Revista Portuguesa de Cardiologia xxx (xxxx) xxx–xxx

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

Early versus late cardiac magnetic resonance in the diagnosis of myocardial infarction with non-obstructive coronary arteries

Inês Macedo Conde[a], Mariana Salazar[b], Vítor Hugo Pereira[a,b,c,d], Catarina Vieira[a], Carlos Galvão Braga[a], Cátia Oliveira[a,b,c,d,*]

[a] *Cardiology Department, Hospital de Braga, Braga, Portugal*
[b] *School of Medicine, University of Minho, Braga, Portugal*
[c] *Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal*
[d] *ICVS/3B's-PT Government Associate Laboratory, Braga, Portugal*

Received 29 August 2023; accepted 2 December 2023

KEYWORDS
MINOC;
CMR

Abstract
Introduction and objectives: Myocardial infarction with non-obstructive coronary arteries (MINOCA) is responsible for about 10% of all acute myocardial infarctions (AMI). Therapeutic strategies and prognosis depend on the underlying etiology, and a multimodal approach is essential. The objectives of this study were to characterize the group of patients diagnosed with MINOCA and to valuate the diagnostic yield of cardiovascular magnetic resonance (CMR).
Methods: This was a retrospective, observational, and analytical study, including 516 patients admitted for a non-ST-elevation MI and with no significant coronary disease on coronary angiography between January 2016 and September 2021.
Results: After the inclusion criteria, 163 patients remained of the 516 admitted to the study. They were divided into four groups based on the CMR results: MINOCA (n=51), Takotsubo syndrome (n=37), myocarditis (n=33), and without diagnosis (n=42). Most patients diagnosed with MINOCA were female with a mean age of 61.06±13.83 years. CMR identified the diagnosis in 74.2% of patients admitted for suspected acute MI, in which coronary angiography showed the absence of significant obstructions. The median time between hospital admission and CMR was significantly shorter in the groups that had a diagnosis compared with the group with no diagnosis (p=0.038), with a significant increase in diagnostic profitability if CMR was performed up to 14 days after admission (p=0.022). There were no deaths of cardiovascular etiology during the follow-up period.
Conclusions: CMR was fundamental as it identified the diagnosis in three out of four patients; it should be performed in the first 14 days.
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* Corresponding author.
E-mail address: catiaandreiaoliveira@gmail.com (C. Oliveira).

https://doi.org/10.1016/j.repc.2023.12.010
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Please cite this article as: I. Macedo Conde, M. Salazar, V.H. Pereira et al., Early versus late cardiac magnetic resonance in the diagnosis of myocardial infarction with non-obstructive coronary arteries, Revista Portuguesa de Cardiologia, https://doi.org/10.1016/j.repc.2023.12.010

PALAVRAS-CHAVE
MINOC;
CMR

Ressonância magnética cardíaca precoce *versus* tardia no diagnóstico de MINOCA

Resumo
Introdução e objetivos: O enfarte agudo do miocárdio com artérias coronárias não obstrutivas (MINOCA) é responsável por cerca de 10% de todos os enfartes agudos do miocárdio. As estratégias terapêuticas e o prognóstico dependem da etiologia subjacente, sendo essencial uma abordagem multimodal. Caracterizar um grupo de doentes diagnosticados com MINOCA. Avaliar o rendimento diagnóstico da ressonância magnética cardiovascular (RMC).
Métodos: Estudo retrospetivo, observacional e analítico, incluindo 516 doentes admitidos por EAM sem elevação do segmento ST e sem doença coronária significativa na coronariografia, entre janeiro de 2016 e setembro de 2021.
Resultados: Após os critérios de inclusão, permaneceram 163 pacientes dos 516 admitidos no estudo, que foram divididos em quatro grupos com base nos resultados da RMC: MINOCA (n = 51), síndrome de Takotsubo (n = 37), miocardite (n = 33) e sem diagnóstico (n = 42). A maioria dos pacientes com diagnóstico de MINOCA era do sexo feminino, com idade média de 61,06 ± 13,83 anos. A RMC identificou o diagnóstico em 74,2% dos doentes admitidos por suspeita de enfarte agudo do miocárdio, nos quais a coronariografia mostrou ausência de obstruções significativas. A mediana do tempo entre a admissão hospitalar e a RMC foi significativamente menor nos grupos que tiveram um diagnóstico comparativamente ao grupo sem diagnóstico (p = 0,038), com um aumento significativo da rentabilidade diagnóstica se a RMC fosse realizada até 14 dias após a admissão (p = 0,022). Não se registaram óbitos de etiologia cardiovascular durante o período de seguimento.
Conclusões: A RMC foi fundamental, pois identificou o diagnóstico em três de quatro doentes e deve ser efetuada nos primeiros 14 dias.
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Introduction

