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Review

Myocardial infarction with angiographically normal coronary arteries

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ABSTRACT

Myocardial Infarction with Normal Coronary Arteries (MINCA) is an important subgroup of myocardial infarction with a frequency of at least 3–4% of all myocardial infarctions. The interest and awareness of MINCA have increased recently due to the frequent use of coronary angiography, the description of Takotsubo stress cardiomyopathy and new sensitive troponin assays. Since myocarditis may mimic myocardial infarction it is essential to exclude this in patients with myocardial infarction with angiographically normal coronary arteries. Cardiac magnetic resonance imaging is a cornerstone not only to establish the diagnosis but also an important tool in the search for different causes of myocardial damage. In the future, atherosclerotic burden, hemostatic function, characterization of stressors and inflammation will be important targets for research in this group of patients.

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1. Introduction

Myocardial Infarction with Normal Coronary Arteries (MINCA) is now recognized as an important and fairly common subgroup of myocardial infarction [1]. There are several reasons for this. First, during more than two decades coronary angiography has been an important tool in the investigation of patients with Non-ST-Elevation Myocardial Infarction (NSTEMI) or ST-Elevation Myocardial Infarction (STEMI). Second, during the last 5 years, stress cardiomyopathy or Takotsubo syndrome, fulfilling the diagnostic criteria of myocardial infarction has received much attention. Third, the new definition of myocardial infarction, including sensitive and specific troponin assays, has increased the accuracy to detect myocardial infarction and thus increased the total number of events. The proportion of MINCA of all myocardial infarctions is uncertain and dependent on the age of the

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Table 1
Causes of elevations of troponin in the absence of ischemic heart disease.

Congestive heart failure, acute and chronic	Renal insufficiency
Chronic obstructive lung disease	Sepsis
Extreme exertion	Stress cardiomyopathy
Infiltrative myocardial disease	Symphaticomimetic drugs
Myocarditis	Tachyarythmias
Pulmonary embolism	

Modified from the expert consensus document by Thygesen et al. on the universal definition of myocardial infarction [1].

patients, the diagnostic work-up and the type of myocardial infarction (NSTEMI/STEMI) with a likely frequency of 3–4% [2,3]. Whether the proportion of MINCA will increase in patients with small elevations of high-sensitive troponin is unknown.

2. Diagnosis

An increased troponin concentration in plasma is the basis of the diagnosis of myocardial infarction today. The universal definition of myocardial infarction states that there should be a rise and/or fall of a cardiac marker above the 99th percentile of the upper reference value together with either symptoms or ECG changes suggestive of ischemia or imaging showing loss of functional myocardium [1]. The majority of patients receive their diagnosis of myocardial infarction from a combination of a troponin increase and symptoms suggesting of myocardial infarction. In addition to a troponin elevation and typical symptoms, such as chest pain, the majority of MINCA patients have a pathological ECG and left ventricular wall motion defects on either echocardiography or left ventriculography [4,8]. Thus, ECG and echocardiography have limited value to identify MINCA patients in the acute setting.

The knowledge behind current treatment of myocardial infarction is based on the assumption that it is caused by underlying coronary artery disease (CAD) with thrombosis superimposed on a plaque rupture or endothelial erosion. However, there are several other reasons for a troponin increase with symptoms suggesting of a myocardial infarction (Table 1). From a prognostic and therapeutic point-of-view pulmonary embolism and myocarditis are of major importance.

A misdiagnosis of myocardial infarction instead of pulmonary embolism might have fatal consequences since the current treatment of myocardial infarction offers limited protection against recurrent pulmonary embolism. In the on-going Stockholm Myocardial Infarction Normal Coronaries (SMINC) study, the first 100 patients were investigated with chest computed tomography (CT). However, since all CT examinations were negative (unpublished data), the protocol was changed to D-dimer and chest CT only upon a remaining suspicion of pulmonary embolism.

