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Review Article

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Myocardial infarction with non-obstructive coronary arteries (MINOCA): current concepts in pathophysiology, diagnosis, management, and prognosis

Abstract

Myocardial infarction with non-obstructive coronary arteries (MINOCA) describes a heterogeneous clinical syndrome in which patients fulfill diagnostic criteria for acute myocardial infarction despite the absence of obstructive coronary artery disease on angiography. Once considered an uncommon and relatively benign condition, MINOCA is now recognized as a clinically significant entity associated with substantial morbidity and non-negligible mortality. Its diagnostic and therapeutic complexity stems from the wide spectrum of underlying mechanisms, including atherosclerotic plaque disruption, coronary vasomotor disorders, microvascular dysfunction, coronary thromboembolism, and spontaneous coronary artery dissection, as well as the frequent coexistence of myocardial conditions that mimic ischemic injury. Accurate evaluation of MINOCA requires a paradigm shift from an angiography-centered approach to a mechanism-oriented framework. Multimodality imaging plays a central role in this process, with cardiac magnetic resonance imaging enabling tissue-level characterization and differentiation between ischemic and non-ischemic myocardial injury, and intravascular and functional coronary testing allowing detection of occult coronary pathology. This structured diagnostic strategy facilitates etiological classification in a substantial proportion of patients and provides the foundation for individualized management. Therapeutic decision-making in MINOCA remains challenging due to limited randomized evidence and marked biological heterogeneity. While selected patients benefit from conventional secondary prevention strategies, others require tailored treatments targeting vasospasm, microvascular dysfunction, thromboembolic sources, or dissection-related pathology. Prognosis varies considerably according to the underlying mechanism, underscoring the importance of accurate diagnosis and long-term risk stratification. Future advances will depend on precision phenotyping, standardized diagnostic pathways, and dedicated clinical trials to inform evidence-based, mechanism-specific care.

Keywords: myocardial infarction with non-obstructive coronary arteries, atherosclerotic plaque disruption, coronary vasospasm, coronary microvascular dysfunction, coronary thromboembolism, spontaneous coronary artery dissection, intravascular imaging (OCT, IVUS), cardiac magnetic resonance imaging, multimodality diagnostic strategy, mechanism-based management, prognosis and long-term outcomes

Volume 19 Issue 1 - 2026

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Received: January 15, 2026 | **Published:** February 5, 2026

Abbreviations

MINOCA, myocardial infarction with non-obstructive coronary arteries; MI, myocardial infarction; ACS, acute coronary syndrome; SCAD, spontaneous coronary artery dissection; CMD, coronary microvascular dysfunction; INOCA, ischemia with non-obstructive coronary arteries; CMR, cardiac magnetic resonance; OCT, optical coherence tomography; IVUS, intravascular ultrasound; CFR, coronary flow reserve; IMR, index of microvascular resistance; LGE, late gadolinium enhancement; ACEI/ARB, angiotensin-converting enzyme inhibitor / angiotensin receptor blocker

Introduction

Acute myocardial infarction has traditionally been conceptualized as the clinical consequence of an obstructive atherosclerotic lesion complicated by plaque rupture and coronary thrombosis. This paradigm has shaped diagnostic pathways, therapeutic strategies, and clinical research for decades. However, the widespread use of coronary angiography in patients presenting with MI has revealed a substantial subgroup in whom no obstructive coronary artery disease can be identified, challenging an obstruction-centered definition of myocardial infarction and exposing important limitations in conventional thinking.[1]

Myocardial infarction with non-obstructive coronary arteries (MINOCA) has emerged from this clinical observation as a distinct and increasingly recognized entity. MINOCA is not a rare curiosity; rather, it represents a clinically meaningful syndrome encompassing a broad spectrum of underlying mechanisms. The introduction of MINOCA into contemporary classifications has underscored the need to move beyond angiographic appearances alone and to integrate pathophysiological, imaging, and clinical data into the evaluation of patients with MI.[1,2]

Epidemiological studies indicate that MINOCA accounts for approximately 5–10% of all MI presentations, with consistent findings across registries and clinical cohorts.[3] Patients with MINOCA tend to be younger and are more frequently women compared with those with obstructive MI, while traditional cardiovascular risk factors are often

less prevalent, though not absent.[3,4] These demographic differences, together with heterogeneous clinical presentations, have historically contributed to diagnostic uncertainty and therapeutic inconsistency.

A persistent misconception is that MINOCA represents a benign or low-risk form of MI. Accumulating evidence has decisively challenged this view. Large observational studies have demonstrated that patients with MINOCA experience substantial rates of all-cause mortality, recurrent MI, and heart failure, with outcomes that, while generally more favorable than those of obstructive MI, are far from trivial.[4,5] Importantly, prognosis varies widely according to the underlying mechanism, emphasizing that MINOCA is not a single disease but a syndrome with heterogeneous biological drivers.

The clinical complexity of MINOCA is further amplified by the fact that it is best regarded as a working diagnosis rather than a final one. The absence of obstructive coronary lesions at angiography should prompt a structured diagnostic approach aimed at identifying the specific mechanism responsible for myocardial injury. Advances in multimodality imaging, including intravascular imaging and cardiac magnetic resonance, as well as invasive functional coronary testing, have transformed the diagnostic landscape and now allow for more precise phenotyping in a substantial proportion of patients.[2,5]

The aim of this review is to provide a comprehensive and contemporary overview of MINOCA, synthesizing current concepts in its pathophysiology, diagnostic evaluation, management strategies, and prognosis. By emphasizing a mechanism-based framework, this review seeks to support a more rational, individualized approach to the care of patients with MINOCA and to highlight key evidence gaps that should inform future research and guideline development.