It has become increasingly recognized that there is a group of patients with acute myocardial infarction (AMI) without obstructive coronary artery disease (CAD) on coronary angiography (stenosis ≥50% in an epicardial artery). The designation acute myocardial infarction without obstructive coronary artery disease (MINOCA) has been adopted for this group of patients.[1]

Studies indicate a prevalence of MINOCA of 10% in all AMI.[2] Patients diagnosed with MINOCA are more often female and younger compared with those with AMI with obstructive CAD.[1,3] The prevalence of CAD risk factors and clinical features also varied between patients with MINOCA versus AMI with obstructive CAD. Patients with MINOCA more often present without ST-segment elevation and have lower troponin elevation than patients with AMI with obstructive CAD.[1,4–6]

In the evaluation of patients with suspected MINOCA, it is critical to exclude other etiologies of troponin elevation.[2,7] Both the European Society of Cardiology and the American Heart Association have recognized the central role of cardiac magnetic resonance imaging (CMR) in the diagnostic approach for patients with suspected MINOCA, as it allows the diagnosis of non-ischemic causes of myocardial injury, such as myocarditis and Takotsubo syndrome. CMR also enables the diagnosis of infarction by providing the location of the area of myocardial injury/ischemia. It may also suggest the underlying etiology, thus further influencing the subsequent management of the patient diagnosed with MINOCA.[1,2,8–10]

The diagnostic accuracy of CMR is higher when it is performed within 7–14 days of symptom presentation.[2,9,11,12] Dastidar et al. compared retrospective imaging findings in patients diagnosed with MINOCA, showing that performing CMR early, within two weeks of admission, increases the diagnostic rate to 84%, due to the ability to detect transient, reversible myocardial changes that usually resolve after a few weeks and are therefore not subsequently detectable. This is particularly relevant in potentially reversible conditions, as in acute myocarditis and Takotsubo syndrome.[8,10] Unchanged, i.e. ''normal,'' CMR may be present in 15–25% of patients with suspected MINOCA.[10]

Numerous pathophysiological mechanisms underlying the diagnosis of MINOCA have been proposed, and a multimodal approach should therefore be considered next in all patients, enabling, where possible, the prescription of specific therapies and the consequent improvement in clinical prognosis.[13–15] In a significant proportion of patients diagnosed with MINOCA, the underlying mechanism may remain unclear, even after extensive investigation.[8]

The underlying pathophysiological mechanisms that cause MINOCA are still poorly understood, and several different mechanisms have been proposed. The most common causes of MINOCA can be divided into atherosclerotic and non-atherosclerotic causes. Atherosclerotic causes

include plaque rupture and erosion. The most common non-atherosclerotic causes include coronary vasospasm, coronary microvascular dysfunction, coronary thrombosis/embolism, and spontaneous coronary artery dissection.[9]

Intra-coronary imaging, preferably high-resolution optical coherence tomography (OCT) or, to a lesser extent, coronary intravascular ultrasound (IVUS), may be important to ascertain the etiology of coronary plaque rupture, plaque erosion, or spontaneous coronary artery dissection. Coronary plaque rupture is common among patients with MINOCA, and spontaneous coronary artery dissection is a frequent cause in women aged <50 years.[2,16] For the diagnosis of coronary vasospasm, provocative testing may be necessary.[1] The late passage of contrast through the coronary arteries has been used as a marker of microvascular dysfunction.[14]

In recent years, interest in the diagnosis of MINOCA has increased rapidly, yet there are still many significant gaps in current knowledge, especially regarding the specific treatment for each etiology.[7,8] One of the reasons is that most of the studies performed include patients based only on the diagnosis of MINOCA, and do not group them by underlying etiologies, making it difficult to build a consensus to decide on the best specific therapy and its prognostic impact. All patients with AMI with obstructive CAD undergo secondary prevention cardio-protective therapies, such as antiplatelet drugs and statins. The focus of these drugs is the atherosclerosis process, however the atherosclerotic burden in most patients with MINOCA is low and there are multiple possible pathological mechanisms, calling into question the routine use of these drugs and therefore, meaning therapy should be individualized.[1]

The prognosis of patients with MINOCA depends on the underlying cause. Several studies indicate that the prognosis is better compared with that of patients with AMI with obstructive CAD; however, it is still not benign.[4,17] A recent meta-analysis showed an annual mortality rate of 2.0%.[8] Other studies have shown an increased risk of experiencing new AMI and re-hospitalization for heart failure (HF) or stroke.[8] The absence of obstructive coronary artery disease should not falsely reassure healthcare professionals because as patients with MINOCA are generally younger, there is a greater likelihood of future disability and early retirement from work.[2,18]

Thus, it was considered pertinent to characterize the group of patients diagnosed with MINOCA, regarding its prevalence, clinical, laboratory, imaging data, and prognosis at discharge, and to study the diagnostic profitability of CMR in patients admitted for suspected AMI without obstructive CAD.

