

Value of Cardiac Magnetic Resonance in the Diagnosis and Prognosis of Patients with Acute Myocardial Infarction with Nonobstructive Coronary Artery Disease (MINOCA)

Valor da Ressonância Magnética Cardíaca no Diagnóstico e no Prognóstico de Pacientes com Infarto Agudo do Miocárdio sem Doença Arterial Coronariana Obstrutiva (MINOCA)

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Abstract

Background: Myocardial infarction is one of the major causes of morbidity and mortality worldwide and 13.2% of patients with acute coronary syndrome have normal or unobstructed coronary arteries, called MINOCA (Myocardial Infarction with Non-Obstructive Coronary Artery). Cardiac magnetic resonance (CMR) is the gold standard for investigating the etiology of acute coronary syndrome. Although MINOCA has a more benign evolution than myocardial infarction due to coronary obstruction, its prognostic factors are not completely elucidated.

Objective: To evaluate prognosis, predictive factors and describe the incidence of major adverse cardiovascular events in patients with MINOCA.

Methods: Prospective cohort through data collection of patients admitted to the emergency department of a tertiary hospital, diagnosed with MINOCA from 2012 to 2019. The mean follow-up was 45 months, the outcomes considered were: death, rehospitalization due to cardiac causes, recurrence of chest pain, myocardial revascularization (MACE).

Results: Of the 179 patients, 52% were male, with a mean standard deviation age of 57.3 ± 15.5 years. A MACE rate of 17.9% was observed during a mean follow-up of 45 ± 21 months. Mortality at the end of follow-up was 3.8%. In the multivariate analysis using the Cox regression model, patients with normal CMR was shown to be a predictor of good prognosis (HR 0.09; 95% CI 0.01 – 0.88; $p = 0.04$). The Kaplan-Meier curve showed a significant difference (Log Rank $\chi^2 = 9.83$ $p = 0.02$) in the prediction of free MACE.

Conclusion: Normal CMR was an independent predictor of good prognosis in this sample and could be useful in the risk stratification of patients with MINOCA.

Keywords: Acute Coronary Syndrome; Magnetic Resonance Imaging; Prognosis.

Resumo

Fundamento: O infarto do miocárdio é uma das principais causas de morbimortalidade no mundo, e 13,2% dos pacientes com síndrome coronariana aguda apresentam coronárias sem obstrução significativa, denominada MINOCA (do inglês Myocardial Infarction with Non-Obstructive Coronary Artery, Infarto do Miocárdio sem Doença Coronariana Obstrutiva). Apesar do MINOCA ter evolução mais favorável que o infarto do miocárdio por obstrução coronariana, seu prognóstico não é benigno. A ressonância magnética cardíaca é o exame que apresenta importância no diagnóstico das diversas causas de MINOCA, e seu valor prognóstico não está completamente elucidado.

Objetivo: Avaliar o valor prognóstico da ressonância magnética cardíaca na detecção de eventos adversos maiores em pacientes com MINOCA.

Métodos: Coorte prospectiva por meio de coleta de dados de pacientes admitidos na urgência de pacientes com hospital terciário, diagnosticados com MINOCA, no período de 2012 a 2019.

Resultados: Foram avaliados 179 pacientes com seguimento médio de 45 ± 21 meses, sendo 52% do sexo masculino, com idade média de

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57,3 ± 15,5 anos. Observou-se incidência de eventos adversos maiores de 17,9%. A taxa de mortalidade ao final do acompanhamento foi de 3,8%. Na análise multivariada, apenas a ressonância magnética cardíaca com resultado normal se mostrou como preditor independente de bom prognóstico (hazard ratio: 0,09; intervalo de confiança de 95% 0,01-0,88; $p = 0,04$), com curva de Kaplan-Meier apresentando diferença significativa (log-rank $\chi^2 = 9,83$; $p = 0,02$) na predição de eventos adversos maiores.

Conclusão: A ressonância magnética cardíaca normal mostrou-se como variável independente de bom prognóstico nessa população, podendo ser útil na estratificação de risco de pacientes com MINOCA.

Palavras-chave: Síndrome Coronariana Aguda; Imagem por Ressonância Magnética; Prognóstico.

Introduction

Acute myocardial infarction (AMI) is a main cause of morbidity and mortality worldwide.¹ Of the affected patients, about 5–15% present with clinical and laboratory findings suggestive of AMI (chest pain, changes in plasma troponin levels, and/or electrocardiographic abnormalities) without significant coronary obstruction on coronary angiography, which is known as myocardial infarction with nonobstructive coronary artery (MINOCA).^{2,3}

The pathophysiological mechanisms involved in the diagnosis of MINOCA are complex and heterogeneous since it has several causes related or unrelated to coronary atherosclerosis, and the identification of the underlying etiology is important in its clinical management. Although the prognosis of patients with MINOCA is more favorable than that of patients with AMI associated with obstructive coronary artery disease (CAD), a recent study demonstrated an annual mortality rate of 3.5%.⁴

According to the 2017 European Society of Cardiology guidelines for the management of acute myocardial infarction, MINOCA is now recognized as an entity distinct from AMI that requires special attention. The therapeutic approach is identified through a safe and accurate differential diagnosis of AMI and its underlying causes.³

Cardiac magnetic resonance (CMR) represents a particularly useful tool in the identification of the causes of MINOCA, such as AMI with spontaneous recanalization/embolism, acute myocarditis, stress cardiomyopathy (Takotsubo), or other cardiomyopathies, and is useful for stratifying risk factors for these patients.⁵⁻⁷

This study aimed to evaluate the role of CMR in the diagnostic and prognostic evaluation of a cohort of MINOCA patients.