Definition and diagnostic criteria

The definition of MINOCA is grounded in the Universal Definition of Myocardial Infarction, which establishes myocardial infarction as evidence of acute myocardial injury with a rise and/or fall in cardiac troponin values above the 99th percentile upper reference limit in the context of clinical myocardial ischemia.[1] Within this framework, MINOCA is diagnosed when three key criteria are fulfilled: fulfillment of MI criteria, demonstration of non-obstructive coronary arteries (<50% stenosis), and absence of an alternative overt diagnosis explaining the clinical presentation at the time of initial evaluation.[2,6] The key components required for the diagnosis of MINOCA, emphasizing its role as a working diagnosis rather than a final etiologic entity, are summarized in Table 1.

Table 1 Definition and diagnostic criteria of MINOCA

Component	Description
MI criteria	Rise/fall of cardiac troponin with evidence of myocardial ischemia
Coronary angiography	Non-obstructive coronary arteries (<50% stenosis)
Alternative diagnosis	No overt alternative diagnosis at initial evaluation
Nature of diagnosis	Working diagnosis requiring further evaluation
Clinical relevance	Etiology guides prognosis and management

Abbreviations: MINOCA, myocardial infarction with non-obstructive coronary arteries; MI, myocardial infarction

The angiographic threshold of <50% stenosis reflects a pragmatic compromise rather than a pathophysiological boundary. While severe flow-limiting lesions are excluded by definition, this criterion does not preclude the presence of atherosclerotic disease, plaque disruption, or functionally significant coronary pathology. Indeed, plaque rupture or erosion may occur in vessels with mild-to-moderate luminal narrowing, and dynamic mechanisms such as vasospasm or microvascular dysfunction are not captured by angiographic severity alone.[2]

Accurate diagnosis of MINOCA requires careful exclusion of entities that mimic acute MI but differ fundamentally in mechanism and management. A key distinction must be made between MINOCA and type 2 MI, which results from an imbalance between myocardial oxygen supply and demand unrelated to an acute coronary process, such as severe anemia, tachyarrhythmia, hypoxia, or hypotension.[1] Although type 2 MI may occur in the setting of non-obstructive coronary arteries, it represents a distinct clinical construct and should not be subsumed under the MINOCA umbrella.

Similarly, non-ischemic myocardial injury must be excluded. Acute myocarditis and Takotsubo syndrome frequently present with chest pain, electrocardiographic abnormalities, and troponin elevation, closely resembling acute MI. However, these conditions are characterized by inflammatory or stress-mediated myocardial injury rather than ischemic necrosis and should not be classified as MINOCA once identified.[7,8] The increasing availability of cardiac magnetic resonance imaging (CMR) has substantially improved diagnostic discrimination, allowing reliable differentiation between ischemic and non-ischemic injury patterns in many cases.[7]

A defining conceptual feature of MINOCA is its designation as a working diagnosis rather than a final one. The identification of non-obstructive coronary arteries at angiography represents the beginning, not the end, of the diagnostic process. This paradigm acknowledges the inherent limitations of angiography and emphasizes the need for downstream investigations to uncover the specific mechanism responsible for myocardial injury.[2,6]

This working-diagnosis framework has important clinical implications. It mandates systematic use of advanced imaging and, when appropriate, invasive testing to achieve etiologic classification, enables mechanism-based treatment selection, and prevents inappropriate reassurance based solely on angiographic findings. Failure to pursue further diagnostic clarification risks misclassification, undertreatment, and inaccurate prognostic assessment.

Epidemiology and clinical characteristics

MINOCA accounts for approximately 5–10% of all acute myocardial infarction presentations, with relatively consistent prevalence reported across registries, clinical trials, and healthcare systems.[3,6] Variability in reported rates largely reflects differences in case definitions, angiographic thresholds, and the intensity of downstream diagnostic evaluation. Importantly, the persistent prevalence of MINOCA over time indicates that it represents a stable and clinically relevant phenotype rather than a diagnostic artifact.

A hallmark epidemiological feature of MINOCA is its sex distribution. Women account for a disproportionately high proportion of MINOCA cases, often representing nearly half of all presentations, in contrast to obstructive MI, which predominantly affects men.[9] Patients with MINOCA are also younger on average, although the condition spans a wide age range and should not be regarded as confined to young individuals.[10] These demographic patterns have historically contributed to under-recognition and misperception of disease severity.

The cardiovascular risk profile of MINOCA differs quantitatively, but not qualitatively, from that of obstructive MI. Traditional risk factors such as hypertension, diabetes mellitus, dyslipidemia, and smoking are generally less prevalent, yet remain common, underscoring that MINOCA frequently occurs in patients with established cardiovascular risk.[3,10] Notably, specific mechanisms—such as coronary vasomotor disorders and spontaneous coronary artery dissection—exhibit weaker associations with conventional atherosclerotic risk factors.

Clinically, patients with MINOCA present with symptoms indistinguishable from those of obstructive MI, including acute chest pain, dyspnea, and autonomic symptoms. Electrocardiographic findings are heterogeneous and may include ST-segment elevation, ST-segment depression, T-wave inversion, or nonspecific changes.[9,11] Importantly, ST-segment elevation is observed in a substantial minority of cases and does not exclude the diagnosis of MINOCA.