Objectives

The aim of our study was to characterize the group of patients diagnosed with MINOCA in terms of prevalence, laboratory, echocardiographic and imaging variables, and prognosis at discharge. Additionally, we aimed to evaluate the diagnostic profitability of CMR in patients admitted for suspected AMI without obstructive coronary disease.

Methods

This was an observational and retrospective study. It included all the patients with suspected AMI admitted to the Braga Hospital for coronary angiography between 1 January 2016 and 31 September 2021.

Patients with clinical evidence of AMI, according to the Fourth Universal Definition of Myocardial Infarction, without ST-segment elevation on electrocardiogram (ECG), without obstructive CAD on angiography (without coronary stenosis equal to or greater than 50% in any artery), and who underwent CMR within 180 days of hospital admission were included. Patients with ST-segment elevation on ECG, patients with CAD on angiography, and patients who had CMR after 180 days of hospital admission were excluded from our sample (Figure 1).

The final sample was divided into four subgroups based on CMR results: MINOCA, Takotsubo syndrome, myocarditis, and no diagnosis. The latter corresponds to a normal CMR with no pathological changes identified.

The study sample was initially selected from the Cath Lab records of the Braga Hospital, where patients with evidence of AMI without ST-segment elevation on ECG and who underwent coronary angiography between 1 January 2016 and 31 September 2021 were included. Data were then collected by consulting the computerized clinical records, always taking patient confidentiality and anonymity as a priority.

The variables collected for each patient were: anthropometric and demographic data, previous medical history, lifestyle and habits, clinical data during hospitalization, including length of stay, symptoms on admission, laboratory data and findings on echocardiography and coronary angiography, imaging data with respect to the timing of CMR and its results, clinical data at the time of discharge and 12 months after.

Arrhythmia was defined by the presence of atrial fibrillation/flutter, ventricular fibrillation, or ventricular tachycardia. HF was defined by the presence of typical symptoms/signs and objective evidence of cardiac dysfunction by imaging or increased natriuretic peptide levels.[19]

Cardiac MR imaging was conducted using clinical 3T scanner (Magnetom Verio, Siemens Healthcare) and a 1.5 Tesla scanner (Avanto, Siemens). Cine images were acquired utilizing balanced steady-state free precession (bSSFP) sequences during breath-hold. The short-axis stack and three standard long-axis views (2-, 3-, and 4-chambers) were obtained with the following parameters: field of view=300–340 mm^2, slice thickness=8 mm with a 25% gap, repetition time ~50 ms, echo time ~1.10 ms, flip angle=30–50°, acquisition matrix=192×156. The acquisition was ECG-g and images were retrospectively reconstructed in 25 frames. The late gadolinium images were acquired approximately 10 minutes after the administration of Gadobutrol (Gadovist) at a dose of 0.2 mmol/kg. Mapping sequences were not locally available at the time of the scans.

Statistical analysis

In the descriptive statistics, we used frequencies (n) and percentages (%) in categorical variables, means (M) and

