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Short communication

ST-segment elevation and cardiac magnetic resonance imaging findings in myocardial infarction with non-obstructive coronary arteries

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ABSTRACT

Purpose: Patients with myocardial infarction and non-obstructive coronary arteries (MINOCA) may present with or without ST-elevation (STE) on the electrocardiogram (ECG). Previous studies have shown that STE was associated with higher risk of early mortality and long-term major adverse coronary events, and that cardiac magnetic resonance imaging (CMR) can help to determine whether the cause of a MINOCA presentation is ischemic or non-ischemic. We set out to determine the relationship between STE and CMR findings in patients presenting with MINOCA.

Design: Patients who underwent CMR based on a provisional diagnosis of MINOCA were pooled from three prospective cohort studies: the multicenter Stockholm Myocardial Infarction with Normal Coronaries, a prospective University of Adelaide study, and a prospective NYU School of Medicine diagnostic imaging study. STE was defined as ≥1 mm in ≥2 contiguous leads.

Results: Among 292 patients, average age was 57.0 years (±11.9), and 68% were female. Fifty-seven had STE, 231 had no STE and four had left bundle branch block. There was no difference between patients with vs. without STE in the likelihood of the CMR findings of infarction (21% vs. 18%), myocarditis (10% vs. 14%), left ventricular wall motion pattern consistent with takotsubo syndrome on CMR (16% vs. 14%).

Conclusion: STE on the presenting ECG was not associated with CMR findings in patients with a provisional diagnosis of MINOCA. Based on these findings, increased risk among MINOCA patients with STE does not appear to be related to variation in these CMR findings.

1. Introduction

At the time of coronary angiography, 3–15% of patients with acute myocardial infarction (MI) have non-obstructive coronary artery disease (CAD) (≤50% diameter stenosis in the major epicardial vessels) [1–3]. Patients meeting the universal definition of MI who have non-obstructive CAD receive a provisional diagnosis of myocardial infarction and non-obstructive coronary arteries (MINOCA) [4–6]. MINOCA is associated with adverse outcomes, with up to 5% one-year death or recurrent MI [1,7,8]. This diagnosis should prompt the clinician to search for an underlying cause such as plaque rupture, coronary artery spasm, or myocarditis [6]. Cardiac magnetic resonance imaging (CMR) is useful in patients presenting with MINOCA, to help define whether the underlying cause is ischemic or non-ischemic Patients with plaque rupture or coronary artery spasm may have an ischemic pattern of late gadolinium enhancement (LGE) on CMR, while patients with myocarditis typically have LGE in a non-ischemic pattern [10].

Patients with ST-segment elevation (STE) on the electrocardiogram (ECG) are less likely to have non-obstructive CAD. MINOCA patients

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who do have STE are at increased risk of in-hospital death, 30-day mortality and major adverse cardiovascular events over 4.5 years [3,8]. Given the differences in frequency and outcomes of patients presenting with MINOCA related to the finding of STE on the ECG, we hypothesized that CMR findings might vary by ECG presentation.

2. Methods

A total of 292 patients with a provisional diagnosis of MINOCA with available CMR data were pooled from a prospective, multicenter, diagnostic imaging study conducted in Sweden (n = 152, the Stockholm Myocardial Infarction with Normal Coronaries [11] between June 2007–May 2011), from a prospective study at the University of Adelaide (n = 96, conducted January 2012–December 2013), and from a prospective diagnostic imaging study at NYU School of Medicine (n = 44, restricted to women, enrolled July 2007–August 2010). Adults with a provisional diagnosis of MINOCA based on ESC criteria with interpretable LGE images on CMR were eligible.

2.1. ECG criteria

ECGs from presentation were reviewed by independent cardiologists. ST-segment elevation was defined according to the Universal Definition of MI [4]. Patients with left bundle branch block (LBBB) are described separately (n = 4) given that the chronicity of LBBB could not be determined.