Biomarker profiles further reflect the heterogeneity of this syndrome. Peak troponin concentrations and estimated infarct size are, on average, lower than in obstructive MI, but overlap extensively between groups.[9,11] Lower biomarker release should not be interpreted as benign disease, as clinical outcomes are more strongly determined by the underlying mechanism than by infarct size alone.

Collectively, the epidemiological and clinical features of MINOCA highlight its heterogeneity and underscore the need for heightened clinical suspicion, systematic diagnostic evaluation, and individualized management strategies.

Pathophysiological mechanisms

MINOCA represents a heterogeneous syndrome encompassing multiple pathophysiological mechanisms that ultimately lead to myocardial ischemia and necrosis in the absence of obstructive epicardial coronary artery disease. Identification of the underlying mechanism is of paramount importance, as it directly influences diagnostic strategies, therapeutic decisions, and prognostic assessment. Contemporary evidence supports a mechanism-based classification broadly divided into atherosclerotic and non-atherosclerotic causes, with partial overlap between categories.[2,6] The principal ischemic mechanisms underlying MINOCA, along with their key clinical and diagnostic features, are outlined in Table 2.

Table 2 Pathophysiological mechanisms of MINOCA

Mechanism	Key features	Diagnostic clues
Plaque disruption	Rupture or erosion with transient thrombosis	OCT/IVUS findings
Coronary vasospasm	Transient epicardial or microvascular spasm	Provocative testing
Microvascular dysfunction	Impaired coronary flow reserve	CFR / IMR measurements
Coronary thromboembolism	Embolic occlusion from systemic sources	Source identification
SCAD	Intramural hematoma or intimal tear	Characteristic angiographic patterns

Abbreviations: MINOCA, myocardial infarction with non-obstructive coronary arteries; OCT, optical coherence tomography; IVUS, intravascular ultrasound; CFR, coronary flow reserve; IMR, index of microvascular resistance; SCAD, spontaneous coronary artery dissection

A significant proportion of MINOCA cases are attributable to atherosclerotic plaque disruption that is not apparent on conventional coronary angiography. Plaque rupture, plaque erosion, and, less commonly, calcified nodules may result in transient thrombosis, distal embolization, or spontaneous thrombus dissolution without leaving angiographically significant residual stenosis.[12,13] Because coronary angiography is limited to luminographic assessment, these culprit lesions frequently remain undetected.

Intravascular imaging has substantially improved mechanistic understanding in this context. Optical coherence tomography (OCT), owing to its high spatial resolution, can identify fibrous cap disruption, intracoronary thrombus, and plaque erosion in patients with angiographically non-obstructive coronary arteries.[12] Intravascular ultrasound (IVUS), while less sensitive for superficial plaque characteristics, allows visualization of deeper plaque components and positive remodeling, further supporting an atherosclerotic substrate in selected MINOCA patients.[13] Collectively, these observations challenge the assumption that non-obstructive coronary arteries equate to non-atherosclerotic disease.

Coronary artery spasm is a well-established and frequently underdiagnosed cause of MINOCA. Transient, intense vasoconstriction of the epicardial coronary arteries can produce severe myocardial ischemia and infarction, yet resolve before angiographic evaluation.[14] Vasospasm may occur spontaneously or be triggered by emotional stress, cold exposure, or vasoactive substances.

Beyond epicardial spasm, microvascular spasm involving the coronary resistance vessels may also induce ischemia without angiographically visible abnormalities.[15] Endothelial dysfunction, heightened smooth muscle cell reactivity, and autonomic dysregulation play central roles in the pathophysiology of vasomotor disorders. Systematic provocative testing with acetylcholine has demonstrated that epicardial and microvascular spasm account for a substantial proportion of ACS presentations in patients with non-obstructive coronary arteries, highlighting vasospasm as a key mechanism of MINOCA when actively investigated.[14,15]

Coronary microvascular dysfunction constitutes another important mechanism underlying MINOCA. CMD may be structural, characterized by microvascular remodeling and rarefaction, or functional, resulting from impaired vasodilatory capacity and increased microvascular resistance.[16] These abnormalities limit myocardial perfusion and predispose to ischemia even in the absence of epicardial coronary disease.

CMD shares pathophysiological overlap with ischemia and no obstructive coronary artery disease (INOCA), suggesting a continuum rather than distinct disease entities.[16,17] Invasive physiological studies have demonstrated impaired coronary flow reserve and elevated index of microvascular resistance in selected patients with MINOCA, supporting a causal role for microvascular disease in myocardial injury.[17]

Coronary thromboembolism represents an infrequent but clinically significant cause of MINOCA. Embolic material may originate from atrial fibrillation, valvular heart disease, intracardiac thrombus, or paradoxical embolism through a patent foramen ovale.[18,19] Hypercoagulable states, including inherited thrombophilias, malignancy, and antiphospholipid syndrome, further increase embolic risk.

Embolic occlusion is often transient or distal, leading to myocardial necrosis without persistent epicardial obstruction. Recognition of

this mechanism has important therapeutic implications, particularly with respect to anticoagulation and targeted evaluation for systemic embolic sources.[18,19]

Spontaneous coronary artery dissection is a distinct non-atherosclerotic cause of MINOCA that predominantly affects younger women and is frequently associated with pregnancy, the postpartum period, or fibromuscular dysplasia.[20] SCAD results from intramural hematoma formation or intimal disruption, leading to dynamic compression of the true lumen.

