

Approximation of the Incidence of Myocarditis by Systematic Screening With Cardiac Magnetic Resonance Imaging

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ABSTRACT

OBJECTIVES This study sought to obtain an approximation of the true incidence of myocarditis by systematic screening of patients at risk using cardiac magnetic resonance imaging (CMR) in a tertiary care center.

BACKGROUND Underdiagnosis of myocarditis and resulting uncertainty about its incidence remain a clinical dilemma. The authors hypothesized that systematic screening of patients presenting with angina-like symptoms, elevated troponin T, and no significant coronary artery disease using cardiac CMR will provide an approximation of the true incidence of myocarditis.

METHODS The authors performed a retrospective chart review of patients presenting with angina-like symptoms and elevated high-sensitivity troponin T (TnT-hs ≥ 14 ng/L) in 2015 and 2016. During the year 2015, only patients with elevated TnT-hs, no significant coronary artery disease, and moderate-to-high clinical likelihood of myocarditis underwent CMR. Starting in 2016, CMR was obtained in patients with similar presentation, but independent of clinical likelihood of myocarditis.

RESULTS A total of 1,788 patients (74% male, age 69 ± 14 years) qualified for our analysis. In 2015, 521 patients presented with angina-like symptoms and TnT-hs elevation. In 2016, the number increased to 1,267 patients. Although in the year 2015, a total of 4 of 88 (5%) CMRs were positive for myocarditis, the percentage of positive CMRs doubled (26 of 199; 13%; $p = 0.03$) in 2016.

CONCLUSIONS A novel diagnostic screening algorithm led to a 6.3-fold increase of the incidence of myocarditis in our hospital. Furthermore, the percentage of CMRs positive for myocarditis doubled, supporting the diagnostic value of this method. Considering the potentially lethal adverse events of myocarditis if left untreated, we recommend a low threshold for the use of CMR in patients with angina-like symptoms and elevated TnT-hs after exclusion of coronary artery disease. (J Am Coll Cardiol HF 2018;■:■-■) © 2018 by the American College of Cardiology Foundation.

Chest pain is currently 1 of the most common causes for patient visits in the emergency department (1). Although acute coronary syndrome remains the leading cause in mortality worldwide (2), approximately 3% to 13% of patients presenting with chest pain and suspected myocardial infarction (MI) have unobstructed coronaries (3-5). Remarkably, patients with unobstructed coronary artery disease or MI with nonobstructed coronary

arteries (MINOCA) have poor prognosis with a 12-month all-cause mortality rate of 4.7% (4). The lack of guidelines for those “culprit free”-patients creates diagnostic and therapeutic challenges. Maddox et al. (6) showed that in contrast to patients with coronary artery disease, this population typically does not receive specific therapy to reduce risk for future cardiovascular events, suggesting potential for therapeutic improvement in this

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**ABBREVIATIONS
AND ACRONYMS****CABG** = coronary artery bypass graft**CMR** = cardiac magnetic resonance imaging**CT** = computed tomography**EMB** = endomyocardial biopsy**HCM** = hypertrophic obstructive cardiomyopathy**MI** = myocardial infarction**MINOCA** = myocardial infarction with nonobstructed coronary arteries**PCI** = percutaneous coronary intervention**Tnt-hs** = high-sensitivity troponin T

population. Differential diagnoses in the setting of angina and unobstructed coronary arteries include microvascular disease, Takotsubo syndrome, spontaneous recanalization of thrombotic occlusion or embolisms, and acute myocarditis (4,7). Assomull et al. (8) found myocarditis to be the most frequent diagnosis in this population. Additionally, most cases of acute myocarditis in young men seem to mimic an MI (9). Moreover, studies in patients with angina-like symptoms, elevated high-sensitivity troponin T (TnT-hs), and unobstructed coronaries have estimated the prevalence of myocarditis to range from 16% to 56% (10-12). Postmortem data have revealed myocarditis in sudden cardiac death at a rate of 8.6% up to 42%, suggesting that a considerable number of cases remain undiagnosed and thus untreated (13-15).

Discrepancy in the published data about the incidence of myocarditis emphasizes the need for effective standardized diagnostic screening. Early accurate diagnosis is crucial to introduce therapy and lifestyle modifications in a timely manner (16,17). Whereas the gold standard for definitive diagnosis of myocarditis remains endomyocardial biopsy (EMB) (7,18,19), cardiac magnetic resonance imaging (CMR) has evolved as a valuable diagnostic alternative to EMB and helps stratifying the risk in patients with suspected myocarditis (20-24).

In the present study, we sought to test the hypothesis of whether systematic screening using CMR of patients presenting with angina-like symptoms, elevated TnT-hs (≥ 14 ng/l), and no significant coronary artery disease will improve detection of myocarditis and provide an approximation of its true incidence in a tertiary medical center.

METHODS

STUDY DESIGN. We performed a retrospective single-center registry study investigating the incidence of myocarditis. Our chart review included patients who presented during the years between 2015 and 2016 (from January 2015 to January 2017) to the University Hospital Zurich with angina-like symptoms and elevated levels of TnT-hs (normal range 0 to 14 ng/l), and who had significant coronary artery disease ($>50\%$ stenosis) excluded by coronary angiography or computed tomography (CT) coronary angiography. No patients were excluded.

OUTCOME MEASUREMENTS. The primary outcome measure was to obtain an approximation of the true

incidence of myocarditis among patients with angina-like symptoms, elevated TnT-hs, and unobstructed coronary arteries by systematic CMR screening in our institution at the University of Zurich. To evaluate effectiveness of screening in 2016, results were compared with the previous year during which no systematic screening was performed. In addition, secondary outcome measures included: 1) number of patients presenting to our hospital with angina-like symptoms, elevated TnT-hs, and unobstructed coronary arteries per year; 2) number of CMRs performed in the years 2015 versus 2016, when the threshold for screening was lowered; 3) percentage of CMRs positive for myocarditis in 2015 versus 2016; and 4) incidence of other diagnoses in this patient population.

CLINICAL DATABASE. Clinical data was retrieved from the electronic medical records database of the University Hospital Zurich. All patients were de-identified and continuously numbered before analysis. Calculation and analysis were performed using IBM SPSS Statistics version 21 (Zurich, Switzerland). The study was approved by the regional ethics committee, and all patients provided their written informed consent.

DIAGNOSTIC SCREENING ALGORITHM. In patients presenting with angina-like symptoms and elevated TnT-hs, coronary artery disease was excluded by coronary angiography in the majority of patients. In cases of very low pretest probability for coronary artery disease, screening methods for coronary artery disease included CT coronary angiography or stress CMR with adenosine. In 2015, patients with moderate-to-high clinical suspicion for myocarditis underwent further diagnostic evaluation with CMR. Moderate-to-high clinical suspicion was raised in patients with classic symptoms of myocarditis such as chest pain, dyspnea, palpitations, syncope after viral prodrome (25,26) in the context of elevated TnT-hs, and unobstructed coronary arteries. In 2016, the threshold for obtaining CMRs was lowered and all patients with angina-like symptoms, elevated TnT-hs, and without obstructive coronary artery disease were screened with CMR unless another apparent etiology for their symptoms and TnT-hs elevation was identified (e.g., pulmonary embolism, severe hypertension, etc.). All CMRs were performed within 1 month of symptom onset.

CMR EXAMINATION. CMR examinations were performed either on a 1.5-T or 3.0-T scanner (SiemensSkyra, Erlangen, Germany, or Philips Achieva, Best, the Netherlands) with the help of electrocardiography-gated breath-hold protocol

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