2.2. CMR definitions

Infarction was defined on CMR based on an ischemic LGE pattern (e.g., subendocardial/transmural, in a coronary territory). Takotsubo syndrome was defined on CMR by typical wall motion pattern extending beyond a single coronary territory in the absence of LGE. Myocarditis was defined on CMR based on a non-ischemic LGE pattern (e.g., linear centromyocardial or subepicardial LGE), typically with T2 signal hyperintensity.

2.3. CMR imaging protocol

All patients were imaged using a 1.5-Tesla MRI system with a phased-array body coil and standard ECG monitoring. Images were acquired during repeated end-expiratory breath holds. LGE images covering the left ventricle in short axes and in two- and four-chamber views were acquired in all patients after administration of an approved gadolinium-based contrast agent. T2-weighted imaging for myocardial edema was recommended. CMR images were assessed by experienced certified readers at the local institutions.

2.4. Statistical analysis

The variability of continuous measures was represented as means and standard deviations when following a normal distribution and with medians and interquartile ranges when following non-normal distribution. Continuous variables were compared using two-sample *t*-tests and non-parametric Wilcoxon rank sum tests, as appropriate (Vassar Stats). Dichotomous variables were compared using chi-square tests.

3. Results

A total of 292 patients met the inclusion criteria for the study. 57 (20%) presented with STEMI, 231 (79%) presented with NSTEMI and 4 (1%) had LBBB. Patient characteristics are presented in Table 1. CMR was performed 1–121 days (median 7, IQR: 3–17) after presentation, with 239 CMR studies performed within 30 days of MI. Consistent with prior literature, NSTEMI patients were older with lower troponin values as compared to STEMI patients [12,13]. There was no difference between groups in left ventricular ejection fraction or atherosclerotic risk factors.

3.1. CMR Results (Fig. 1)

There was no difference in the likelihood of CMR diagnosis of infarction, takotsubo, myocarditis or normal CMR between patients with and without ST elevation. CMR abnormalities other than infarction, myocarditis or takotsubo were identified in 9% of STEMI and 9% of NSTEMI. Other CMR findings (n = 9 in Sweden cohort, n = 10 in Adelaide cohort, n = 6 in the NYU cohort) included areas of LGE that were difficult to characterize and/or very small, patchy areas of T2 signal hyperintensity, edema in a pattern not consistent with takotsubo syndrome, and previously undiagnosed hypertrophic or dilated cardiomyopathy.

Among 4 patients with LBBB, one had myocarditis, one normal CMR, one non-compaction cardiomyopathy, and one cardiomyopathy with a wall motion pattern not consistent with takotsubo, without LGE.

Despite similar age, sex and peak troponin levels in patients across sites, the Swedish cohort had more normal scans as compared to NYU and Adelaide (67% vs. 20%). This remained true when the analysis was restricted to CMR scans performed within 7 days; 59% of the CMR studies performed in the Swedish cohort were normal when done within one week. This likely relates to the lack of takotsubo diagnoses on CMR in this cohort; this cohort was enrolled before establishment of standardized CMR criteria for takotsubo. As previously published, 32% of Swedish cohort patients with normal CMR met Mayo Clinic criteria for takotsubo syndrome [11]. The Swedish cohort excluded patients with >30% angiographic stenosis while a 50% threshold was used at NYU and Adelaide. As an additional sensitivity analysis, we analyzed CMR findings in patients with vs. without STE excluding Swedish patients, and still found no difference in CMR findings between groups.

4. Discussion

We found that infarction or myocarditis was identified on CMR in 32% of patients with a provisional diagnosis of MINOCA, though ST elevation on the ECG was not associated with any particular CMR finding, including presence of infarction. CMR is recommended in the evaluation of MINOCA patients because it provides information which may influence management [6]. For example, patients with myocarditis do not require the typical secondary prevention medications appropriate for atherothrombotic MI.

Table 1
Baseline characteristics of MINOCA patients with and without ST elevation.