Angiographic diagnosis may be challenging, as SCAD can mimic atherosclerotic disease or present with subtle luminal irregularities. Awareness of characteristic angiographic patterns and judicious use of intravascular imaging are essential to avoid misdiagnosis and potentially harmful interventions.[20,21]

Several myocardial disorders may initially present as MINOCA but represent fundamentally different disease processes. Myocarditis and Takotsubo syndrome are the most prominent mimickers, often indistinguishable from acute MI at presentation.[7,8] While these entities are not mechanisms of MINOCA per se, their frequent overlap in the differential diagnosis underscores the importance of systematic evaluation and accurate classification.

Diagnostic approach and multimodality imaging

A structured diagnostic strategy is central to contemporary MINOCA care. Because MINOCA is a working diagnosis rather than a definitive one, the demonstration of non-obstructive coronary arteries should trigger a systematic, mechanism-oriented evaluation to determine the cause of ischemic myocardial injury. Multimodality imaging and targeted invasive testing are complementary and can establish a specific diagnosis in a substantial proportion of patients.[2,6] A stepwise, multimodality diagnostic strategy integrating anatomical, functional, and tissue-level assessment is central to MINOCA evaluation, as summarized in Table 3.

Table 3 Diagnostic modalities in MINOCA

Modality	Purpose	Clinical value
Coronary angiography	Exclude obstructive CAD	Initial diagnostic step
OCT / IVUS	Detect occult plaque pathology	Identify atherosclerotic MINOCA
Cardiac MRI	Tissue characterization	Differentiate ischemic vs non-ischemic injury
Provocative testing	Assess vasomotor disorders	Mechanism-specific diagnosis
Echocardiography	LV function and wall motion	Supportive but non-specific

Abbreviations: MINOCA, myocardial infarction with non-obstructive coronary arteries; CAD, coronary artery disease; OCT, optical coherence tomography; IVUS, intravascular ultrasound; MRI, magnetic resonance imaging; LV, left ventricular

The initial assessment parallels that of acute coronary syndrome and includes electrocardiography, serial cardiac biomarkers, and transthoracic echocardiography. ECG findings are heterogeneous and cannot reliably distinguish among underlying mechanisms.[11] Echocardiography is essential to assess left ventricular function and regional wall motion abnormalities and to identify alternative explanations for hemodynamic instability or overt cardiomyopathy. However, routine testing alone is rarely sufficient to define the mechanism in MINOCA, and normal or near-normal angiography should prompt escalation of diagnostic work-up rather than therapeutic de-escalation.

Coronary angiography is pivotal because it confirms the absence of obstructive coronary artery disease and may reveal diagnoses such as SCAD when angiographic features are evident. Nonetheless, angiography is a luminographic technique and lacks sensitivity for plaque disruption, small thrombus, distal embolization, or dynamic vasomotor abnormalities.[12,13] Clinicians should suspect missed culprit lesions in the presence of subtle angiographic irregularities, focal ECG changes, or congruent regional dysfunction on echocardiography.

Intravascular imaging can uncover occult coronary pathology and refine mechanism-based classification. OCT provides superior spatial resolution and can identify plaque rupture, plaque erosion, and intracoronary thrombus—findings that are frequently angiographically silent.[12] IVUS remains useful for assessing plaque burden, positive remodeling, and deeper plaque architecture, supporting an atherosclerotic substrate in selected MINOCA presentations.[13] When clinical suspicion for an atherosclerotic mechanism is high, intravascular imaging—performed during index angiography or as a staged procedure—can materially improve diagnostic yield, although routine use is limited by availability, operator expertise, and procedural considerations.

Cardiac magnetic resonance (CMR) has a central role in the evaluation of MINOCA and is recommended when an explanatory mechanism is not established after initial angiography.[6] CMR provides noninvasive tissue characterization that differentiates ischemic injury from mimickers and alternative myocardial diseases. In practice, diagnostic yield is highest when CMR is performed early after presentation; in a cohort of troponin-positive acute chest pain with unobstructed coronaries, CMR performed at approximately one week provided a conclusive diagnosis in about three-quarters of patients.[22]

Late gadolinium enhancement (LGE) patterns are particularly informative: subendocardial or transmural LGE supports an ischemic mechanism, whereas mid-wall or epicardial enhancement suggests myocarditis, with edema-sensitive sequences aiding assessment of acuity.[7] In larger MINOCA cohorts, CMR has similarly identified a specific cause for troponin elevation in roughly three-quarters of patients and provided prognostic stratification based on the final CMR phenotype.[23]

When CMR supports an ischemic mechanism but a specific coronary cause remains unclear, invasive functional assessment can diagnose vasomotor and microvascular disorders. Provocative testing with acetylcholine or ergonovine may elicit epicardial or microvascular spasm, while CFR and IMR quantify microvascular function.[14,15] Although routine implementation is limited by logistics and expertise, contemporary evidence supports feasibility and safety when performed in experienced centers.[15]

Current evidence supports a stepwise, mechanism-oriented diagnostic algorithm. After confirming MI and non-obstructive coronary arteries, early CMR should be prioritized to differentiate ischemic injury from myocardial mimickers and to establish a working phenotype.[6,22] If ischemic injury is confirmed without a clear mechanism, intravascular imaging should be considered to detect plaque disruption, and coronary functional testing should be pursued when vasomotor or microvascular disease is suspected.[12,15]

This structured approach enables individualized treatment and more accurate prognostic assessment. Accordingly, a structured, mechanism-oriented diagnostic algorithm integrating multimodality imaging and functional coronary testing is essential for accurate etiologic classification in MINOCA (Figure 1).

