DIAGNOSIS AND TREATMENT OF MICROVASCULAR ANGINA

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Abstract: Microvascular angina (MVA) represents a complex clinical phenotype characterized by symptoms of myocardial ischemia resulting from structural or functional abnormalities of the coronary microcirculation, rather than obstructive epicardial coronary artery disease. Historically underdiagnosed due to the limitations of standard macroscopic imaging techniques, MVA is now recognized as a major subtype of Ischemia with Non-Obstructive Coronary Arteries (INOCA). This article provides a comprehensive overview of the pathophysiology, multi-step diagnostic criteria, and contemporary multi-faceted treatment strategies for MVA, emphasizing a shift toward personalized, mechanism-guided cardiovascular care.

Keywords: Microvascular angina, coronary microvascular dysfunction, INOCA, myocardial ischemia, endothelial dysfunction, coronary flow reserve, index of microcirculatory resistance, anti-anginal therapy.

Ischemic heart disease has historically been synonymously linked with obstructive atherosclerosis of the epicardial coronary arteries, a perspective that long overshadowed other significant causes of myocardial ischemia. However, extensive clinical research over the past few decades has revealed a substantial cohort of patients who present with typical anginal symptoms and objective evidence of myocardial ischemia but exhibit no angiographically significant epicardial narrowing. This clinical entity, broadly classified as Ischemia with Non-Obstructive Coronary Arteries, frequently stems from pathological alterations within the pre-arterioles and arterioles that constitute the coronary microcirculation. When chest pain or discomfort is directly attributable to the impairment of these microscopic branching vessels, which are smaller than five hundred micrometers in diameter and therefore invisible during standard invasive angiography, the condition is formally

diagnosed as microvascular angina. Managing this condition is of paramount importance because it not only severely compromises a patient's quality of life through recurrent episodes of debilitating pain and frequent emergency department visits but also carries a documented risk of major adverse cardiovascular events, including myocardial infarction, heart failure, and cardiovascular mortality.

The underlying pathophysiology of microvascular angina is rooted in coronary microvascular dysfunction, a complex process involving both structural and functional abnormalities of the microvasculature. Structurally, the microvessels may undergo adverse remodeling characterized by luminal narrowing, medial hypertrophy, perivascular fibrosis, and capillary rarefaction, which is a physical reduction in the density of functional capillaries supplying the myocardium. Functionally, the primary driver is endothelial dysfunction, where the vascular endothelium fails to synthesize and release adequate amounts of nitric oxide and other vasodilatory substances, preventing the microvessels from dilating appropriately in response to increased cardiac workload. Furthermore, smooth muscle hyper-reactivity within the microvessels can lead to localized or diffuse microvascular spasms, which abruptly restrict coronary blood flow even in the absence of physical exertion. Collectively, these structural and functional impairments disturb coronary autoregulation, elevate coronary microvascular resistance, and severely limit the heart's ability to augment coronary blood flow during periods of physical exercise or emotional stress, resulting in transient but repeated episodes of myocardial tissue ischemia.

To establish a definitive diagnosis of microvascular angina, clinical guidelines require a rigorous and standardized diagnostic framework consisting of four interconnected criteria. First, the patient must demonstrate typical clinical symptoms of angina pectoris, which usually manifest as retrosternal chest pain, pressure, or tightness that may radiate to the left arm or jaw and is classically triggered by exertion or stress, although it can also occur atypically at rest. Second, there must be objective evidence of myocardial ischemia verified through non-invasive imaging

techniques such as stress echocardiography, nuclear perfusion imaging, or advanced cardiac magnetic resonance imaging and positron emission tomography, which reveal perfusion deficits under stress conditions. Third, coronary angiography or computed tomography coronary angiography must confirm the absence of obstructive epicardial coronary artery disease, which is defined as having less than fifty percent luminal stenosis and a fractional flow reserve greater than 0.80 in all major epicardial arteries. Fourth, and most crucially, there must be objective, quantifiable proof of microvascular dysfunction itself. This is typically achieved during invasive diagnostic coronary reactivity testing by measuring a restricted Coronary Flow Reserve, defined as a ratio of hyperemic to baseline coronary blood flow of less than 2.0, or by identifying an elevated Index of Microcirculatory Resistance of twenty-five or greater, which directly points to abnormally high resistance within the microscopic vessels of the heart.

Once a diagnosis is confirmed, treating microvascular angina requires an aggressive, multi-faceted therapeutic approach that targets systemic cardiovascular health, stabilizes the endothelium, and directly addresses the physical symptoms of ischemia. The baseline of this strategy is comprehensive lifestyle modification and rigorous risk factor control, since the microvasculature is highly sensitive to systemic metabolic stress. Absolute smoking cessation is mandatory because nicotine directly damages the endothelial lining and promotes acute microvascular constriction, while transitioning to a low-fat, nutrient-dense Mediterranean diet helps suppress systemic vascular inflammation. Patients are also encouraged to participate in regular, supervised physical exercise programs, which have been shown to enhance endothelial nitric oxide production and stimulate beneficial microvascular remodeling over time. Additionally, meticulous clinical management of co-existing conditions, such as maintaining strict target levels for blood pressure, lipid profiles, and glycemic control in diabetic patients, is essential to halt the progression of microcirculatory damage.

Pharmacological management is divided between systemic cardioprotective therapies and targeted anti-anginal medications. Statins are prescribed not only for their lipid-lowering capabilities but also for their potent pleiotropic properties, which reduce vascular inflammation and directly improve endothelial function by enhancing nitric oxide bioavailability. Low-dose aspirin is utilized to prevent microvascular thrombosis and suppress platelet activation, which can worsen flow dynamics in restricted vessels. Angiotensin-converting enzyme inhibitors, such as quinapril, are highly valuable because they block tissue-level angiotensin II, thereby reducing arterial stiffness, reversing vascular remodeling, and facilitating better endothelial-dependent vasodilation. To manage active chest pain, first-line anti-anginal therapy includes beta-blockers, which reduce the resting and exertional heart rate to decrease myocardial oxygen demand, and calcium channel blockers, which relax the smooth muscles of the coronary arterioles to prevent microvascular spasms and improve diastolic perfusion. In patients with refractory symptoms despite standard therapy, second-line agents like ranolazine are introduced to inhibit the late inward sodium current, thereby reducing intracellular calcium overload and improving myocardial relaxation, while ivabradine can be used to selectively slow the heart rate without compromising myocardial contractility or lowering systemic blood pressure. Ultimately, adhering to these structured diagnostic and therapeutic algorithms, as advocated by major cardiovascular societies, allows clinicians to move away from empirical treatment toward targeted, mechanism-based care that substantially improves both the clinical outcomes and the daily lives of those living with microvascular angina.

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