	All patients (n = 288)	STE (n = 57) *Sweden N = 27* *Adelaide N = 20* *NYU N = 10*	NSTE (n = 231) *Sweden N = 122* *Adelaide N = 76* *NYU N = 33*	*P* value
Age (mean ± SD)	57.0 ± 11.9	54.0 ± 13.4	58.0 ± 11.4	0.02
Troponin (multiple of ULN), median, IQR	19.8 (6.9–48.2)	26.7 (11.9–54.0)	16.6 (6.0–45.4)	<0.01
Female (%)	197 (68%)	35 (61%)	162 (70%)	0.20
HTN (%)	137 (48%)	26 (46%)	111 (48%)	0.74
DM (%)	35 (12%)	7 (12%)	28 (12%)	0.97
Current smoking (%)	54 (19%)	10 (18%)	44 (19%)	0.79
EF (mean ± SD)	57.0 ± 10.4	58 ± 10.04	54 ± 11.78	0.06
Days from event to CMR(median)	7 (IQR: 3-17)	5 (IQR: 3-10)	8 (IQR: 4-18)	0.01
CMR-infarction (%)	54 (19%)	12 (21%)	42 (18%)	0.62
CMR- myocarditis (%)	38 (13%)	6 (10%)	32 (14%)	0.51
CMR- normal (%)	129 (45%)	25 (44%)	104 (45%)	0.87
CMR- other (%)	25 (9%)	5 (9%)	20 (9%)	0.98
Takotsubo (%)	42 (14%)	9 (16%)	33 (14%)	0.77

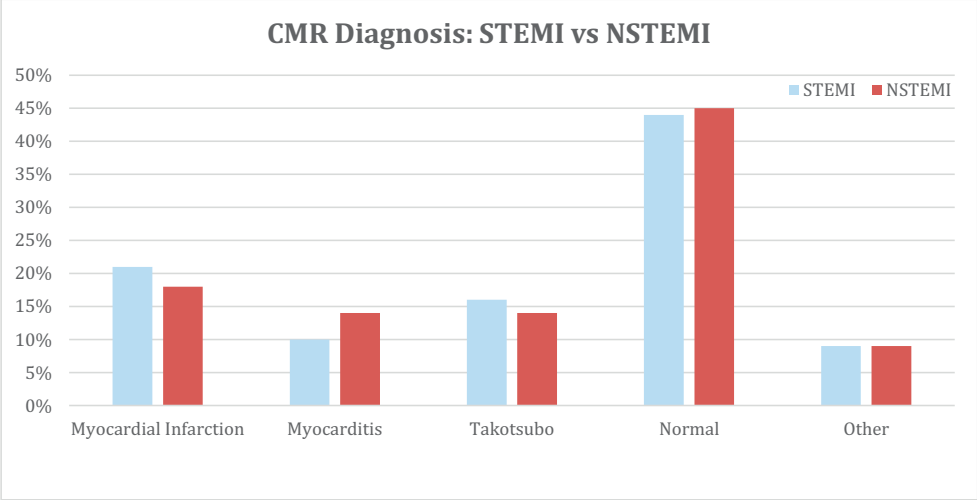

Fig. 1. Proportion of MINOCA patients with/without ST elevation at the time of presentation who have different findings on cardiac MRI.

Two large studies have shown that STE is present in 16–17% of patients with MINOCA [3,8], while a pooled analysis of clinical trials in acute coronary syndrome found that 33% of patients with MINOCA had STE [1]. Given the increased risk of mortality among MINOCA patients with STE in the short- and long-term, we anticipated differences in the underlying pathophysiological mechanisms between the two presentations would be detected on CMR [3,9]. Thus our findings are contrary to hypothesis. It is possible that our findings are limited by bias relating to survival to undergo CMR. Alternatively the increased risk associated with STE in MINOCA may be mediated by factors other than CMR findings. These could include lipid levels, renal function and C-reactive protein, because after introduction of these parameters into a multivariate model for outcomes among MINOCA patients, STE was no longer a significant predictor [8]. Prior studies have shown that STE is associated with death and composite major adverse cardiovascular events, but not with recurrent MI; however, when recurrent MI does occur and angiography is performed, new obstructive CAD is more likely if the initial MINOCA event included STE [14]. Thus it remains possible that underlying atherosclerosis is more common when there is STE with MINOCA.

