A pragmatic diagnostic approach to myocardial infarction with non-obstructive coronary arteries
Ammar J Alsamarrai, Jocelyne R Benatar, Eun Soo Chung, Jithendra B Somaratne

Most myocardial infarctions (MI) are caused by plaque disruption of underlying atherosclerotic coronary artery disease (CAD). This pathophysiologic model of acute coronary syndrome lends itself to effective treatment strategies, including pharmacologic measures and percutaneous interventions. However, an increasingly recognised phenomenon is that of patients who present with MI but do not have obstructive CAD at the time of coronary angiography. This is defined as having met the universal criteria of MI, but having no stenosis ≥50% on angiography. In such cases, the term MI with non-obstructive coronary arteries (MINOCA) is applied.

MINOCA should be considered a working diagnosis rather than a final diagnosis. It is increasingly clinically recognised and accounts for approximately 10% of presentations of all MI. It is more common in women, particularly young women, and associated with fewer traditional risk factors, and usually presents as non–ST elevation MI. While the absence of significant stenosis appears to be reassuring, conflicting data exists regarding the risk of further major adverse outcomes in this group. Some studies show either reduced or similar risk of death to those with MI. Reasons for this are complex; for example, women are less likely to receive cardioprotective medication, broad definitions for MINOCA are used where the specific aetiology is not precisely elucidated and there is a difference in the incidence of specific conditions, like coronary artery spasm, within different population groups. In the New Zealand setting, patients with MINOCA have a lower risk of adverse outcomes and death compared to patients with obstructive CAD, but a significantly higher event rate and mortality risk than patients without cardiovascular disease.
A myriad of conditions can cause MINOCA (Table 1) and each requires a unique diagnostic and management approach. The incidence of each condition that contributes to MINOCA is low in the general population, which means that there is little evidence available on how to both diagnose and treat each condition. However, accurate diagnosis remains crucial to ensure patients are on the most appropriate treatments.

Proposed diagnostic algorithm

As MINOCA accounts for a significant proportion of patients with MI and is increasingly recognised, there needs to be a unified and systematic approach to the tests that ensue to reach the final diagnosis. Furthermore, as the individual conditions that cause MINOCA are relatively infrequent, they should all be considered during the workup process, particularly the commoner causes. We also emphasise that the absence of obstructive CAD on angiography is not a satisfactory end-point in the workup of patients with ACS.

We propose a simplified and pragmatic diagnostic approach, adapted from the American Heart Association guidelines, to facilitate clinical decision making regarding appropriate investigations following coronary angiography (Figure 1).

The presence of MINOCA should prompt a thorough review of the clinical history and angiogram. Alternative causes of raised serum troponin (with or without chest pain) should always be considered, such as pulmonary embolism and sepsis. A clinical review of the patient should be undertaken to exclude anaemia, hypotension and sustained tachycardia, all of which may cause type 2 MI (due to supply-demand mismatch). An assessment of the left ventricle either at angiography or with echocardiography can diagnose cardiomyopathies such as Takotsubo syndrome.

If this is not helpful, the angiogram should be carefully reviewed to exclude spontaneous coronary artery dissection (SCAD) and coronary thrombus or embolism. SCAD can be difficult to diagnose as angiographic appearance can be subtle and initially missed. Only a small proportion of SCAD have the classic angiographic appearance of a double lumen artery with a visible intimal flap (type 1). Most may have diffuse stenosis of varying severity (type 2) and some have lesions that mimic atherosclerosis (type 3). Intracoronary imaging is useful if angiographic diagnosis is not obvious. SCAD is more frequent in women with few traditional cardiac risk factors. The median age

Table 1: Overview of the causes of myocardial infarction with non-obstructive coronary arteries.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Proportion of MINOCA</th>
<th>Diagnostic standard</th>
<th>Management</th>
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<tbody>
<tr>
<td>Coronary artery spasm</td>
<td>46%(^1)</td>
<td>Coronary provocative testing</td>
<td>Calcium channel blockers, nitrates</td>
</tr>
<tr>
<td>Plaque disruption</td>
<td>36%(^1)</td>
<td>Intracoronary imaging</td>
<td>Standard acute coronary syndrome treatments</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>33%(^1)</td>
<td>Endomyocardial biopsy or cardiac magnetic resonance imaging</td>
<td>Supportive care, immunosuppression, transplantation</td>
</tr>
<tr>
<td>Coronary thrombosis and embolism</td>
<td>24%(^1)</td>
<td>Intracoronary imaging, thrombophilia screen</td>
<td>Anticoagulation in some cases</td>
</tr>
<tr>
<td>Spontaneous coronary artery dissection</td>
<td>7%(^2)</td>
<td>Intracoronary imaging</td>
<td>Aspirin, beta-blockers, revascularization in some cases</td>
</tr>
<tr>
<td>Takotsubo syndrome</td>
<td>7%(^2)</td>
<td>Left ventriculography</td>
<td>Supportive care, ACE inhibitors</td>
</tr>
</tbody>
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MINOCA: myocardial infarction with non-obstructive coronary arteries, ACE: angiotensin converting enzyme.

\(^1\)Proportions reflect findings of individual studies and are not additive.
Figure 1: Proposed diagnostic algorithm for myocardial infarction with non-obstructive coronary arteries (adapted from 10).

is 50 years old but there is also an increased risk in the antenatal and peripartum periods. SCAD does not always strictly meet the ‘non-obstructive’ criteria of MINOCA as there is usually luminal narrowing; however, initial angiographic views can miss subtle SCAD.

Thrombosis and thromboembolism in the coronary arteries can also be diagnosed with intracoronary imaging. This is usually seen in young patients with few traditional cardiovascular risk factors who often have an underlying thrombophilia. One study of 84 patients with MINOCA found that ¼ had an inherited thrombophilia. This diagnosis is crucial to make because of the high risk of recurrence and the possible need for long-term anticoagulation such as in antiphospholipid syndrome.

If review of the angiogram reveals no diagnosis, cardiac magnetic resonance (CMR) imaging is recommended. The diagnostic yield of CMR is as high as 87% in the workup of MINOCA. It is able to characterise myocardial tissue, quantify chamber volumes and ejection fraction. It can accurately diagnose myocardial infarction, myocarditis, and non-ischemic cardiomyopathy such as Takotsubo syndrome and hypertrophic cardiomyopathy.

If the CMR is normal, coronary artery spasm (CAS) needs to be considered. Spasm can affect a spectrum of vessels from epicardial to microvascular vessels. It is more common in females, in certain ethnic groups (for example Japanese) and usually presents with angina at rest. When it presents with angina, empirical treatment with calcium channel blockers and nitrates can be considered, but in the setting of MINOCA, provocative testing with intracoronary acetylcholine could be used to confirm the diagnosis. While this test has lower sensitivity in young patients, sequential vasoreactivity provocation tests can improve the accuracy. Microvascular spasm is a component of coronary microvascular dysfunction, and usually presents with angina rather than MI. A patient is only labelled with “unclassified MINOCA” once all other possibilities are actively excluded.

**Conclusion**

MINOCA is more common in women with no traditional risk factors for heart disease and has an increased risk of mortality compared to healthy individuals. It is a working diagnosis and further investigations should be undertaken to establish a specific cause to ensure appropriate treatment. When done within a short time of presentation, CMR is particularly useful to establish the diagnosis in the majority of patients and should be routinely undertaken if no cause of MINOCA is found.

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REFERENCES:


