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Myocardial infarction with non-obstructive coronary arteries: Novelties and perspectives

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Abstract
The aim of current study is review of Myocardial infarction with non-obstructive coronary arteries (MINOCA) diagnostic and treatment strategies.
Material and Methods: This study used a comprehensive structured systematic approach that included a methodical literature search.
Results: Varies observational studies shows that a sizeable proportion of myocardial infarctions (MI), ranging between 1–14%, occur in the absence of obstructive (>50% stenosis) coronary artery disease. The potential mechanisms responsible for MI in MINOCA patients are structural myocardial dysfunction, coronary artery spasm and trombophilia disorders. Identifying treatable causes of MINOCA is fundamental to its clinical assessment as these may have prognostic implications and may impact on its guarded prognosis.
Conclusion: Myocardial infarction with non-obstructive coronary arteries is identified using a working diagnosis made following coronary angiography in the assessment of patients with an AMI. In patients in whom no specific cause is found, further studies are warranted to assess the most effective treatment.

Keywords: Myocardial infarction with non-obstructive coronary arteries, myocardial infarction, treatment, diagnosis

Introduction
Ischaemic heart disease (IHD) is the single most common cause of death and its frequency is increasing. However, in Europe, there has been an overall trend for a reduction in its mortality over the past three decades [1]. IHD at present time accounts for almost 1.8 million annual deaths, or 20% of all deaths in Europe, although with large variations between countries [2].
In 2017 the guidelines for diagnostic and treatment of myocardial infarction with ST elevation (STEMI) were updated by European Cardiology Society (ESC) [3]. One of important part of this document was devoted to Myocardial infarction with non-obstructive coronary arteries (MINOCA).
The aim of current study is review of Myocardial infarction with non-obstructive coronary arteries (MINOCA) diagnostic and treatment strategies.

Material and Methods
This study used a comprehensive structured systematic approach that included a methodical literature search, well-defined inclusion criteria for MINOCA, extraction of available raw data, and pooling of the data to determine the frequency of each of the predetermined study end points.

Results and Discussion
Results of varies observational studies shows that a sizeable proportion of myocardial infarctions (MI), ranging between 1–14%, occur in the absence of obstructive (>50% stenosis) coronary artery disease (CAD) [4, 5].
It's important, that demonstration of non-obstructive (<50%) CAD in a patient presenting with symptoms suggestive of ischaemia and ST-segment elevation or equivalent does not preclude an atherothrombosis aetiology, as thrombosis is a very dynamic phenomenon and the underlying atherosclerotic plaque can be non-obstructive [3].

The diagnostic criteria of MINOCA are [3, 6]

1. Universal MI criteria;
2. Non-obstructive coronary arteries by angiography (no coronary stenosis more 50% in any potential infarct-related artery);
3. No clinically overt specific cause for acute presentation.

The potential mechanisms responsible for MI in MINOCA patients are structural myocardial dysfunction, coronary artery spasm and trombophilia disorders.

Pooled analyses of the 26 cardiac magnetic resonance (CMR) imaging publications involving MINOCA patients revealed features consistent with a subendocardial infarct on delayed hyper-enhancement in only 24% of 1801 MINOCA patients studied. The most common finding in the CMR imaging studies was myocarditis, with 33% of the 1676 MINOCA patients having features of this condition. Other myocardial abnormalities reported in the MINOCA CMR imaging studies included Tako-tsubo cardiomyopathy (18% of 1529 patients), hypertrophic cardiomyopathy (3% of 1074 patients), dilated cardiomyopathy (2% of 625 patients), and other causes (7% of 760 patients) such as pericarditis and amyloidosis. Importantly, 26% of 1592 MINOCA patients undergoing contrast CMR imaging did not have detectable myocardial abnormalities [4].

More than a quarter of patients with MINOCA undergoing provocative spasm testing have inducible spasm [4]. Unfortunately there are no suitable studies directly comparing provocative spasm testing between MINOCA and MI-CAD patients, although several have reported inducible spasm in 20% to 80% of MI-CAD patients [7]. Thus the relative contribution of coronary spasm to the pathophysiology of MINOCA requires further investigation.

Some genetic thrombophilia disorders have been observed in MINOCA. Factor V Leiden is a single point mutation with a prevalence of 3% to 7% in Western populations but was observed in 12% of MINOCA patients [4]. Furthermore, comparative studies with MI patients also report a higher prevalence in MINOCA – approximately for 3 times [8, 9]. Protein C&S deficiency are autosomal dominant disorders with a population prevalence of 0.1% to 1%,yet occur in 2.6% of MINOCA patients and similarly those with MI [10].

These associations with the genetic thrombophilia disorders are based on small studies and require confirmation with larger multicenter prospective studies. Furthermore, investigation of acquired thrombophilia disorders should be considered because these may also occur in the context of acute MI and could exacerbate the genetic disorders. Irrespective of the prevalence of these thrombophilia disorders in MINOCA, their detection may influence subsequent management thereby justifying their routine evaluation in patients with MINOCA [4].

Due ESC recommendation MINOCA is a working diagnosis and should lead the treating physician to investigate underlying causes. Failure to identify the underlying cause may result in inadequate and inappropriate therapy in these patients [3].

There are markedly different aetiologies causing MINOCA and they can be grouped into: (I) secondary to epicardial coronary artery disorders (e.g. atherosclerotic plaque rupture, ulceration, fissuring, erosion, or coronary dissection with non-obstructive or no CAD) (MI type 1); (II) imbalance between oxygen supply and demand (e.g. coronary artery spasm and coronary embolism) (MI type 2); (III) coronary endothelial dysfunction (e.g. microvascular spasm) (MI type 2); and (IV) secondary to myocardial disorders without involvement of the coronary arteries (e.g. myocarditis or Takotsubo syndrome). The last two entities may mimic MI but are better classified as myocardial injury conditions. The identification of the underlying cause of MINOCA should lead to specific treatment strategies. Although the outcome of MINOCA strongly depends on the underlying cause, its overall prognosis is serious, with a 1 year mortality of about 3.5% [3].

Recommended diagnostic and therapeutic algorithm for myocardial infarction with non-obstructive coronary arteries is presented on Fig. 1.

Identifying treatable causes of MINOCA is fundamental to its clinical assessment as these may have prognostic implications and may impact on its guarded prognosis. For example, coronary artery spasm is effectively treated with nitrates and calcium channel blockers, with use of the latter shown to be a survival determinant in patients with MINOCA [11]. Additionally, identification of thrombophilia disorders may influence treatment and could impact on the patient's offspring in the case of hereditary thrombophilia.

The management of MINOCA with no specific underlying aetiology identified requires further investigation.

Statins, ACE inhibitors/angiotensin receptor blockers (ACEI/ARB), beta blockers and dual antiplatelet therapy (DAPT) are treatments given following an MI or those at risk of MI. In new observational study of MINOCA patients recorded in the SWEDEHEART registry (the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapy) the associations between treatment with these medications, and long-term cardiovascular events were observed. At discharge, 84.5%, 64.1%, 83.4%, and 66.4% of the patients were on statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and dual antiplatelet therapy, respectively. During the follow-up of a mean of 4.1 years, 2183 (23.9%) patients experienced a major adverse cardiac event. The hazard ratios (95% confidence intervals) for major adverse cardiac events were 0.77 (0.68-0.87), 0.82 (0.73-0.93), and 0.86 (0.74-1.01) in patients on statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and β-blockers, respectively. For patients on dual antiplatelet therapy followed for 1 year, the hazard ratio was 0.90 (0.74-1.08) [11]. The authors concluded about long-term beneficial effects of treatment with statins and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers on outcome in patients with MINOCA, a trend toward a positive effect of β-blocker treatment, and a neutral effect of dual antiplatelet therapy.

Multi-centre clinical trials of diagnostic and therapeutic strategies are needed in cohort of MINOCA patients. These results will have great impact on both treatment and prognosis of these patients.

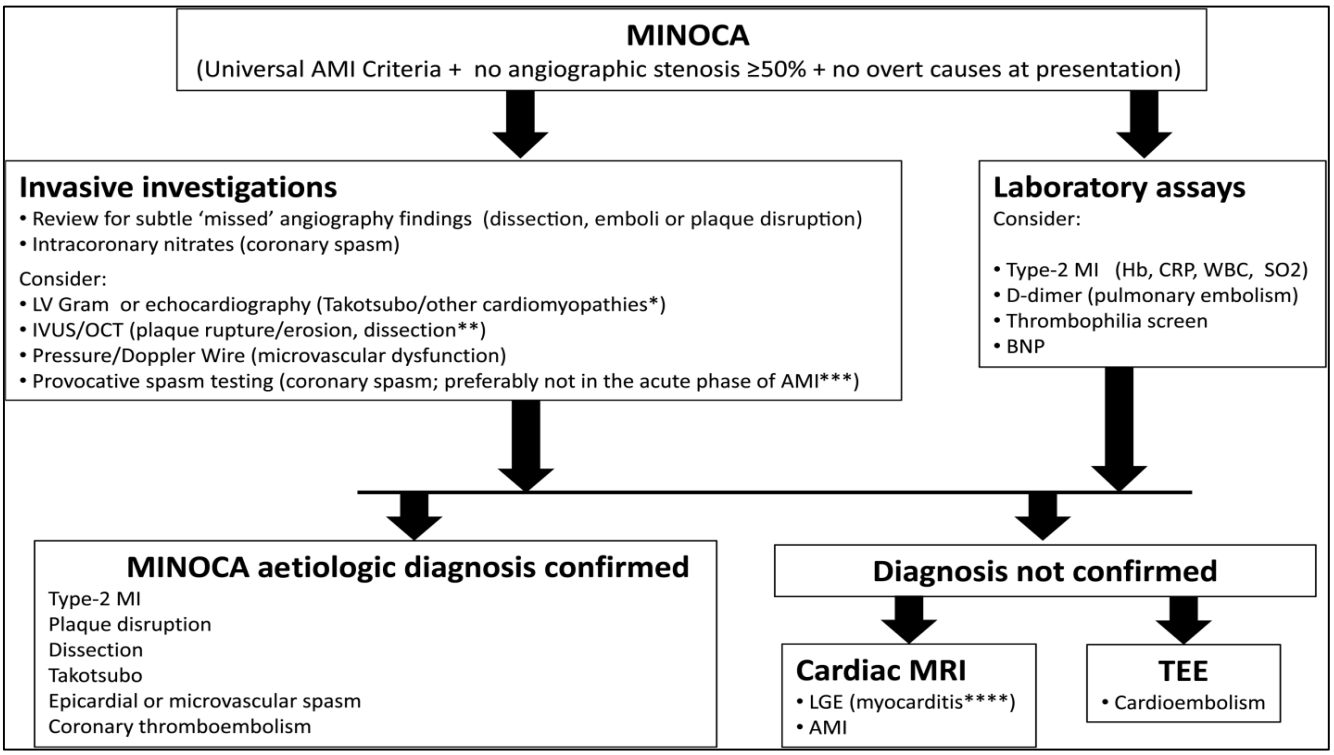

Fig 1: Recommended diagnostic and therapeutic algorithm for myocardial infarction with non-obstructive coronary arteries [6].

Conclusion

Myocardial infarction with non-obstructive coronary arteries is identified using a working diagnosis made following coronary angiography in the assessment of patients with an AMI. In patients in whom no specific cause is found, further studies are warranted to assess the most effective treatment.

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