A diagnosis of myocarditis, instead of myocardial infarction, results in no need for specific anti-coagulation and anti-platelet therapy minimising the risk of bleeding as well as treatment with betablockers and statins. Previously, the diagnosis of myocarditis was dependent on endocardial biopsies. However, the accuracy of myocardial biopsises is very low with a potential risk of complications and is therefore limited to patients with severe heart failure necessitating active treatment [5]. Today, the diagnosis of myocarditis is based on magnetic resonance imaging (MRI) of the heart. Cardiac MRI has been shown to be able to distinguish between myocarditis and myocardial infarction [6]. At present, there are four series of patients with MINCA investigated with cardiac MRI showing an incidence of myocarditis of 5–60% [3,7–9] (Table 2). The reason for the wide variation is presumably explained by the age of the patients. In two of the studies, the patients with acute myocarditis were considerably younger (mean 35 years) than the rest of the cohorts [3,8]. To summarize the data on myocarditis; in potential MINCA patients below the age of 45 the prevalence of myocarditis is high and very common in patients below 35. In the latter age group, a group with a low risk of myocardial infarction due to CAD, cardiac MRI could be chosen before coronary angiography as the primary investigation if supported by clinical findings such as elevated CRP or fever. A suggestion of a diagnostic algorithm, modified from the SMINC study, is presented in Fig. 1. In the future, it can be possible to use cardiac MRI protocols that also can exclude pulmonary embolism [10].

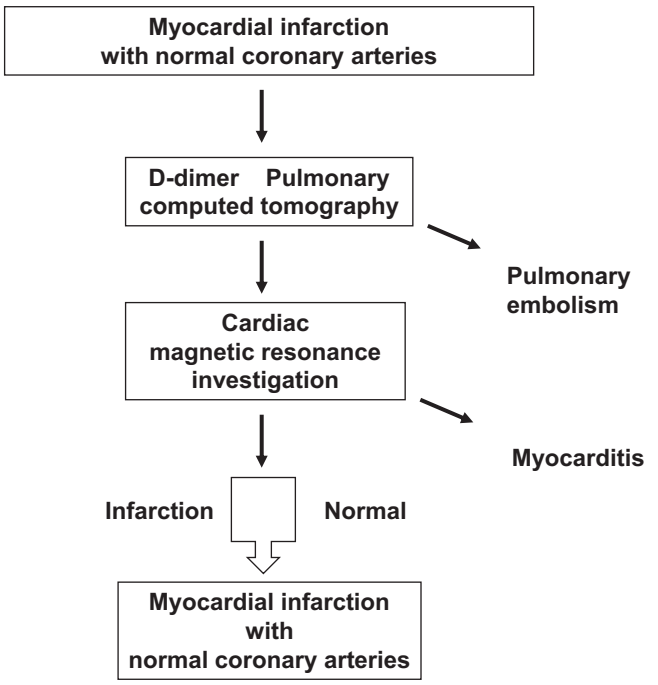

Fig. 1. Diagnostic algorithm for investigation of patients with myocardial infarction that have angiographic normal coronary arteries.

2.1. Subgroups

MINCA patients are likely a heterogeneous group of patients with different ethiologies. There are two special reasons for myocardial infarction that are obvious from the angiogram and should receive special attention; myocardial bridging and

Table 2
Studies of Myocardial Infarction with Normal Coronary Arteries using magnetic resonance imaging (MRI).

Patients, no	Age, mean	Myocarditis	Myocardial necrosis	Normal	Reference
23	54	1 (4%)	7 (30%)	15 (65%)	[7]
60	44	30 (50%)	7 (12%)	21 (35%)[a]	[8]
80	48	51 (63%)	12 (15%)	17 (21%)	[9]
49	45	14 (29%)	None	5 (10%)[b]	[3]

[a] Two patients were diagnosed with cardiomyopathy.
[b] The remaining patients were classified as pericarditis, stress cardiomyopathy, dilated cardiomyopathy or non-diagnostic using an integrated approach using clinical findings, ECG, biomarkers and MRI.