Methods

Patients diagnosed with MINOCA^{2,3} were prospectively selected from January 2012 to July 2019. All patients were admitted with clinical AMI (chest pain and/or electrocardiographic changes suggestive of myocardial ischemia and elevated troponin T) and underwent urgent angiography, which showed coronary arteries without significant obstruction, and subsequently underwent CMR for diagnostic definition.

The study exclusion criteria were age <18 years; a previous history of obstructive CAD, AMI, or myocardial revascularization; or unwillingness to participate in

the study for any reason or failed to leave any contact information in hospital records, preventing them from being found for follow-up.

Upon admission, each patient completed a standardized data collection form on the presence of cardiac risk factors. Systemic arterial hypertension was defined as a documented history of high blood pressure or treatment with antihypertensive drugs. The presence of diabetes mellitus was defined as a previous diagnosis of diabetes and/or the use of insulin or oral hypoglycemic agents. Dyslipidemia was defined as a previous history of dyslipidemia or current treatment with lipid-lowering drugs. Smoking was considered the current smoking habit or smoking cessation within three months of the exam.

Adverse clinical outcomes were obtained through telephone interviews and classified as the occurrence of death of cardiac origin; myocardial infarction; unstable angina associated with hospitalization and revascularization; or hospitalization for cardiac reasons.

CMR was performed using a 1.5-T device (MAGNETOM Avanto, Siemens Healthineers, Erlangen, Germany). A comprehensive protocol included the study of ventricular function and the evaluation of edema and myocardial fibrosis. The presence of myocardial edema was analyzed using T2-weighted short-axis images with a short tau inversion recovery (STIR) sequence. Myocardial edema was considered present when the ratio between the signal intensity of the myocardium and the mean signal intensity of the skeletal muscle was >2 in T2-STIR images. Short-axis cine-CMR (steady-state free precession) was used to measure the left ventricular (LV) ejection fraction. The most basal short-axis cut was positioned just after the atrioventricular ring, and all subsequent respiratory pauses at maximum expiration were acquired with 8-mm thickness and 2-mm spacing between the other cuts up to the LV apex. A long- and short-axis gradient-echo sequence with inversion recovery (delayed enhancement technique) was performed 10–20 minutes after a gadolinium injection of 0.1–0.2 mmol/kg (Dotarem®, Guerbet) to identify myocardial fibrosis. Myocardial segments were evaluated in 17 segments. LV measurement and calculations were performed on a dedicated CMR workstation using specific software.

The patients were grouped into four categories based on CMR characteristics: normal (Figure 1A), ischemic (infarction; Figure 1B), myocarditis (Figure 1C), and cardiomyopathy (Figure 1D). The normal study corresponded to a heart without the evidence of contractile changes (except

desynchrony secondary to the left bundle branch block) and no edema or myocardial fibrosis. Myocarditis was diagnosed based on T2-STIR sequence changes and the detection of myocardial edema and the late epicardial or medium-myocardial enhancement pattern, according to the Lake Louise criteria.⁸ The ischemic pattern (infarction) was diagnosed based on the presence of the late enhancement of a subendocardial or transmural pattern in the coronary territory. Takotsubo cardiomyopathy was diagnosed based on T2-STIR images detecting myocardial edema and medium-apical contractile changes without the evidence of significant myocardial fibrosis due to late enhancement. Dilated, hypertrophic, and restrictive cardiopathies were detected based on the specific characteristics of each pathology and grouped under cardiomyopathy together with Takotsubo cardiomyopathy. The extent of delayed enhancement and myocardial edema was quantified by the calculation of the number of involved segments.

The data were encoded, entered into a Microsoft Excel™ database, and subsequently analyzed using the Statistical Package for Social Science software version 20.0 (SPSS Inc., Chicago, IL, USA), with values of $p < 0.05$ considered statistically significant.

The study groups were compared using bilateral hypothesis tests with a significance level of 5% ($\alpha = 0.05$).

The Cox proportional-hazards model was used to estimate the survival of MINOCA patients. The hazard ratio was calculated with a 95% confidence interval as an estimated risk associated with a selected variable. The multivariate analysis included all variables selected in the univariate analysis. The survival analysis is expressed using the Kaplan–Meier plot, and the p values of the curves were compared using the log-rank test.

This study was approved by the Ethics Committee of the Health and Human Ecology College (no. CAAE66664017.0.0000.5101).