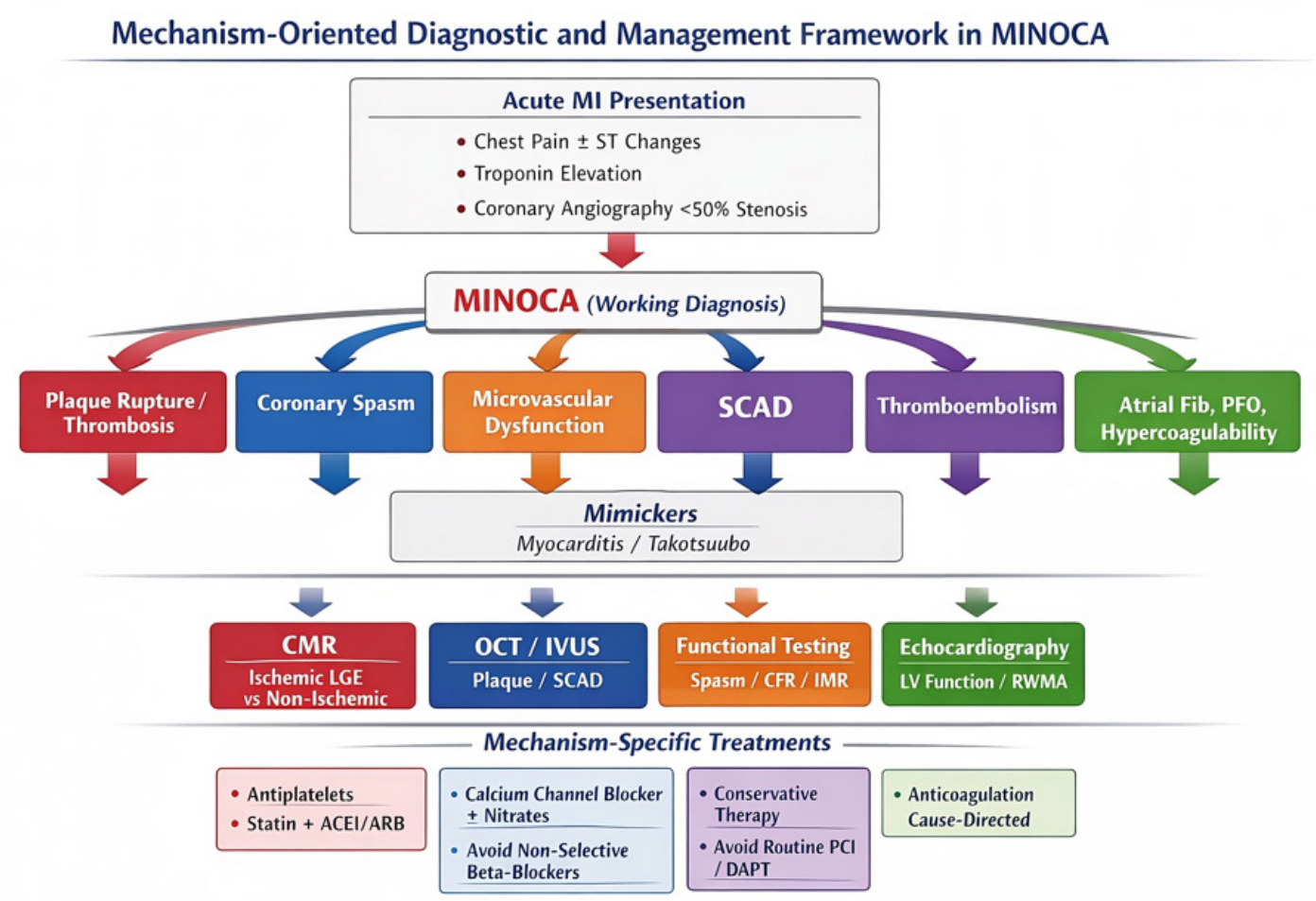

Figure 1 Mechanism-oriented diagnostic and management framework in MINOCA

This figure illustrates a structured, mechanism-oriented approach to the diagnosis and management of MINOCA. Following an acute myocardial infarction presentation with elevated cardiac biomarkers and non-obstructive coronary arteries on angiography, MINOCA should be considered a working diagnosis rather than a final etiologic entity. A systematic evaluation using multimodality imaging and functional coronary testing enables identification of underlying mechanisms, including plaque rupture or erosion, coronary vasospasm, microvascular dysfunction, coronary thromboembolism, and spontaneous coronary artery dissection. Cardiac magnetic resonance imaging plays a central role in differentiating ischemic from non-ischemic myocardial injury, while intravascular imaging and functional testing further refine etiologic classification. Identification of the underlying mechanism allows individualized, mechanism-specific management and more accurate prognostic stratification (MINOCA, myocardial infarction with non-obstructive coronary arteries; MI, myocardial infarction; CMR, cardiac magnetic resonance imaging; LGE, late gadolinium enhancement; OCT, optical coherence tomography; IVUS, intravascular ultrasound; CFR, coronary flow reserve; IMR, index of microvascular resistance; SCAD, spontaneous coronary artery dissection; LV, left ventricular; RWMA, regional wall motion abnormality; PCI, percutaneous coronary intervention; DAPT, dual antiplatelet therapy; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; PFO, patent foramen ovale)

