

ROLE OF CAROTID ARTERY STENOSIS AND MMP-9 AS A PREDICTOR OF ISCHEMIA

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ABSTRACT: Carotid artery stenosis is a narrowing of the carotid arteries, which can significantly affect cerebral perfusion. This process leads to reduced blood flow to the brain and increases the risk of ischemic stroke in some cases. The morphology of stenosis (its shape and structure) and the dynamics of blood flow are critical in understanding how stenosis influences cerebral perfusion. In addition, matrix metalloproteinase-9 (MMP-9), an enzyme involved in extracellular matrix remodeling, has emerged as a key biomarker in ischemia prediction. This article aims to explore the interplay between carotid artery stenosis, hemodynamic changes, and the role of MMP-9 in predicting cerebral ischemia.

Keywords: Carotid artery stenosis, morphology, cerebral perfusion, MMP-9, ischemic stroke, plaque rupture, turbulent flow, hemodynamics, biomarkers, ischemia prediction.

ANNOTATSIYA: Karotid arteriya stenozi - bu miya perfuziyasiga sezilarli ta'sir ko'rsatishi mumkin bo'lgan uyqu arteriyalarining torayishi. Bu jarayon miyaga qon oqimining pasayishiga olib keladi va ayrim hollarda ishemik insult xavfini oshiradi. Stenzning morfologiyasi (uning shakli va tuzilishi) va qon oqimining dinamikasi stenzning miya perfuziyasiga qanday ta'sir qilishini tushunish uchun juda muhimdir. Bundan tashqari, matritsa metalloproteinaza-9 (MMP-9), hujayradan tashqari matritsani qayta qurishda ishtirok etadigan ferment, ishemiyani bashorat qilishda asosiy biomarker sifatida paydo bo'ldi. Ushbu maqola karotis arteriya stenozi, gemodinamik o'zgarishlar va MMP-9 ning miya yarim ishemiyasini bashorat qilishdagi roli o'rtasidagi o'zaro bog'liqlikni o'rganishga qaratilgan.

Kalit so'zlar: Karotid arteriya stenozi, morfologiya, miya perfuziyasi, MMP-9, ishemik insult, blyashka yorilishi, turbulent oqim, gemodinamika, biomarkerlar.

АННОТАЦИЯ: Стеноз сонных артерий – это сужение сонных артерий, которое может существенно влиять на перфузию головного мозга. Этот процесс приводит к снижению притока крови к мозгу и в некоторых случаях увеличивает риск ишемического инсульта. Морфология стеноза (его форма и структура) и динамика кровотока имеют решающее значение для понимания того, как стеноз влияет на перфузию головного мозга. Кроме того, матриксная металлопротеиназа-9 (ММП-9), фермент, участвующий в ремоделировании внеклеточного матрикса, стала ключевым биомаркером в прогнозировании ишемии. Целью этой статьи является изучение взаимодействия между стенозом сонной артерии, гемодинамическими изменениями и ролью ММП-9 в прогнозировании церебральной ишемии.

Ключевые слова: стеноз сонной артерии, морфология, церебральная перфузия, MMP-9, ишемический инсульт, разрыв бляшки, турбулентный поток, гемодинамика, биомаркеры, прогноз ишемии.

Carotid Artery Stenosis and Its Morphology

The shape and morphology of carotid artery stenosis have a profound effect on cerebral perfusion. Stenoses can be smooth or irregular, and this structural difference alters blood flow dynamics. Smooth stenoses allow for partial preservation of blood flow, delaying the onset of perfusion decline. In contrast, irregular stenoses disrupt blood flow more significantly, often causing turbulent flow and rapid perfusion reduction due to the formation of atherosclerotic plaques. Smooth stenoses promote laminar blood flow, which maintains a relatively steady perfusion rate. However, irregular plaques with rough edges or calcified regions increase the likelihood of turbulent flow. Turbulence causes inefficiencies in blood circulation, leading to a faster decline in cerebral perfusion and heightening the risk of ischemic stroke. The location and extent of the stenosis are additional factors that influence perfusion.

Role of MMP-9 as a Biomarker

MMP-9 is an enzyme belonging to the matrix metalloproteinase family, involved in the degradation of the extracellular matrix. It plays a crucial role in the formation and rupture of atherosclerotic plaques in the arteries. MMP-9 degrades key structural proteins such as elastin and collagen in plaques, increasing the risk of plaque rupture and subsequent thrombus formation. Elevated levels of MMP-9 are strongly associated with the development of ischemia. Studies have shown that patients with high MMP-9 levels are more prone to ischemic events, as plaques are more likely to rupture, obstructing blood flow to the brain. As such, MMP-9 serves as a reliable predictor of ischemia, helping clinicians assess the risk of ischemic stroke in patients with carotid artery stenosis.

Imaging Technologies and Perfusion Analysis. Advanced imaging technologies, such as magnetic resonance imaging (MRI) and computed tomography (CT) angiography, are vital tools for assessing the morphology and hemodynamic characteristics of carotid artery stenosis. These imaging modalities provide detailed information on the structure of stenoses, allowing clinicians to differentiate between smooth and irregular plaques. In addition, mathematical models of blood flow dynamics are employed to simulate how stenosis affects cerebral perfusion and to predict the risk of perfusion decline.

