Risk Factors and Markers for Acute Myocardial Infarction With Angiographically Normal Coronary Arteries

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Myocardial Infarction with normal coronary arteries (MINCA) is common with a prevalence of 1% to 12% of all myocardial infarctions. The pathogenic mechanisms of MINCA are still unknown, but endothelial dysfunction has been suggested as a possible cause. To investigate risk factors and markers for MINCA, we conducted a case−control study. Considering the reported low prevalence of classical risk factors for coronary heart disease (CHD) in some but not all studies, our hypothesis was that endothelial function and intima−media thickness (IMT) were better, respectively lower, than CHD controls. One hundred patients with MINCA fulfilling diagnostic criteria according to the European Society of Cardiology/American Collage of Cardiology/American Heart Association universal definition of myocardial infarction with myocarditis excluded by cardiac magnetic resonance imaging were investigated. Risk factors, endothelial function (EndoPAT), and IMT were compared to gender- and age-matched patients with myocardial infarction and CHD, respectively healthy controls. Smoking, hypertension, impaired glucose tolerance and diabetes mellitus, inflammatory disease, and psychiatric disorders were more common in patients with MINCA than in healthy controls. In contrast to patients with CHD, the lipid profile was antiatherogenic with low low-density lipoprotein and high high-density lipoprotein cholesterol. There were no major differences between the groups regarding endothelial function and IMT that were in the normal range. In conclusion, the present study showed that MINCA was associated with many established cardiovascular risk factors without major differences in atherosclerosis markers. MINCA patients recalled a high prevalence of emotional stress before admission that together with previous psychiatric vulnerability and female gender speaks strongly in favor of Takotsubo syndrome being an important cause of MINCA. **(Am J Cardiol 2015;116:838−844)**

To investigate risk factors and markers for myocardial infarction with normal coronary arteries (MINCA), we conducted a case−control study. In the Stockholm Myocardial Infarction with Normal Coronaries (SMINC) study, we compared patients with MINCA with age- and gender-matched patients with coronary heart disease (CHD) and healthy controls. Considering a reported low prevalence of classical risk factors for CHD in some but not all studies,[1−3] our hypothesis was that endothelial function and intima−media thickness (IMT) were better, respectively lower, than CHD controls.

Methods

From June 2007 to May 2011, a total of 176 patients were screened at five coronary care units in the Stockholm metropolitan area. Patients aged from 35 to 70 years fulfilling the diagnostic criteria of acute myocardial infarction and a coronary angiogram with no or minimal signs of atheromatosis were eligible for the study; thus patients with Takotsubo Syndrome (TS) were included. Minimal atheromatosis was defined as small irregularities in the coronary vessel wall, giving rise to <30% reduction of the vessel lumen with all coronary angiograms independently examined by a second angiographer. Acute myocardial infarction was diagnosed according to the European Society of Cardiology/American Collage of Cardiology/American Heart Association universal definition of myocardial infarction,[4]

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The Stockholm Myocardial Infarction with Normal Coronaries study was supported by grants provided by the Stockholm County Council (ALF project) (grant number: 20110179) and the Swedish Heart and Lung Association (grant number: 20100327).

See page 843 for disclosure information.

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0002-9149/15/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2015.06.011