Management strategies

The management of MINOCA remains challenging because of its etiological heterogeneity and the relative paucity of randomized clinical trial data. Unlike obstructive MI, where treatment algorithms are well established, therapeutic decisions in MINOCA must be individualized and guided by the underlying mechanism whenever possible. Accordingly, contemporary management can be conceptualized across three domains: acute management, mechanism-specific therapy, and secondary prevention. Accordingly, management in MINOCA should be individualized according to the underlying mechanism, with commonly used mechanism-based treatment strategies summarized in Table 4.

Citation: ŞAHİN MM, SARIHAN A, BİRGÜN A, et al. Myocardial infarction with non-obstructive coronary arteries (MINOCA): current concepts in pathophysiology, diagnosis, management, and prognosis. *J Cardiol Curr Res.* 2026;19(1):13–21. DOI: 10.15406/jccr.2026.19.00637

Table 4 Mechanism-based management strategies in MINOCA

Mechanism	Recommended treatment	Avoid
Plaque disruption	Antiplatelets, statins, ACEI/ARB	—
Vasospasm	Calcium channel blockers, nitrates	Non-selective beta-blockers
Microvascular dysfunction	Beta-blockers, ACEI, statins	Unproven aggressive therapy
SCAD	Conservative management, beta-blockers	Routine PCI, prolonged DAPT
Thromboembolism	Anticoagulation	Antiplatelet monotherapy

Abbreviations: MINOCA, myocardial infarction with non-obstructive coronary arteries; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention; DAPT, dual antiplatelet therapy; SCAD, spontaneous coronary artery dissection

In the acute setting, patients with suspected MINOCA should initially be treated according to standard acute coronary syndrome (ACS) protocols until obstructive coronary artery disease has been excluded and alternative diagnoses are considered. This approach is justified by the clinical and electrocardiographic overlap with obstructive MI and by the need to avoid undertreatment during the early, high-risk phase.[2,6]

However, once MINOCA is established, it becomes evident that certain components of routine MI therapy may be inappropriate or even harmful in specific subgroups. For example, aggressive antithrombotic therapy may be unnecessary in patients with non-ischemic myocardial injury, while early coronary intervention may be contraindicated in conditions such as spontaneous coronary artery dissection (SCAD). These considerations underscore the importance of early diagnostic clarification and avoidance of a "one-size-fits-all" approach.

In patients with evidence of plaque disruption identified by intravascular imaging or inferred from clinical presentation, treatment strategies largely mirror those used in obstructive MI. Antiplatelet therapy, statins, and renin–angiotensin system inhibition are generally recommended, given their established benefits in atherosclerotic disease.[4,24] Although direct randomized evidence in MINOCA is lacking, observational data support improved outcomes with statins and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in this subgroup.[4]

For patients with epicardial or microvascular coronary spasm, calcium channel blockers constitute the cornerstone of therapy, often in combination with long-acting nitrates.[14,25] These agents reduce vasomotor tone and prevent recurrent ischemic episodes. In contrast, beta-blockers—particularly non-selective agents—may exacerbate vasospasm and should generally be avoided unless compelling indications exist.[25] Smoking cessation and avoidance of known triggers are essential components of management.

Management of MINOCA related to coronary microvascular dysfunction is less well defined. Therapeutic strategies are extrapolated from studies in INOCA and include beta-blockers, angiotensin-converting enzyme inhibitors, statins, and, in selected cases, calcium channel blockers.[16,17] Symptom control and improvement in microvascular function remain the primary goals, as robust outcome data are limited.

In SCAD-related MINOCA, conservative management is preferred in the absence of ongoing ischemia or hemodynamic instability. Spontaneous healing of the dissected vessel is common, and percutaneous coronary intervention is associated with high complication rates.[20,21] Beta-blockers are often prescribed to reduce arterial shear stress, while prolonged dual antiplatelet therapy is generally avoided unless stenting has been performed.

When coronary embolism is identified or strongly suspected, treatment should focus on the underlying embolic source. Anticoagulation is indicated in patients with atrial fibrillation, intracardiac thrombus, or hypercoagulable states, whereas routine antiplatelet therapy alone may be insufficient.[18,19] Evaluation for systemic embolic sources is essential to prevent recurrence.

Secondary prevention in MINOCA remains an area of ongoing debate. Observational registry data suggest that treatment with statins and renin–angiotensin system inhibitors is associated with lower rates of major adverse cardiovascular events, whereas the benefit of beta-blockers and dual antiplatelet therapy is less consistent.[4,24]

Antiplatelet therapy should be individualized based on the presumed mechanism. While aspirin is commonly prescribed, the routine use of prolonged dual antiplatelet therapy in all MINOCA patients is not supported by current evidence and may expose patients to unnecessary bleeding risk.[6,24] Lifestyle modification and aggressive management of cardiovascular risk factors should be emphasized, regardless of the identified mechanism.

Overall, the optimal management of MINOCA requires a personalized strategy that integrates diagnostic findings, pathophysiological understanding, and patient-specific risk, highlighting the urgent need for dedicated randomized trials to guide therapy.