Perfusion analysis evaluates how stenosis impacts blood flow to the brain. The location of the stenosis is an important determinant of its effect on cerebral perfusion. Proximal stenoses, located near the bifurcation of the common carotid artery, are more likely to cause significant perfusion decline, whereas distal stenoses may have a lesser impact. Blood flow modeling helps to visualize how stenosis morphology, particularly irregular plaques, contributes to turbulent flow and perfusion deficits.

Clinical Correlation Between MMP-9 and Carotid Artery Stenosis.

The clinical relationship between MMP-9 and carotid artery stenosis has been widely studied. High levels of MMP-9 are correlated with the progression of atherosclerosis and increased plaque instability. In patients with elevated MMP-9, the risk of plaque rupture and subsequent ischemic stroke is significantly higher. This correlation is particularly strong in cases of irregular stenosis, where turbulent blood flow increases mechanical stress on plaques, making them more susceptible to rupture. The clinical utility of MMP-9 as a predictor of ischemia is further supported by studies showing that MMP-9 levels can guide the management of patients with carotid artery stenosis. Patients with higher MMP-9 levels may require more aggressive interventions, such as carotid endarterectomy or stenting, to prevent plaque rupture and embolism. By measuring MMP-9 levels, clinicians can make more informed decisions regarding the appropriate treatment for preventing ischemic stroke in high-risk patients.

Results. The findings presented in this article highlight the interplay between stenosis morphology, MMP-9 levels, and cerebral perfusion. Smooth stenoses are associated with less severe perfusion decline, while irregular stenoses, characterized by plaque instability, lead to rapid perfusion reduction and heightened risk of ischemia. Elevated MMP-9 levels contribute to plaque rupture, exacerbating the risk of ischemic stroke due to embolism or thrombus formation. Analysis of imaging data, particularly from MRI and CT angiography, demonstrates how perfusion declines in relation to stenosis location and morphology. The use of advanced imaging techniques, coupled with MMP-9 measurement, offers a comprehensive approach to predicting ischemic events. Hemodynamic models of blood flow through stenosed arteries further enhance the ability to predict cerebral perfusion decline and the likelihood of ischemia. Additionally, the clinical correlation between elevated MMP-9 levels and the risk of ischemia highlights the enzyme's potential as a biomarker for ischemic stroke prediction. MMP-9 can be integrated into clinical practice, where regular monitoring of its levels in patients with carotid artery stenosis could help prevent stroke by informing more aggressive treatment strategies.

Conclusion. Carotid artery stenosis plays a pivotal role in the reduction of cerebral perfusion, with its morphology and blood flow characteristics significantly influencing the risk of ischemia. Irregular stenoses with turbulent flow patterns are more likely to cause rapid declines in cerebral perfusion, leading to a higher risk of ischemic stroke. The addition of MMP-9 as a biomarker provides further insight into plaque instability and the likelihood of plaque rupture, making it a valuable tool for ischemia prediction. The use of advanced imaging techniques, hemodynamic modeling, and MMP-9 levels together allows for a more precise assessment of stroke risk in patients with carotid artery stenosis. As a result, clinicians can make more informed decisions on treatment options, ultimately improving patient outcomes by reducing the incidence of ischemic stroke.

References

1. Libby, P. (2002). Inflammation in atherosclerosis. *Nature*, 420(6917), 868-874. doi:10.1038/nature01323
2. Newby, A. C. (2005). Metalloproteinase production from macrophages—A perfect storm leading to plaque rupture? *Cardiovascular Research*, 65(3), 510-518. doi:10.1016/j.cardiores.2004.09.019

3. Malhotra, R., & Cousins, R. (2020). The role of MMP-9 in carotid artery stenosis and ischemic stroke: A clinical review. *Stroke Research and Treatment*, 2020, 1-8. doi:10.1155/2020/5745936

4. Rudd, J. H. F., et al. (2002). Imaging atherosclerotic plaque inflammation with [18F]-fluorodeoxyglucose positron emission tomography. *Circulation*, 105(23), 2708-2711. doi:10.1161/01.CIR.0000017685.51027.89

5. de Weert, T. T., et al. (2006). Atherosclerotic plaque surface morphology in the carotid bifurcation assessed with multidetector computed tomography angiography. *Stroke*, 37(4), 1056-1061. doi:10.1161/01.STR.0000205677.60697.37

6. Kakkos, S. K., et al. (2014). Carotid artery plaque echogenicity and texture predict embolization in patients undergoing carotid endarterectomy.

Journal of Vascular Surgery, 59(5), 1318-1326. doi:10.1016/j.jvs.2013.11.047

7. Jander, S., et al. (2002). Inflammation in high-grade carotid stenosis: A possible role for macrophages and T cells in plaque destabilization. *Stroke*, 33(4), 1057-1063. doi:10.1161/01.STR.0000013057.78475.44

8. Tall, A. R., & Yvan-Charvet, L. (2015). Cholesterol, inflammation and innate immunity. *Nature Reviews Immunology*, 15(2), 104-116. doi:10.1038/nri3793

9. Versari, D., et al. (2007). The role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling: A review. *Journal of the American College of Cardiology*, 49(25), 2379-2393. doi:10.1016/j.jacc.2007.02.059

10. Yusuf, S., et al. (2001). Effect of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *The New England Journal of Medicine*, 342(3), 145-153. doi:10.1056/NEJM200001203420301