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Review article

MINOCA: Myocardial infarction no obstructive coronary artery disease☆

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ABSTRACT

Myocardial infarction without obstructive coronary artery disease (MINOCA) is defined as myocardial infarction with mild or no obstructive coronary artery disease (CAD) on angiogram. MINOCA has a number of heterogeneous causes, including coronary disruption, coronary vasospasm, coronary embolism, spontaneous coronary artery dissection (SCAD), and coronary microvascular dysfunction (CMD). Even though MINOCA might have a better prognosis than MI with obstructive CAD, it is not benign. A stepwise diagnostic approach is crucial to identifying the underlying cause of MINOCA or conditions mimicking it. A cause-specific treatment approach is the key to managing MINOCA.

1. Introduction

MINOCA, Myocardial Infarction with No Obstructive Coronary Artery disease, describes patients who meet the criteria for myocardial infarction (MI) by the fourth universal definition, but coronary angiogram does not show any obstructive coronary artery disease (≥50 % stenosis) [1]. Additionally, alternative etiologies like sepsis and pulmonary embolism do not explain their acute presentation [2]. Clinical findings of these patients are often mislabeled as "false positive" [3]. This mini review will focus on the understanding that there are many possible causes of MINOCA. Finding the underlying etiology of MINOCA is the crucial step to initiating an appropriate disease-specific treatment.

2. MINOCA: etiologies and diagnosis

During the development of the TIMI frame count method over thirty years ago, I (CMG) observed slower blood flow in some non-culprit arteries in the MI patients [4]. This was considered a sign of microvascular dysfunction. Since then, especially in the past ten years, tremendous progress has been made in the recognition, classification, and study of MINOCA. MINOCA affects about 5 to 15 % of patients undergoing cardiac catheterization for MI [5].The prevalence of MINOCA is much higher in COVID-19 patients compared with non-Covid-19 patients [6]. The majority of patients present with non-ST segment elevation MI (NSTEMI) [7]. Compared with patients with MI secondary to coronary artery disease (MI-CAD), MINOCA patients are more likely to be women and younger, and less likely to have dyslipidemia [3].

Coronary plaque disruption is considered one of the most common causes of MINOCA, along with coronary vasospasm, coronary embolism, spontaneous coronary artery dissection (SCAD), and coronary microvascular dysfunction (CMD) [8]. Plaque disruption, including plaque erosion, plaque rupture, or calcific nodules, can lead to MI-CAD if there is a complete or near complete occlusion secondary to thrombosis. However, if the thrombosis is not significant enough to cause an obstructive lesion, MINOCA will result [9]. As well as these underlying causes, there are also conditions that are not a MI, but mimic MINOCA. Therefore, it is essential to recognize MINOCA mimics, including stress-induced cardiomyopathy, non-ischemic cardiomyopathy, and myocarditis [10].

It is crucial to thoroughly review all angiographic images before labeling a patient with MINOCA to ensure there are no overlooked obstructive lesions [5]. If there is any uncertainty about plaque disruption or SCAD, intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are essential tools for further evaluation (Fig. 1) [1]. Cardiac Magnetic Resonance Imaging (CMR) can determine whether the distribution of any gadolinium enhancement is consistent with MI and exclude MINOCA mimics [3]. In a study of women with MINOCA, Reynolds et al. identified a cause for MINOCA in 85 % of the cases using OCT and CMR [11]. The vast majority of the participants (64 %) had an ischemic cause, >20 % had MINOCA mimics, including

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myocarditis (14.7 %), stress-induced cardiomyopathy (3.4 %), and non-ischemic cardiomyopathy (2.6 %). These findings emphasize the importance of further investigation beyond coronary angiography in patients with MINOCA. It is important to note that very few STEMI patients were included in this study because of a time constraint to obtain research consent prior to an emergent coronary angiogram. As a result of this limitation, the incidence of stress-induced cardiomyopathy may have been lower in this study.

Another important finding of the study was that the severity of a non-obstructive stenosis in a vessel was not significantly associated with a higher probability of finding the culprit lesion in the same vessel [11]. The results suggest that we should consider doing OCT or IVUS of all coronary arteries in patients with MINOCA, irrespective of the severity of the stenosis, to help narrow down the list of differential diagnoses. OCT and IVUS can help to identify plaque rupture, plaque erosion, and SCAD [5,12].OCT can also help identify vasospasm in certain cases, however, the gold standard test for diagnosing coronary vasospasm is to detect it angiographically after administration of intra-coronary acetylcholine [5]. Finally, CMD can be diagnosed by measuring coronary flow reserve (CFR < 2) and index of microvascular resistance (IMR ≥ 25) [1].

3. Management

The goal in patients with MINOCA is to find the underlying etiology and focus on cause-specific therapy [5]. Secondary prevention for cardiovascular disease is recommended in the majority of patients with true MINOCA [8]. Lindahl et al., in a large and unique observational study of 9466 patients with MINOCA in the SWEDEHEART registry, showed that statins and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers were associated with a lower rate of recurrent major adverse cardiac events and β-blockers showed a trend toward a beneficial effect [13]. Dual antiplatelet therapy was not associated with a lower MACE rate at one-year follow-up. The therapeutic role of antiplatelets in coronary plaque disruption is more well-defined compared with coronary vasospasm [14], in which calcium channel blockers are the mainstay of treatment [9]. No randomized trial data are available to guide therapeutic recommendations or define optimal medical management for MINOCA patients.

