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REVIEW ARTICLE

Anemia as an Under-Recognized Cause of Angina Pectoris: Pathophysiological Mechanisms, Clinical Implications, and Management Strategies

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Abstract

Background: *Angina pectoris is traditionally attributed to obstructive coronary artery disease (1,2); however, myocardial ischemia may arise from systemic factors that impair oxygen delivery. Anemia, highly prevalent in South Asia and other low- and middle-income regions (6), reduces arterial oxygen content and can precipitate angina even in the absence of significant epicardial coronary stenosis (10,11). Despite its frequency, anemia remains insufficiently emphasized in routine cardiology evaluation.*

Objective: *To examine the mechanisms by which anemia induces myocardial ischemia and angina, and to outline its diagnostic, therapeutic, and prognostic implications in contemporary cardiovascular practice.*

Methods: *A focused review of cardiovascular and hematologic literature was performed, emphasizing oxygen transport physiology, coronary hemodynamics, and clinical studies linking anemia with ischemic symptoms (4,6).*

Results: *Reduced hemoglobin concentration lowers arterial oxygen content, prompting compensatory increases in heart rate and cardiac output that raise myocardial oxygen demand (1,7). When coronary vasodilatory reserve is limited due to epicardial disease or microvascular dysfunction (10,11), these adaptations fail, resulting in oxygen supply–demand mismatch and angina. Correction of anemia improves functional capacity and anginal burden in selected populations (4,8).*

Conclusion: *Anemia is a clinically important and potentially reversible contributor to angina pectoris.*

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Introduction

Angina pectoris is a hallmark manifestation of myocardial ischemia and is commonly attributed to obstructive coronary artery disease.[1,2] However, ischemia may occur in the absence of flow-limiting coronary lesions (10,11), highlighting the importance of non-coronary determinants of myocardial oxygen balance.

Anemia is defined by reduced hemoglobin concentration and diminished oxygen-carrying capacity of blood (6). It frequently coexists with cardiovascular disease, particularly heart failure and chronic kidney disease.[4,5,7]

Myocardial oxygen delivery depends on coronary blood flow and arterial oxygen content (1,2). In anemia, compensatory cardiovascular responses increase cardiac output and heart rate.[7] While initially adaptive, these responses increase myocardial workload and oxygen demand, lowering the ischemic threshold.

Failure to recognize anemia may lead to misinterpretation of stress tests and unnecessary invasive procedures.[10]

Epidemiology and Clinical Significance

Anemia affects more than one-quarter of the global population (6). Among patients with stable ischemic heart disease, anemia is reported in approximately 15–30%[5,7] In acute coronary syndromes, anemia at presentation is common and independently associated with adverse outcomes.[5]

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Reduced hemoglobin concentration correlates with earlier onset of ischemia during exercise testing and greater symptom burden (4,8). In patients with non-obstructive coronary disease, limited coronary flow reserve or microvascular dysfunction amplifies the ischemic impact of reduced oxygen content.[11,12]

Pathophysiological Mechanisms of Anemia-Induced Angina

Reduced Arterial Oxygen Content

Hemoglobin accounts for nearly all oxygen transport in blood (1,2). A decline in hemoglobin concentration leads to proportional reduction in arterial oxygen content, even when saturation is normal.

Compensatory Hemodynamic Responses

Anemia triggers sympathetic activation, resulting in tachycardia and increased stroke volume (7). Tachycardia shortens diastole, reducing coronary perfusion time (1).

Coronary Vasodilatation and Limited Reserve

Anemia induces coronary vasodilatation. However, in patients with epicardial CAD or microvascular dysfunction, coronary flow reserve is already impaired (10,11), limiting compensatory capacity.

Oxygen Supply–Demand Mismatch

The convergence of reduced oxygen supply and increased myocardial demand produces subendocardial ischemia, often manifested as exertional ST-segment depression (10).

Hemodynamic and Oxygen Transport Considerations

Reduced blood viscosity lowers systemic vascular resistance but increases venous return and cardiac workload (6,7). Despite increased cardiac output, oxygen delivery remains compromised due to reduced hemoglobin concentration (1).

Coronary Circulation and Functional Ischemia

In anemia, resting coronary blood flow may be elevated, consuming a substantial portion of coronary flow reserve. During stress, inability to augment flow results in ischemia (11).

Microvascular and endothelial dysfunction further impair adaptive vasodilatation (11,12). In patients with angina and non-obstructive coronary arteries, anemia may unmask latent microvascular disease (12).

Types of Anemia Relevant to Angina

Iron deficiency anemia: Impairs hemoglobin synthesis and iron-dependent myocardial metabolism (4,8).

Anemia of chronic disease / heart failure–related anemia: Associated with blunted erythropoietin response and reduced iron availability (3,4,7).

Chronic kidney disease–related anemia: Linked with LV hypertrophy and worse cardiovascular outcomes (4,5).

Hemolytic anemia: Rapid hemoglobin decline may provoke acute ischemia due to nitric oxide depletion.

Megaloblastic anemia: May contribute via endothelial dysfunction.

Clinical Presentation

Anemia-related angina typically presents with exertional chest discomfort at low workloads. ECG may demonstrate subendocardial ischemic changes (10).

Symptoms disproportionate to angiographic findings should raise suspicion for contributory anemia (11).

Diagnostic and Management Approach

Evaluation of angina should include routine hemoglobin assessment (6). Interpretation of stress testing must consider oxygen-carrying capacity (10).

Iron supplementation improves exercise capacity in selected patients (4,8). Erythropoiesis-stimulating agents have been evaluated with mixed results (9). Blood transfusion is reserved for severe or symptomatic anemia with active ischemia (6).

Anti-anginal therapy remains important but may be insufficient without correction of anemia.

Prognosis

Anemia in patients with ischemic heart disease is associated with increased hospitalization and worse outcomes (5,7). Correction of hemoglobin levels improves functional capacity in selected populations (4,8).

Conclusion

Anemia reduces arterial oxygen content and increases myocardial oxygen demand, resulting in ischemic imbalance in patients with and without obstructive coronary disease (1,10). Routine hemoglobin assessment should be integrated into angina evaluation, particularly in high-prevalence regions.

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