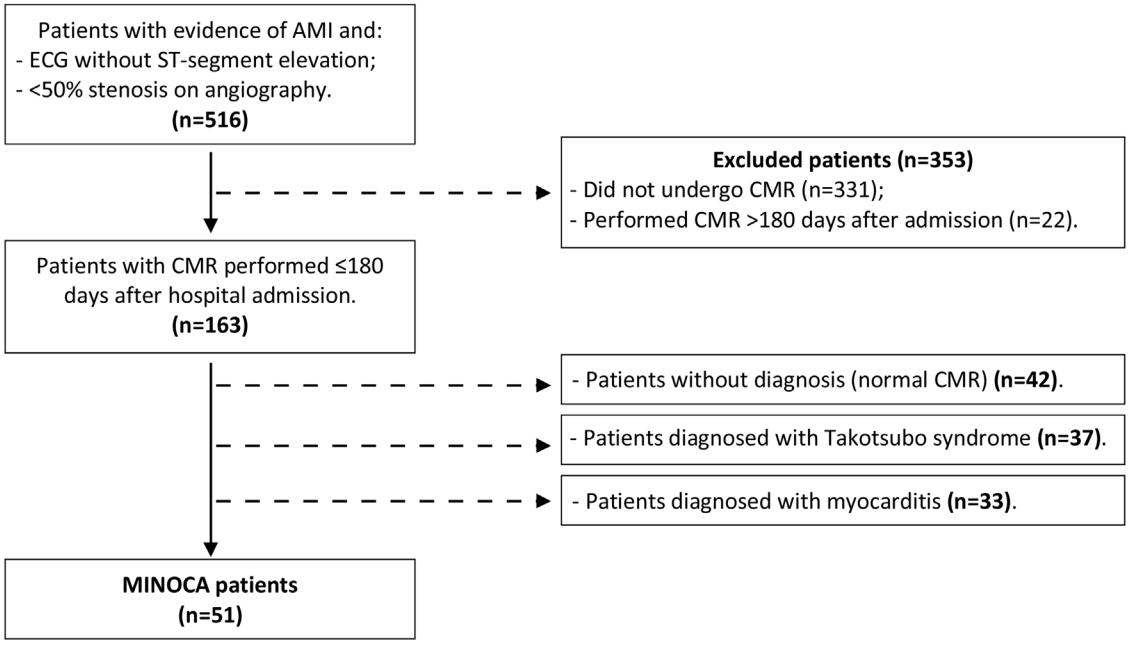

Figure 1 Flowchart of the selection of the sample of patients diagnosed with MINOCA.

standard deviations (SD) in continuous variables with symmetrical distribution and medians (Mdn) and quartiles (Q1−Q3) in continuous variables with an asymmetrical distribution. Symmetry was established by observing the histogram and by calculating the asymmetry coefficient falling within the interval [−1, 1].

The Mann−Whitney test was used to compare the time from admission to CMR by type of diagnosis. This type of non-parametric test was chosen because the distribution of time from the date of admission to CMR was very asymmetric, with Kolmogorov−Smirnov test, $p<0.05$. The association of categorical variables was performed using chi-square tests or Fisher's tests, in case of non-compliance with Cochran's rules.

Effect sizes were calculated according to Cohen's (1988) recommendations.[20] Thus, for the chi-square tests, phi (φ) were calculated with 0.2 (small effect), 0.5 (moderate effect), and 0.8 (high effect) as cutoff points. For the Mann−Whitney tests the calculated effect size was the rank-biserial correlation (r) with cutoff points 0.10 (small effect), 0.24 (moderate effect) and 0.37 (high effect).[21]

All tests were considered statistically significant for a significance level (p-value) of less than 0.05.

Results

Characterization of the group of patients diagnosed with MINOCA

Clinical and demographic characterization

By applying the previously mentioned inclusion and exclusion criteria, we obtained a sample of 51 patients diagnosed with MINOCA, of which 27 (52.9%) were female. The study sample had a mean age of 61.06 years (SD=13.83). The mean body mass index (BMI) was 27.15 (SD=4.04) kg/m^2. Regarding smoking, there were 9 (17.6%) smokers and 11 (21.6%) ex-smokers. The prevalence of diabetes mellitus was 11.8% (n=6), hypertension was 49% (n=25) and dyslipidemia was 58.8% (n=30). Regarding past cardiovascular medical history, 3 (5.9%) patients had previous history of AMI or stroke, 1 (2%) patient had a history of HF, and 3 (5.9%) had valvular heart disease. No patient had peripheral arterial disease (PAD) or chronic kidney failure (CKF). Seven (13.7%) patients had a family history of early cardiovascular (CV) disease.

Table 1 summarizes the clinical and demographic characteristics of patients diagnosed with MINOCA.

Clinical characterization during hospitalization

At the time of hospital admission, the most reported symptom was chest pain, in 49 (96.1%) patients. Regarding laboratory tests, the median troponin value was 8.9 (3.6−18.2) ng/mL. The median total cholesterol was 184.63 (SD=40.16) mg/dL, HDL cholesterol was 48.67 (SD=14.27) mg/dL, and LDL cholesterol was 117.45 (SD=36.13) mg/dL. The median of triglycerides was 125.0 (85.0−160.0) mg/dL.

Regarding echocardiographic variables, the mean left ventricular ejection fraction (LVEF) was 54.78%, and it was possible to observe segmental motility abnormalities in 25 (49%) patients. Coronary angiography revealed normal coronary arteries in 45 (88.2%) patients and non-obstructive CAD in 5 (11.8%). Spontaneous coronary artery dissection was identified by OCT in 1 patient.