The finding of infarction on CMR does not identify which ischemic etiology caused that infarct (e.g., coronary artery spasm, plaque rupture or erosion) [6]. The specific ischemic cause may be identified via intracoronary imaging (such as optical coherence tomography [OCT]) and/or provocative spasm testing. These tests are of potential clinical value and may soon become integral to the diagnostic workup of MINOCA patients, particularly when combined with CMR. Further studies investigating diagnostic strategies in patients are needed to better define the role of intracoronary imaging, and one is ongoing (NCT#02905357). Until additional data are available, infarction on CMR should prompt physicians to treat for the most common ischemic causes of MINOCA (i.e., plaque disruption and spasm), such as with a statin, calcium channel blocker and aspirin [6,15].

5. Limitations

While all patients in the NYU and Swedish cohorts underwent CMR routinely as part of a research protocol, the Australian cohort included clinically ordered CMR, which may have influenced the distribution of imaging findings, particularly toward higher prevalence of takotsubo syndrome. We do not have data on the proportion of STEMI patients with MINOCA who underwent CMR across sites or the degree of ST elevation. ECGs were not reviewed by a central core laboratory. Time from MI to CMR varied between sites and may have led to overestimation of the number of normal or non-diagnostic CMRs. The Swedish cohort was limited by longer period of time from event to CMR, which may have resulted in missed reversible states such as myocarditis or takotsubo. However, a sub-analysis excluding the Swedish cohort did not alter the results of the STE comparison, and analysis excluding CMR after 30 days did not alter results. Given these limitations, further investigation is required to determine the optimal timing to perform CMR to best characterize MINOCA.

6. Conclusion

ST segment elevation on presenting ECG was not related to CMR diagnosis in patients with a provisional diagnosis of MINOCA.

Conflict of interest

Dr. Reynolds received a donation of OCT catheters for an unrelated study from Abbott Vascular.

References

[1] S. Pasupathy, T. Air, R.P. Dreyer, R. Tavella, J.F. Beltrame, Systematic review of patients presenting with suspected myocardial infarction and nonobstructive coronary arteries, Circulation 131 (10) (2015) 861–870.
[2] A.I. Larsen, D.W. Nilsen, J. Yu, R. Mehran, E. Nikolsky, A.J. Lansky, A. Caixeta, H. Parise, M. Fahy, E. Cristea, et al., Long-term prognosis of patients presenting with ST-segment elevation myocardial infarction with no significant coronary artery disease (from the HORIZONS-AMI trial), Am. J. Cardiol. 111 (5) (2013) 643–648.
[3] N.R. Smilowitz, A.M. Mahajan, M.T. Roe, A.S. Hellkamp, K. Chiswell, M. Gulati, H.R. Reynolds, Mortality of myocardial infarction by sex, age, and obstructive coronary artery disease status in the ACTION registry-GWTG (acute coronary treatment and intervention outcomes network registry-get with the guidelines), Circ. Cardiovasc. Qual. Outcomes 10 (12) (2017), e003443.
[4] K. Thygesen, J.S. Alpert, A.S. Jaffe, B.R. Chaitman, J.J. Bax, D.A. Morrow, H.D. White, Group ESCSD, Fourth universal definition of myocardial infarction (2018), Eur. Heart J. 72 (18) (2018) 2231–2264.
[5] H.R. Reynolds, M.B. Srichai, S.N. Iqbal, J.N. Slater, G.B. Mancini, F. Feit, I. Pena-Sing, L. Axel, M.J. Attubato, L. Yatskar, et al., Mechanisms of myocardial infarction in women without angiographically obstructive coronary artery disease, Circulation 124 (13) (2011) 1414–1425.
[6] S. Agewall, J.F. Beltrame, H.R. Reynolds, A. Niessner, G. Rosano, A.L.P. Caforio, R. De Caterina, M. Zimarino, M. Roffi, K. Kjeldsen, et al., ESC working group position paper on myocardial infarction with non-obstructive coronary arteries, Eur. Heart J. 38 (3) (2017) 143–153.
[7] K.R. Bainey, R.C. Welsh, W. Alemayehu, C.M. Westerhout, D. Traboulsi, T. Anderson, N. Brass, P.W. Armstrong, P. Kaul, Population-level incidence and outcomes of myocardial infarction with non-obstructive coronary arteries (MINOCA): insights from the Alberta contemporary acute coronary syndrome patients invasive treatment strategies (COAPT) study, Int. J. Cardiol. 264 (2018) 12–17.
[8] A.M. Nordenskjold, T. Baron, K.M. Eggers, T. Jernberg, B. Lindahl, Predictors of adverse outcome in patients with myocardial infarction with non-obstructive coronary artery (MINOCA) disease, Int. J. Cardiol. 261 (2018) 18–23.
[9] R. Dahmani, R. Ben Said, Y. Arous, H. Mahfoudhi, C. Chourabi, M. Ghommidh, B. Jedaida, N. Ben Mansour, A. Haggui, N. Hajlaoui, et al., Contribution of cardiac