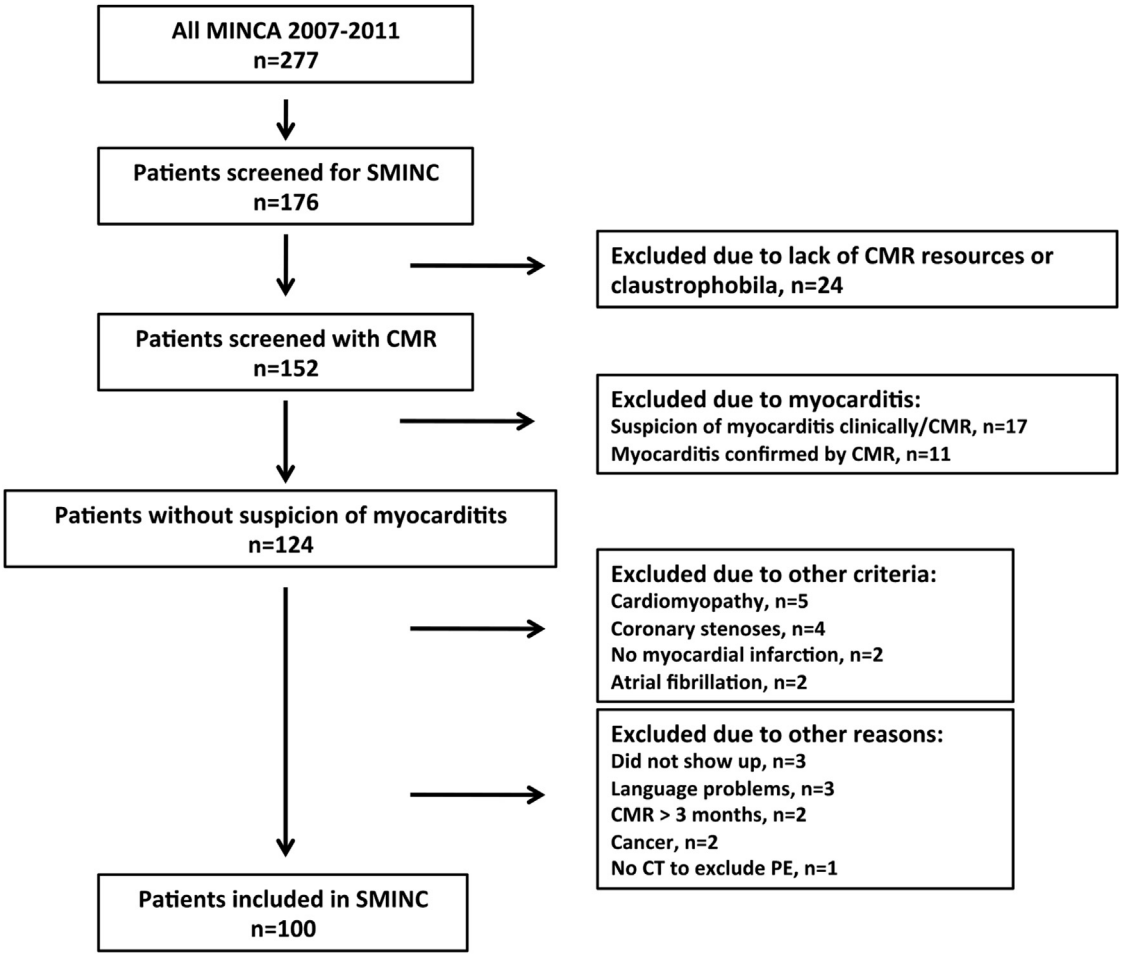

Figure 1. CONSERT diagram of inclusion of patients with MINCA.

and the diagnosis of TS was based on the Mayo clinic diagnostic criteria.[5] Patients with a history of structural heart disease, CHD, pacemaker, severe chronic obstructive pulmonary disease with hypoxemia due to acute exacerbation, severe renal failure (serum creatinine >150 μmol/L), or lack of sinus rhythm on admission were excluded. Medical records of all patients were examined by a cardiologist unrelated to the study to exclude patients not fulfilling the criteria for myocardial infarction. The first 100 patients underwent computed tomography (CT) of the chest to exclude pulmonary embolism, but because all turned out negative, the protocol was changed to measurement of D-dimer and CT only in case of high suspicion of pulmonary embolism. Cardiac magnetic resonance (CMR) imaging was performed in 152 patients mainly to exclude myocarditis. The screening process, including CMR results, has been described.[6] Subsequently a total of 100 patients with MINCA were included (Figure 1).

All 100 patients with MINCA were individually matched by gender and age (within ± 5 years) to 2 control groups: patients with myocardial infarction with CHD and healthy controls. Matching CHD controls were recruited during hospital stay or at follow-up at the respective coronary care unit. Healthy controls were recruited from the Stockholm population registry (2007 to 2008) or from the computer-based medical record system TAKE CARE containing all citizens in Stockholm (2009 to 2012). The controls were selected randomly by date of birth and gender to match cases and contacted for participation by an invitation letter followed by a telephone call. Ten missing healthy controls were recruited among staff, relatives, and controls' friends. The participation proportion was approximately 50%. All healthy controls were free of symptomatic CHD and performed a normal exercise stress test.

The study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice and was approved by the Stockholm Ethics Committee. For inclusion, patients were asked to give written informed consent. Each patient was assigned a study identification number, and a record for information was established and kept secured at the Cardiology Unit at Karolinska University Hospital in Solna, Sweden.

Smoking was defined as any active regular use and ex smoking as any history of regular use. Hypertension and hyperlipidemia were defined as previously diagnosed and medically treated. Diabetes mellitus was defined as previously diagnosed. Inflammatory diseases included diagnosed asthma, chronic obstructive pulmonary disease, rheumatologic diseases, pancreatitis, hepatitis, primary biliary cirrhosis, diverticulitis, collagenous colitis, and chronic