At hospital discharge, 37 (72.5%) patients were treated with aspirin, 30 (58.8%) with P2Y12-receptor inhibitors, 46 (90.2%) with statins. Of the 51 patients admitted to the study, 26 (51.0%) patients were prescribed dual antiplatelet therapy, i.e. aspirin and P2Y12-receptor inhibitor, and 25 (49.0%) patients were prescribed dual antiplatelet therapy plus statins. Anticoagulants were prescribed to 6 (11.8%) patients, 29 (56.9%) patients were prescribed angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor

Table 1 Clinical and demographic characterization of patients diagnosed with MINOCA.

	n (%)	M (SD)	Min–Max
Age		61.06 (13.83)	[30–85]
Female	27 (52.9%)		
BMI		27.15 (4.04)	[18.22–37.56]
CV risk factors			
Smoking			
Current smoker	9 (17.6%)		
Former smoker	11 (21.6%)		
Diabetes mellitus			
Type 1 diabetes	1 (2.0%)		
Type 2 diabetes	5 (9.8%)		
Hypertension	25 (49.0%)		
Dyslipidemia	30 (58.8%)		
Past medical history			
AMI	3 (5.9%)		
Stroke	3 (5.9%)		
Depression	8 (15.7%)		
HF	1 (2.0%)		
Valvular heart disease	3 (5.9%)		
CKF	0 (0.0%)		
PAD	0 (0.0%)		
Hypothyroidism	1 (2.0%)		
Family history of early CV disease	7 (13.7%)		

blocker (ARB), 35 (68.6%) were prescribed beta-blockers (BB) and, 11 (21.6%) were prescribed calcium channel blockers (CCB).

Table 2 summarizes the clinical characteristics of patients diagnosed with MINOCA during hospitalization.

Prognosis 12 months after hospital admission

No patient deaths were reported up to 12 months after hospital admission. After 12 months, there were 4 (7.8%) patients with HF and 3 (5.9%) patients with arrhythmias, none of whom required re-hospitalization.

Diagnostic yield of CMR in patients admitted for suspected AMI without obstructive CAD

Of the 163 patients who underwent CMR within 180 days of hospital admission, it allowed the diagnosis of 121 (74.3%) patients: 51 (31.3%) patients diagnosed with MINOCA, 37 (22.7%) patients with Takotsubo syndrome and 33 (20.2%) patients with myocarditis. In 42 (25.8%) patients, CMR was normal, and therefore, no diagnosis was established (Plate 1).

Figure 2 shows the time distribution, in days, between the date of hospital admission and the performance of CMR, with most patients performing this exam in the first 14 days. The frequency distribution when stratified into 3 time intervals was: up to 14 days (n=83, 50.9%), 15–30 days (n=27, 16.6%), and more than 30 days (n=53, 32.5%).

The median time from hospital admission to CMR in all 4 groups was 14 days (5.0–37.0). The median time from hospital admission to CMR of patients without a diagnosis (Mdn=26.0) was significantly higher (U=1995.0, p=0.038, r=0.22) compared with patients who obtained a diagnosis (Mdn=12.0), which included patients diagnosed with MINOCA, Takotsubo syndrome, and myocarditis.

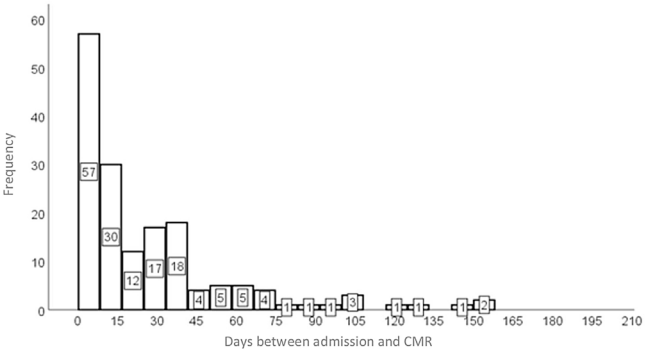

Figure 2 Distribution of time between the date of hospital admission and the performance of CMR.

Table 3 shows a comparative analysis of time from admission to CMR between the groups with and without diagnosis. When stratifying the time to CMR, we observed that only 15 (35.7%) patients without diagnosis underwent CMR in the first 14 days, compared with patients with diagnosis (56.2%). In patients without diagnosis, the percentage of CMR performed after 14 days was higher (64.3%), compared to patients with diagnosis, where the percentage was 43.8%. The association between the undiagnosed and diagnosed groups and the stratified time until CMR was statistically significant ($\chi^2(1)=5.24$, p=0.022, $\varphi=0.18$).