4. Prognosis

Although MINOCA patients may have a better prognosis than MI-CAD patients, their rate of MACE is higher than that of the normal population. Pasupathy et al., in a systematic review, have shown

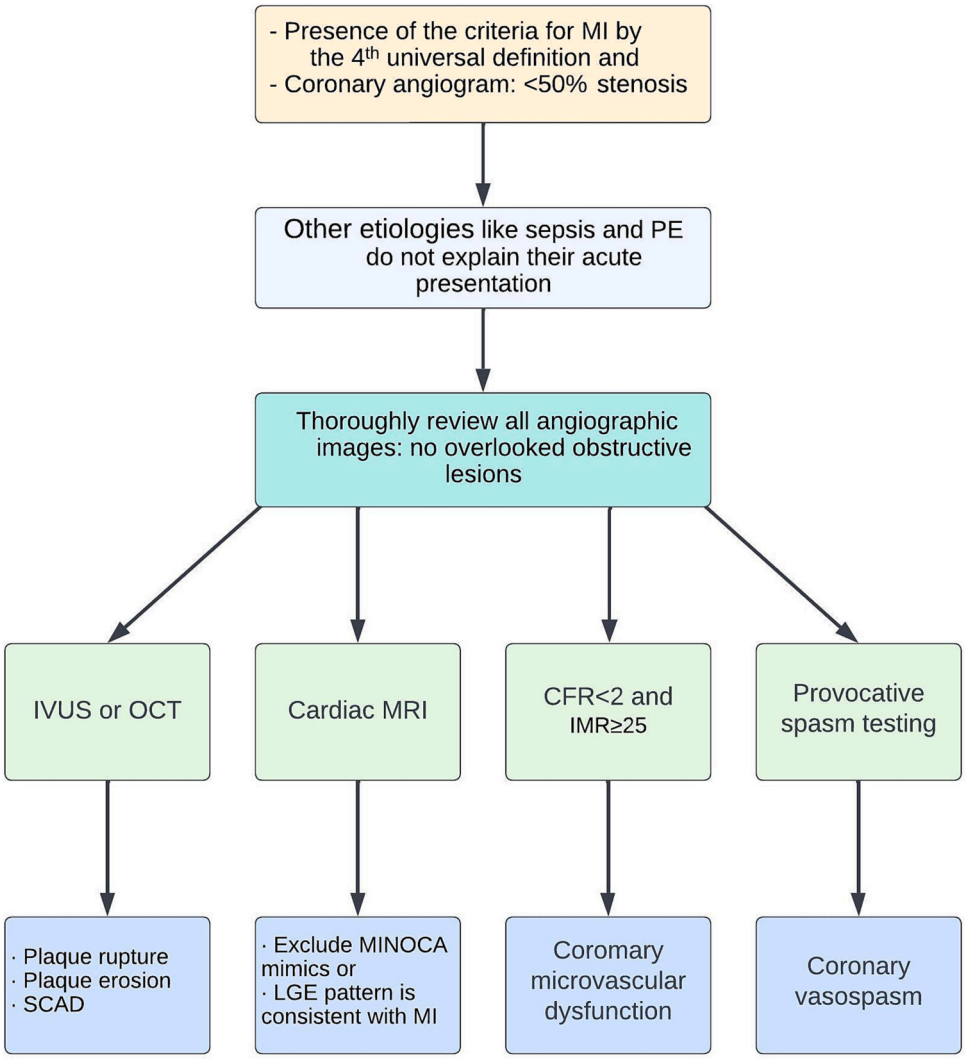

Fig. 1. Simplified diagnostic approach for myocardial infarction without obstructive coronary artery disease (MINOCA). MI: myocardial infarction; CAD: coronary artery disease; IVUS: intravascular ultrasound; OCT: optical coherence tomography; CFR: coronary flow reserve; IMR: index of microvascular resistance; LGE: late gadolinium enhancement; SCAD: spontaneous coronary artery dissection.

MINOCA patients had lower all-cause mortality at 12 months compared with MI-CAD (4.7 % vs. 6.7 %) [15]. On the other hand, Choo et al., in a study of Patients from the KAMIR-NIH (Korean Acute Myocardial Infarction-National Institutes of Health) registry, demonstrated similar 2-year all-cause death comparing MINOCA and MI-CAD (9.1 % versus 8.8 %) [16]. This is a very high mortality rate after acute MI for patients with no obstructive coronary artery disease and highlights the importance of recognizing and treating MINOCA. Moreover, in a study of 4793 patients with STEMI, Andersson et al. showed that patients with non-obstructive CAD and normal coronary arteries had similar and higher long-term hazard of death than patients with obstructive CAD respectively [17]. It should be noted that the cause of mortality was less likely to be cardiovascular in patients who had normal coronary arteries or non-obstructive CAD.

5. Conclusion

In summary, MINOCA consists of 5 to 15 % of patients undergoing cardiac catheterization for MI and is associated with higher adverse outcomes compared with the normal population. Patients with MINOCA should undergo further investigation by IVUS or OCT to rule out plaque disruption or SCAD and, if necessary, measurement of CFR and IMR to rule out CMD and provocative testing to rule out coronary vasospasm. CMR is useful to assess for gadolinium enhancement consistent with MI and to help exclude MINOCA mimics such as stress-induced cardiomyopathy and myocarditis. Targeted therapy can be used once a diagnosis has been established although randomized clinical trials are still needed to help to determine the optimal treatment.

CRediT authorship contribution statement

Hooman Bakhshi: Writing – original draft. **C. Michael Gibson:** Conceptualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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