Prognosis and long-term outcomes

Contrary to earlier assumptions, MINOCA is not a benign clinical entity. Evidence from large registries and observational cohorts consistently shows that patients with MINOCA experience clinically meaningful rates of adverse cardiovascular events, both early and during long-term follow-up. Although outcomes are often more favorable than those observed in obstructive MI, they remain substantial and mandate systematic evaluation and risk-oriented management.[26,27]

Short-term mortality after MINOCA is generally lower than that of obstructive MI but is not negligible. Early events reflect the acute risk associated with myocardial necrosis itself, as well as the potential for misclassification at presentation (e.g., unrecognized myocarditis or stress cardiomyopathy) and incomplete mechanism identification. This reinforces that an angiographic "non-obstructive" result should not lead to therapeutic nihilism or premature discharge from cardiology follow-up.[23,26]

Long-term outcomes further challenge the "benign MI" myth. Across multiple cohorts, MINOCA is associated with sustained risk of all-cause mortality and major adverse cardiovascular events over time, including recurrent MI, heart failure, and stroke. Importantly, in a large study of first-time MINOCA, patients experienced a considerable burden of subsequent morbidity and cause-specific mortality, underscoring that MINOCA carries meaningful prognostic implications and requires careful longitudinal management.[28]

Prognosis in MINOCA is highly heterogeneous and depends strongly on the underlying mechanism. Patients with atherosclerotic

plaque disruption or coronary thromboembolism tend to have higher rates of recurrent ischemic events, whereas vasospastic and microvascular mechanisms may be characterized by recurrent symptoms and repeat healthcare encounters despite variable mortality risk.[15,18] Conversely, when CMR identifies myocarditis or Takotsubo syndrome, the prognostic trajectory and management priorities differ substantially from ischemic MINOCA, further emphasizing the importance of definitive diagnostic classification.[23]

Sex-specific considerations are also important. Women represent a disproportionate share of MINOCA presentations, and outcome differences by sex may reflect heterogeneity in mechanisms as well as potential differences in diagnostic intensity and secondary prevention. Younger patients with MINOCA likewise remain vulnerable to recurrent events over time, highlighting the need for mechanism-based therapy and long-term risk factor management irrespective of age.[10,27]

Collectively, contemporary data establish MINOCA as a prognostically significant syndrome. Accurate identification of the causative mechanism—supported by CMR and, when indicated, invasive coronary imaging and functional testing—provides the basis for individualized therapy and improved risk stratification in long-term follow-up.[2,6]

Special populations and clinical scenarios

Women constitute a disproportionate share of MINOCA presentations and often exhibit a distinct mechanistic distribution compared with men, including higher rates of vasomotor and non-atherosclerotic etiologies. In contemporary cohorts of young MI patients, MINOCA is predominantly observed in women, with heterogeneous mechanisms and clinically meaningful adverse outcomes, reinforcing the need to avoid diagnostic or therapeutic nihilism based on angiographic findings alone.[10] These sex-related patterns heighten the importance of early mechanism clarification—particularly with CMR and, when indicated, coronary functional testing—given the higher prevalence of myocardial mimickers and vasomotor disorders in this group.[6]

MINOCA in younger individuals frequently occurs in the absence of extensive traditional atherosclerotic burden and should prompt consideration of SCAD, vasospasm, thromboembolism, and inherited or acquired prothrombotic conditions. Although infarct size may be smaller on average, recurrent symptoms, rehospitalizations, and long-term events remain clinically relevant, supporting structured etiologic evaluation and risk-factor management even in the absence of obstructive coronary disease.[10]

Autoimmune and systemic inflammatory diseases can intersect with MINOCA through multiple pathways, including endothelial dysfunction with vasomotor abnormalities, microvascular impairment, and thrombotic predisposition.[6] In selected patients—particularly those with prior thrombosis, pregnancy morbidity, or suggestive laboratory history—clinicians should consider acquired hypercoagulable states (e.g., antiphospholipid syndrome) and evaluate for potential embolic sources when clinically indicated, as these mechanisms directly influence the need for anticoagulation and recurrence prevention.[18,19]

Pregnancy-associated myocardial infarction is uncommon but clinically high stakes. SCAD is a leading mechanism in this setting and often presents postpartum with high-risk angiographic patterns and more severe clinical features compared with non–pregnancy-associated SCAD, supporting conservative management whenever feasible and careful multidisciplinary follow-up.[20,29] Recognition of this phenotype is essential because routine ACS interventions may be less effective and can carry higher procedural risk.

Current guidelines, evidence gaps, and ongoing trials

Contemporary guidance increasingly recognizes MINOCA as a clinically important ACS phenotype that requires systematic evaluation rather than reassurance based on "non-obstructive" angiography. The 2023 ESC Acute Coronary Syndromes guideline explicitly incorporates MINOCA within the ACS spectrum and emphasizes a structured diagnostic work-up to establish the underlying mechanism, including early cardiac magnetic resonance (CMR) when the cause is not apparent after angiography.[30] In parallel, the American Heart Association scientific statement frames MINOCA as a working diagnosis and supports a mechanism-oriented algorithm integrating intravascular imaging, CMR, and—when appropriate—invasive functional testing to identify vasomotor and microvascular disorders.[2]

Despite these increasingly detailed diagnostic frameworks, major evidence gaps persist in therapeutic management. Most recommendations for pharmacotherapy in MINOCA are extrapolated from obstructive MI or derived from observational data, and the optimal intensity and duration of antiplatelet therapy, the role of beta-blockers, and the consistency of benefit from renin–angiotensin system inhibition remain uncertain across MINOCA phenotypes.[4,6] This uncertainty reflects, in large part, the biological heterogeneity of MINOCA: treatments likely have differential efficacy in plaque disruption, vasospasm, microvascular dysfunction, coronary embolism, or SCAD, making "all-comer" strategies inherently vulnerable to dilution of benefit.