Table 2 Clinical characterization during hospitalization of patients diagnosed with MINOCA.

	n (%)	M (SD) [Min–Max]	Mdn (Q1–Q3) [Min–Max]
Symptoms at admission			
Chest pain	49 (96.1%)		
Palpitations	3 (5.9%)		
Syncope	1 (2.0%)		
Dyspnea	6 (11.8%)		
Vomiting	3 (5.9%)		
Diarrhea	2 (3.9%)		
Fever	2 (3.9%)		
Laboratory analysis			
Troponin peak I			8.9 (3.6–18.2) [0.9–53.2]
Total cholesterol		184.63 (40.16) [88–288]	
HDL cholesterol		48.67 (14.27) [24–98]	
LDL cholesterol		117.45 (36.13) [40–222]	
Triglycerides			125.0 (85.0–160.0) [42–377]
Coronary heart disease			
0%	45 (88.2%)		
1–49%	6 (11.8%)		
Spontaneous coronary dissection	1 (2.0%)		
Echocardiography			
LVEF		54.78 (9.22) [20–74]	
LV wall motion abnormality	25 (49.0%)		
Outpatient therapy			
Aspirin	37 (72.5%)		
P2Y12-receptor inhibitors	30 (58.8%)		
Statins	46 (90.2%)		
Aspirin and P2Y12-receptor inhibitors	26 (51.0%)		
Aspirin, P2Y12-receptor inhibitors and statins	25 (49.0%)		
Anticoagulants	6 (11.8%)		
ACE inhibitors	29 (56.9%)		
Beta-blockers	35 (68.6%)		
Calcium channel blockers	11 (21.6%)		

Table 3 Comparison of time from admission to CMR between the groups with diagnosis and without diagnosis.

	Undiagnosed	Diagnose established	Chi-square test
Up to 14 days	15 (35.7%)	68 (56.2%)	$\chi^2(1)=5.24$
<14 days	27 (64.3%)	53 (43.8%)	p=0.022*, φ=0.18

* p<0.05.

Prognosis at discharge and 12 months after hospital admission

Table 4 shows the mortality at discharge and 12 months after admission and the comparative analysis of prognosis at 12 months between the groups diagnosed with MINOCA, Takotsubo syndrome, and myocarditis. No deaths were observed at the date of discharge and at 12 months after hospital admission. No differences were noted in the prognosis at 12 months between the 3 groups (p=0.398).

Discussion

In this study, the main goal was to characterize patients diagnosed with MINOCA with regard to its prevalence, clinical, laboratory, echocardiographic and imaging characteristics and prognosis at discharge. A higher prevalence of female patients and a lower prevalence of CV risk factors were noted. The diagnosis of MINOCA was associated with good prognosis and low mortality during the 12 months after hospital admission. However, in comparison with other

