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Mechanisms and Treatment Strategies of Coronary Microvascular Disease

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Abstract: Heart disease remains one of the primary causes of death and disability, particularly with a high incidence of ischemic heart disease, severely impacting people's health and lives. Among the causes of ischemic heart disease, angina and breathlessness are common, yet many patients clinically lack severe obstructive coronary artery disease, often presenting with coronary microvascular disease (CMD). This condition has multifaceted causes, complex mechanisms, high diagnostic challenges, and substantial treatment difficulties. It is elusive and requires careful determination of effective treatment strategies. Therefore, in-depth research into the mechanisms and treatment strategies of coronary microvascular disease is essential for advancing medical standards and positively impacting patient health and recovery.

Keywords: Coronary Microvascular Disease; Mechanisms; Treatment Strategies

Introduction

Following the onset of CMD, cardiovascular function in patients is significantly impaired, contributing to non-obstructive coronary ischemia. Current statistics indicate a high incidence of CMD in clinical settings, elevating the risk of cardiovascular events and endangering patient health. The 2020 Expert Consensus on Non-Obstructive Coronary Ischemia (EAPCI) underscores the criticality of assessing coronary microvascular function to tailor optimal treatment strategies based on clinical diagnoses in China, thereby enhancing treatment efficacy^[1]. Consequently, in-depth investigation into the mechanisms and treatment of CMD is essential for improving medical standards and facilitating the restoration of cardiovascular health in patients.

1. Mechanisms of Coronary Microvascular Disease

1.1 Structural Abnormalities of Microvessels

Histological changes observed during myocardial tissue biopsy of CMD patients reveal phenomena such as myofiber proliferation, intimal thickening, and luminal endothelial cell swelling associated with small coronary artery pathology. These pathological changes may induce luminal obstruction and vascular remodeling. Further analysis suggests that the pathophysiology of acute coronary syndromes may involve microembolic events post-vascular reperfusion, while hypertrophic cardiomyopathy and hypertension patients are more prone to vascular remodeling. These disease processes collectively contribute to microcirculatory structural abnormalities, ultimately leading to narrowing of microvascular lumens and increased resistance in small arteries.

1.2 Functional Abnormalities of Microvessels

In exploring the dysfunction of the microcirculatory system, notable manifestations of microvascular dysfunction include impaired vasodilation and excessive constriction of coronary microvessels. Studies indicate that impaired vasodilation may result from pathological changes in endothelial-dependent and non-endothelial-dependent mechanisms, commonly observed in populations at high cardiovascular risk such as diabetes, obesity, and smokers, suggesting a multifactorial interaction in their pathophysiology. Moreover, another manifestation of microcirculatory dysfunction, excessive vascular constriction, correlates closely with the over-release of vasoconstrictors like endothelin-1 (ET-1) and thromboxane A₂, and increased sensitivity of vascular smooth muscle cells to these constrictive stimuli.

1.3 Extravascular Mechanisms

Studies exploring the pathophysiology of the cardiovascular system reveal direct relationships with abnormalities in extravascular structure and function. These factors encompass conditions such as hypertension and extracellular matrix collagen deposition-induced vascular external compression, as well as reduced diastolic perfusion time due to aortic valve stenosis and critical coronary artery conditions. Furthermore, ischemic hypoxia at the tissue level causing cellular edema, as well as genetic and acquired susceptibility to microcirculatory damage, are integral components of extravascular mechanisms. Therefore, academic research recognizes the combined action of these pathological processes not only revealing the complexity of multifactorial involvement in cardiovascular diseases but also emphasizing the need to consider individual differences and the diversity of pathophysiological mechanisms in treatment strategies.

1.4 Others

While traditional cardiovascular risk factors are acknowledged to have some impact on the pathogenesis of CMD, they clearly do not fully explain the complexity of pathological occurrences. Accordingly, the academic community has expanded the scope of etiological studies, proposing diverse factors including hyperactivity of the adrenergic system, insulin resistance, systemic inflammatory responses, and estrogen deficiency. In clinical practice, it is particularly noteworthy that some CMD patients exhibit significant pain sensitivity. These patients are more susceptible to chest pain during routine procedures such as cardiac catheterization, cardiac electrophysiological stimulation, and contrast agent injection compared to those unaffected by microvascular disease. This heightened pain sensitivity may not only serve as an indicator for assessing disease severity but also holds promise as a crucial therapeutic intervention target for this patient subgroup.

2. Diagnostic Strategies for Coronary Microvascular Disease

2.1 Measurement of Microcirculatory Resistance Index

Currently, the microcirculatory resistance index is considered the "gold standard" for diagnosing CMD in clinical settings. Calculated by assessing the product of the maximum hyperemic state coronary artery pressure and the mean transit time of intracoronary injection of 0.9% saline, a parameter value ≥ 25 generally indicates disease presence. As a diagnostic criterion, the microcirculatory resistance index is minimally influenced by heart rate and arterial conditions, demonstrating strong repeatability despite methodological limitations.