Ongoing randomized trials are therefore central to progress. The MINOCA-BAT program was designed to address the long-standing gap in randomized evidence for conventional secondary prevention therapies in MINOCA, evaluating beta-blockers and ACE inhibitor/ARB strategies in a pragmatic framework.[31] A dedicated MINOCA-BAT substudy further targets symptom-related outcomes (post-infarct angina), reflecting the clinical reality that many MINOCA phenotypes generate recurrent ischemic symptoms and healthcare utilization even when mortality risk is modest.[32] Collectively, these initiatives underscore a broader shift toward phenotype-driven trial design in MINOCA.

In the near term, standardizing care remains challenging because diagnostic capability varies widely across centers (e.g., access to OCT/IVUS, acetylcholine testing, and timely CMR). Future guideline refinements will likely hinge on improved mechanistic adjudication, pragmatic implementation pathways, and randomized evidence aligned with biologically coherent MINOCA subtypes.

Future directions

Future progress in MINOCA will depend on transitioning from a syndromic label to biologically coherent endophenotypes that can be matched to targeted diagnostics and therapies. A practical near-term priority is the broader implementation of standardized, mechanism-oriented pathways that integrate early CMR, intravascular imaging when plaque disruption is suspected, and invasive functional testing when vasomotor or microvascular mechanisms are plausible.[23,33] Systematic approaches are likely to reduce misclassification, enable consistent care across centers, and improve the interpretability of future trials.

Precision medicine in MINOCA will require scalable phenotyping and better linkage between mechanism and treatment response. This

includes harmonized reporting of CMR injury patterns, OCT/IVUS-defined culprit morphology, and functional coronary testing results to define reproducible subtypes. The broader precision-medicine agenda in non-obstructive coronary syndromes—particularly in women—highlights how multimodal diagnostics combined with "pan-omic" profiling may help define mechanistically distinct subgroups suitable for targeted intervention.[34] While much of this framework is still emerging, it provides a clear direction for MINOCA research programs.

Biomarker development is another key frontier. High-sensitivity troponin carries prognostic information even within MINOCA and may support risk stratification beyond conventional clinical variables.[35] Expanding biomarker panels that reflect thrombosis, inflammation, endothelial dysfunction, and microvascular injury could enable earlier mechanistic suspicion and guide selection of downstream tests.

Finally, artificial intelligence (AI) is likely to become an enabling technology rather than a standalone solution. AI-supported interpretation of CMR (including quantitative mapping), angiographic signals, and clinical phenotypes may improve diagnostic efficiency and reduce interobserver variability, particularly in centers with limited subspecialty expertise. However, meaningful clinical impact will require prospective validation in MINOCA-specific cohorts and alignment with actionable mechanistic categories.[23,33]

Conclusions

Myocardial infarction with non-obstructive coronary arteries is no longer considered a benign or exclusionary diagnosis but represents a heterogeneous and prognostically relevant clinical syndrome. Contemporary evidence demonstrates that patients with MINOCA experience substantial morbidity and long-term cardiovascular risk, with outcomes that vary markedly according to the underlying pathophysiological mechanism.[2,4]

This review highlights that coronary angiography alone is insufficient to determine the etiology of myocardial infarction in the absence of obstructive coronary disease. A structured, mechanism-oriented diagnostic strategy—centered on early cardiac magnetic resonance imaging and complemented by intravascular imaging and invasive functional coronary testing when indicated—is essential for accurate etiologic classification.[2,6] Such an approach enables differentiation between ischemic and non-ischemic myocardial injury and informs appropriate therapeutic decision-making.

Management of MINOCA should therefore move beyond uniform application of conventional myocardial infarction therapies. While secondary prevention strategies may be appropriate in patients with evidence of atherosclerotic plaque disruption, alternative mechanisms such as coronary vasomotor disorders, microvascular dysfunction, coronary thromboembolism, and spontaneous coronary artery dissection require tailored treatment approaches.[14,19,20] Aligning therapy with mechanism is crucial to avoid both overtreatment and undertreatment.

Despite advances in diagnostic capability, robust randomized data guiding mechanism-specific therapy remain limited. Future progress will depend on standardized diagnostic pathways, refined phenotypic classification, and dedicated clinical trials designed to inform evidence-based management of this complex syndrome.[31]

Contributorship

All of the authors contributed planning, conduct, and reporting of the work. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

No financial funding was received for this study.

Competing interests

All of the authors have no conflict of interest.

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Citation: ŞAHİN MM, SARIHAN A, BİRGÜN A, et al. Myocardial infarction with non-obstructive coronary arteries (MINOCA): current concepts in pathophysiology, diagnosis, management, and prognosis. *J Cardiol Curr Res*. 2026;19(1):13–21. DOI: 10.15406/jccr.2026.19.00637