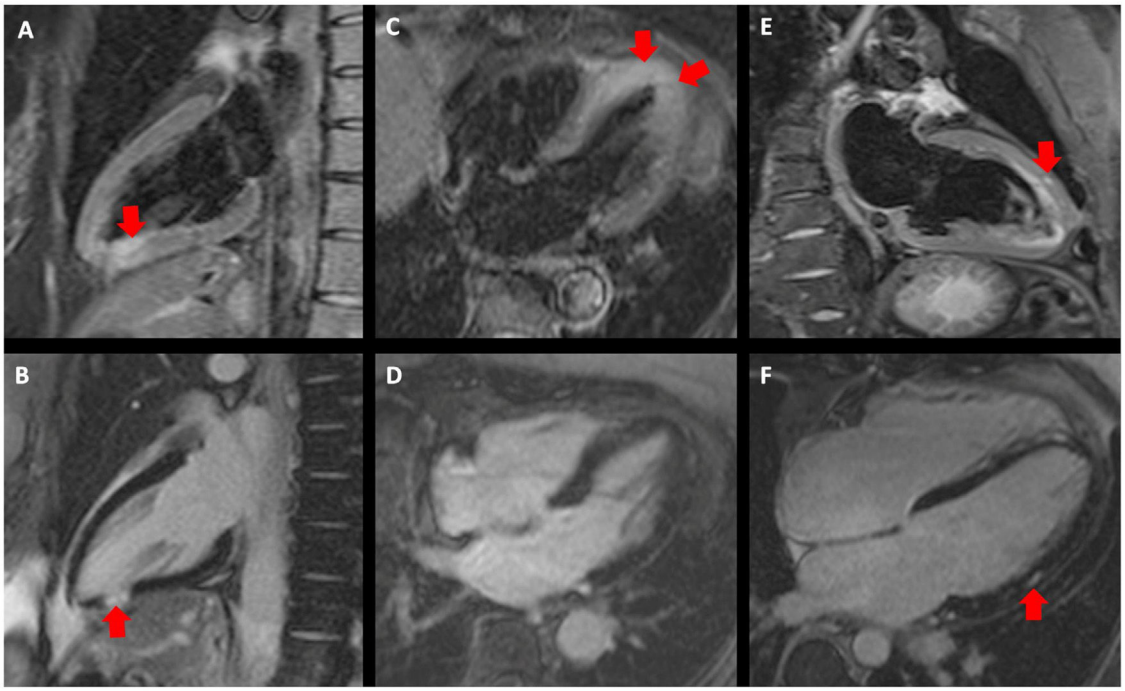

Plate 1 Examples of CMR findings in each subgroup: MINOCA: (A) T2 STIR 2 chamber view showing sub-endocardial edema (arrow) and (B) 2 chamber view showing transmural late gadolinium enhancement (LGE) in the inferior wall (arrow); Takotsubo (C and D): T2 STIR showing apical edema in 4 chamber view (arrows) without LGE; myocarditis (E and F): T2 stir 2 chamber view showing small intramyocardial LGE in the anterior wall (arrow) and 4 chamber view showing intramyocardial edema in the anterolateral wall (arrow).

Table 4 Mortality at discharge and 12 months after admission and comparative analysis of prognosis at 12 months after admission between the group diagnosed with MINOCA, Takotsubo syndrome and myocarditis.

	MINOCA		Takotsubo syndrome		Myocarditis		Fisher's test
Mortality at discharge	0	0.0%	0	0.0%	0	0.0%	
Mortality at 12 months	0	0.0%	0	0.0%	0	0.0%	
Prognosis at 12 months							p=0.398
Non-fatal AMI	0	0.0%	0	0.0%	0	0.0%	
HF	4	7.8%	2	5.4%	1	3.0%	
Arrhythmias	3	5.9%	0	0.0%	0	0.0%	
Stroke	0	0.0%	0	0.0%	0	0.0%	
Re-hospitalization for HF	0	0.0%	1	2.7%	0	0.0%	

differential diagnoses, such as myocarditis or Takotsubo syndrome, it was associated with a greater propensity for developing HF at 12 months. On the other hand, this study analyzed the diagnostic profitability of CMR in patients admitted for suspected AMI without obstructive CAD. In these cases, CMR could establish the diagnosis in 3 of 4 patients, and its diagnostic yield was higher in the first 14 days after admission.

Most patients diagnosed with MINOCA were female, with a mean age of 61.06 years. Half of the patients reported hypertension and more than half (58.8%) reported dyslipidemia. The presence of diabetes mellitus (11.8%) and smoking (17.6%) were less prevalent. Overall, the clinical data are in agreement with the clinical characteristics commonly described in the literature, which state that more than 50% of patients diagnosed with MINOCA are female and have a lower prevalence of previous CV risk factors, except for hypertension, which is more prevalent among patients diagnosed with MINOCA.[17,22–25] However, dyslipidemia was more prevalent than described in most studies. In this study, the mean age of the patients with MINOCA may have influenced this, since in most literature, patients with MINOCA had a lower mean age than in our study, which may have contributed to a higher prevalence of dyslipidemia in our sample.[24–28]

Regarding the therapy instituted after discharge, statins were the most prescribed therapy (90.2%), followed by aspirin (72.5%), BB (68.6%) and, then ACEI/ARB (56.9%). Dual antiplatelet therapy plus statins was prescribed in almost half of the patients diagnosed with MINOCA. According to the literature, treatment with statins or ACEI/ARB has been shown to be associated with lower mortality.[8,18] In clinical

practice, the continued use of dual antiplatelet therapy, which is usual in patients with AMI with obstructive CAD, may be associated with the lack of specific guidelines for the therapeutic approach of patients with MINOCA and the scarcity of published randomized clinical trials, leading clinicians to use the guidelines recommended for AMI with obstructive CAD patients.[8]

In this study, CMR enabled the diagnosis in 74.2% of the patients admitted for suspected AMI, with MINOCA being the most prevalent diagnosis (31.3%). According to the existing literature, the CMR diagnosis rate ranges from 30 to 90%.[22,28,29] Of note, in a recent multicenter prospective study, the diagnosis rate was 77%, like this study.[26] The variation in the diagnostic yield of CMR in the literature may be explained by different criteria in sample selection, the waiting time for CMR, or even the CMR imaging protocol used.[2,12,29] However, in most studies, myocarditis is the most prevalent pathology in CMR, contrary to our results.[10,22,26] The higher prevalence of MINOCA may be related to the higher mean age of patients (59.2 years) included in our study compared to the mean age (50–54 years) of most published studies and a higher prevalence of CV risk factors observed in our study.[22,25,26,28,29]

