interactions in atherosclerotic disease[J]. Thromb Haemost, 2008, 99(3): 480-486.
36. Naik UP. Bacteria exploit platelets[J]. Blood, 2014, 123(20): 3067-3068.

本文引用: 朱慈燕, 韩辉. 口腔疾病与脑血管病的关系[J]. 临床与病理杂志, 2020, 40(12): 3313-3316. doi: 10.3978/j.issn.2095-6959.2020.12.036

Cite this article as: ZHU Ciyan, HAN Hui. Relationship between oral diseases and cerebrovascular diseases[J]. Journal of Clinical and Pathological Research, 2020, 40(12): 3313-3316. doi: 10.3978/j.issn.2095-6959.2020.12.036