2.2 Coronary Flow Reserve Assessment

Coronary flow reserve reflects the critical adjustment of the coronary vascular bed in clinical settings to meet myocardial oxygen demands, serving as a determinant indicator for CMD when excluding epicardial coronary artery stenosis. However, this method is significantly affected by patient age, gender, heart rate, blood pressure, and other factors, limiting its use^[2].

3. Treatment Strategies for Coronary Microvascular Disease

3.1 Lifestyle Modifications

On the basis of clinical research findings, smoking, alcohol consumption, and poor dietary habits are major contributors to CMD. Therefore, treatment involves smoking cessation, alcohol abstinence, achieving optimal weight status, and adjusting dietary habits to improve vascular function, prevent severe angina symptoms, and enhance quality of life^[3]. Additionally, necessary psychological counseling measures help CMD patients alleviate anxiety and depression, promoting normalized vascular flow and expediting physical health recovery.

3.2 β -Blockers

β -Blockers hold significant therapeutic value in clinical cardiovascular diseases by lowering heart rate and prolonging diastole, thereby maintaining adequate vascular flow to meet cardiac functional demands. Research indicates that β -blockers effectively improve cardiac function and are particularly advantageous in treating angina, commonly used as adjunct medications for cardiovascular diseases.

3.3 Nitrate Drugs

Nitrate use promotes vasodilation and enhances blood flow, significantly impacting the treatment of coronary artery stenosis and spasms. Nevertheless, its prognostic effect on CMD treatment remains controversial, especially considering potential risks associated with long-term use.

3.4 Traditional Chinese Medicine Treatments

Combining traditional Chinese medicine with Western medicine facilitates anti-inflammatory and antioxidant effects, positively impacting symptom alleviation and improving patient quality of life to meet cardiovascular functional requirements. Clinical needs in traditional Western medicine treatment, supplemented by Tongxinluo Capsule, Qishe Yiqi Diwan, Shexiang Tongxin Dropping Pill, and other traditional Chinese medicine treatments, effectively improve patient symptoms and enhance treatment efficacy. However, the integration of traditional Chinese and Western medicine treatment methods requires extensive clinical expansion to ensure treatment effectiveness^[4].

3.5 Other Treatment Strategies

In addition to the aforementioned treatment measures, treatment using ranolazine blocks the late sodium channel to reduce sodium and calcium overload, maintaining myocardial relaxation and significantly improving myocardial perfusion capacity. Clinical trials have shown that ranolazine treatment for CMD has high utility in alleviating angina symptoms but requires further research to improve coronary artery flow reserve indicators. Ivabradine in clinical treatment lowers sinus node autonomicity, maintaining sinus rhythm within reasonable limits^[5].

4. Conclusion

Following the onset of coronary microvascular disease, cardiovascular function in patients is compromised. Timely diagnosis and treatment facilitate the restoration of patient health, improving quality of life. As cardiovascular disease research continues to deepen in recent years, understanding the mechanisms and treatment strategies of CMD remains essential. The complexity of CMD's pathogenesis necessitates rigorous clinical research to explore treatment options, enhance treatment standards, and positively impact future medical developments.

References

- [1] The project team of "Expert Consensus on Integrated Diagnosis and Treatment of Coronary Artery Microvascular Disease with Traditional Chinese and Western Medicine". Expert Consensus on Integrated Diagnosis and Treatment of Coronary Artery Microvascular Disease with Traditional Chinese and Western Medicine [J]. Journal of Integrated Chinese and Western Medicine Cardiovascular Disease, 2022, 20 (21): 3841-3850
- [2] Zhu Feng, Wang Hailong. Research progress on the correlation between instantaneous waveform free ratio and coronary artery blood flow reserve fraction [J]. Journal of Practical Cardiovascular, Cerebrovascular, and Pulmonary Vascular Diseases, 2021, 29 (1): 137-140
- [3] The Basic Research Group of the Cardiovascular Branch of the Chinese Medical Association, the Interventional Cardiology Group of the Cardiovascular Branch of the Chinese Medical Association, and the Women's Heart Health Group of the Cardiovascular Branch of the Chinese Medical Association. Chinese Expert Consensus on the Diagnosis and Treatment of Coronary Microvascular Diseases [J]. Chinese Journal of Circulation, 2017, 32 (5): 421-430
- [4] Jin Gangqiang. The therapeutic effect of Nicorandil on microvascular angina and its impact on endothelial function [J]. Contemporary Medicine, 2016, 22 (23): 131-132
- [5] Ma Zhihui, Chen Bin, Zhang Yongjun, et al. The effect and efficacy of rosuvastatin on plasma Hcy levels in patients with microvascular angina [J]. Practical Geriatrics, 2015, 29 (11): 961-962

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