This study also revealed that the median time from hospital admission to CMR was significantly shorter in the groups that obtained a diagnosis compared with the undiagnosed group, with a significant increase in diagnosis when CMR was performed up to 14 days after hospital admission. Generally, several studies show the benefit of performing CMR within 7–14 days of symptom presentation, as it ensures the detection of transient and reversible myocardial changes, which usually resolve after a few weeks, particularly in cases of myocarditis and Takotsubo syndrome, thus increasing the effective rate of diagnosis.[8,12,17,23,26] Our study reinforces the importance of performing CMR and as early as possible after admission, thus enabling a higher diagnostic rate and facilitating the prescription of therapy specific to the underlying etiology of the acute event.

Of note, 25% of patients did not obtain any diagnosis after CMR. This is consistent with the existing literature, which shows that CMR results in 15–30% of patients are normal and a diagnosis cannot be ascertained.[9,10,12,26] However, a recent study showed that the combined use of CMR and OCT identified the underlying etiology in 85% of patients, having superior results than the two imaging tests used alone (44% for OCT and 74% for CMR), thus reinforcing the need to include a multimodality approach in the management of patients with suspected MINOCA.[10,13,29] Normal CMR result may be explained by diffuse myocardial injury, microvascular dysfunction or coronary spasm that may be undetectable on CMR, requiring other more sensitive imaging or functional tests for the mentioned etiologies.[26]

Regarding the prognosis, there were no deaths during hospitalization or after 12 months of admission in patients diagnosed with MINOCA. However, several studies have shown that 12-month mortality was 2–4.7% in patients diagnosed with MINOCA.[12,23,30] Additionally, a recently published large systematic review including 3624 patients from a total of 26 studies revealed that CMR-confirmed diagnosis of MINOCA was associated with an increased risk of MACE at follow-up (pooled OR 2.4).[31] One of the factors for this divergence of results may be related to our sample selection, where we excluded patients with ST-segment elevation on ECG, considered by several studies as a predictor of mortality, and there may have been a selection of low-risk patients.[22,26,28] Currently, researchers and clinicians recognize that the mortality and morbidity of this condition is not benign, and randomized clinical trials are essential for creating a consensus on the diagnostic and therapeutic approach in patients diagnosed with MINOCA, with important prognostic implications.[8]

Looking to assess the prognosis at 12 months after hospital admission, we compared the groups with diagnoses of MINOCA, Takotsubo syndrome, and myocarditis with respect to mortality, development of HF, arrhythmias, non-fatal AMS, and stroke. No differences were found between the groups. However, a higher rate of HF and arrhythmias was found in the group diagnosed with MINOCA. In the largest retrospective study to date, Dastidar et al. showed that patients with Takotsubo syndrome had a significantly worst prognosis, followed by MINOCA (4%), myocarditis (2%) and undiagnosed patients (2%), with a mean follow-up of 3.5 years.[22] The fact that our follow-up was 12 months in patients without ST-segment elevation, while most studies have a longer follow-up period and included patients with and without ST-segment elevation, may be one of the possible factors to consider.

Limitations

The main limitation of this study is that it was a retrospective study since all data had to rely on existing medical records.

This study focused on clinical data records from Braga Hospital, making it difficult to generalize the findings, which might have greater impact in a prospective multicenter study.

Another limitation to be considered is related to the sample selection criteria for our study, where we included only patients without ST-segment elevation on ECG. As such, our results cannot be generalized to all patients diagnosed with MINOCA.

Conclusion

The diagnosis of MINOCA is complex, since there are numerous underlying pathophysiological mechanisms; a multimodal approach should be considered in all patients.

Through this study we were able to establish that CMR plays a key role in the diagnostic approach for these patients, since it can pinpoint the diagnosis in three out of four patients admitted for suspected AMI, in whom angiography demonstrates the absence of obstructive CAD and its diagnostic yield is higher in the first 14 days after admission. In our study, the diagnosis of MINOCA was more prevalent in females, and associated with fewer traditional CV risk factors. In the limited 12-month follow-up, MINOCA initial diagnosis was associated with good prognosis and low mortality. However, a confirmed diagnosis of MINOCA via CMR was associated with a greater propensity to develop HF.

Funding

No funding sources were used in this research.

Conflicts of interest

The authors have no potential conflicts of interest to disclose.

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