magnetic resonance imaging in the diagnosis of acute coronary syndrome with normal coronary angiography, Tunis. Med. 94 (6) (2016) 167–172.
[10] P. Tornvall, E. Gerbaud, A. Behaghel, R. Chopard, O. Collste, E. Laraudogoitia, G. Leurent, N. Meneveau, M. Montaudon, E. Perez-David, et al., Myocarditis or "true" infarction by cardiac magnetic resonance in patients with a clinical diagnosis of myocardial infarction without obstructive coronary disease: a meta-analysis of individual patient data, Atherosclerosis 241 (1) (2015) 87–91.
[11] O. Collste, P. Sorensson, M. Frick, S. Agewall, M. Daniel, L. Henareh, C. Ekenback, L. Eurenius, C. Guiron, T. Jernberg, et al., Myocardial infarction with normal coronary arteries is common and associated with normal findings on cardiovascular magnetic resonance imaging: results from the Stockholm myocardial infarction with normal coronaries study, J. Intern. Med. 273 (2) (2013) 189–196.
[12] D.S. Blondheim, M. Kleiner-Shochat, A. Asif, M. Kazatsker, A. Frimerman, R. Abu-Fanne, E. Neiman, M. Barel, Y. Levy, N. Amsalem, et al., Characteristics, management, and outcome of transient ST-elevation versus persistent ST-elevation and non-ST-elevation myocardial infarction, Am. J. Cardiol. 121 (12) (2018) 1449–1455.
[13] D.D. McManus, J. Gore, J. Yarzebski, F. Spencer, D. Lessard, R.J. Goldberg, Recent trends in the incidence, treatment, and outcomes of patients with STEMI and NSTEMI, Am. J. Med. 124 (1) (2011) 40–47.
[14] A.M. Nordenskjold, B. Lagerqvist, T. Baron, T. Jernberg, N. Hadziosmanovic, H.R. Reynolds, P. Tornvall, B. Lindahl, Reinfarction in patients with myocardial infarction with nonobstructive coronary arteries (MINOCA) : coronary findings and prognosis, Am. J. Med. 132 (3) (2019) 335–346.
[15] M. Alkhalil, J.T. Chai, R.P. Choudhury, Plaque imaging to refine indications for emerging lipid-lowering drugs, Eur. Heart J. Cardiovasc. Pharmacother. 3 (1) (2017) 58–67.