Results

The present study selected 179 patients, of whom 93 (52%) were male, with a mean age of 57.3 ± 15.5 years. Table 1 summarizes the baseline characteristics of the study population. Systemic arterial hypertension was the most common comorbidity (44% of patients). The median follow-up was 45 ± 21 months, with 13% of patients lost to follow-up. During follow-up, 28 (17.9%) adverse events occurred

Table 1 - Baseline characteristics of the studied population with myocardial infarction with nonobstructive coronary artery.

Characteristics	
Male	93 (52)
Age, years	57.3 ± 15.5
Dyslipidemia	52 (28.6)
Smoking	19 (10.4)
Hypertension	80 (44)
Diabetes	22 (12.1)
LVEF	58.1 ± 14.1
SBP, mmHg	126.7 ± 28.3
HR, bpm	75.9 ± 19.3
Follow-up, months	45 ± 21
MACE	28 (17.9)
Final diagnosis	
Normal	62 (35)
Ischemic	61 (34)
Cardiomyopathy	27 (15)
Myocarditis	29 (16)

Values are expressed as n (%) or mean \pm standard deviation. HR, heart rate; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; SBP, systemic blood pressure.

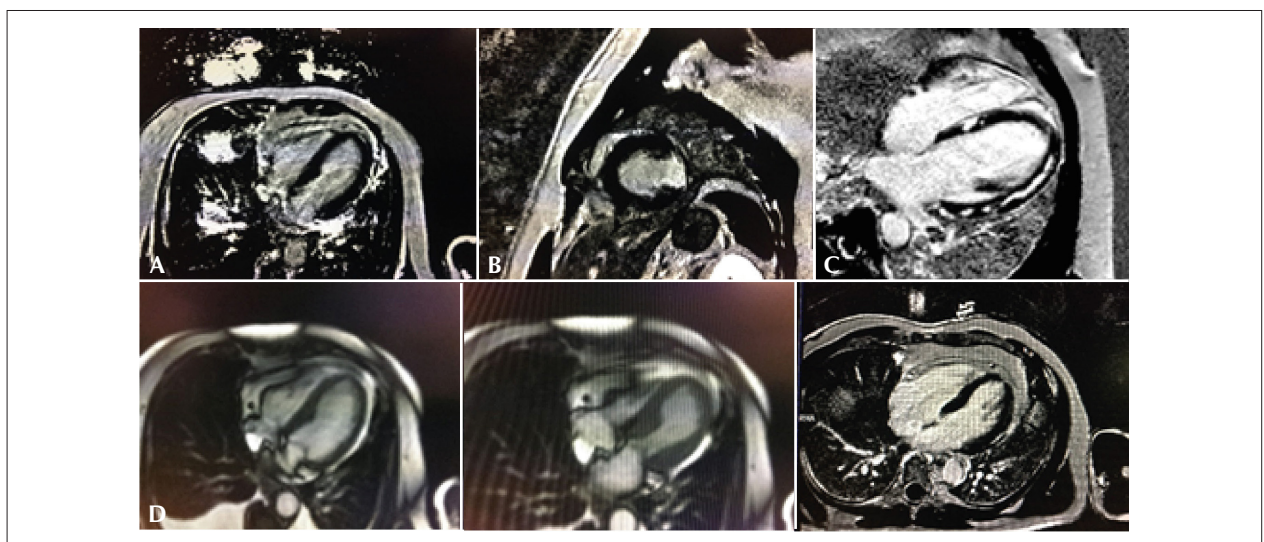


Figure 1 – Cardiac magnetic resonance images of patients with normal study findings using the delayed enhancement technique (1A); transmural infarction in the lateral wall (1B), myocarditis pattern (1C), and Takotsubo cardiomyopathy showing medium-apical contractile deficit and no changes using the delayed enhancement technique (1D).

(selecting only adverse clinical outcomes occurring in the minimum follow-up period of three months), with 12 patients presenting with acute coronary syndrome (ACS), seven deaths, five with myocardial revascularization, and four owing to readmission for cardiac reasons. The mortality rate at the end of the follow-up period was 3.8%. Table 2 shows the univariate analysis of clinical characteristics and CMR to predict adverse events. Table 3 shows the independent predictors of adverse cardiac events, obtained by multivariate analysis using the Cox regression model. Statistical analyses considered normal CMR examination findings as an independent and significant predictor of a good prognosis.

Figure 2 illustrates the different patterns of CMR diagnosis in this cohort. The role of CMR in event-free survival was analyzed to compare normal examination results in relation to other diagnoses (Figure 3A: log-rank $\chi^2 = 9.83$; $p = 0.02$) and the normal and changed examination results (ischemic and nonischemic; Figure 3B: log-rank $\chi^2 = 6.83$; $p = 0.009$).

Discussion

The present study demonstrated important aspects in the evaluation of MINOCA patients, such as: CMR enabling a diagnosis in 65% of the evaluated cases; an adverse event rate of 17.9% and a mortality rate of 3.8% in a mean follow-up of 3.8 years; and the presence of normal CMR study findings demonstrated an excellent prognosis compared with other diagnoses on multivariate analysis.

The population group most affected by ACS with nonobstructive coronary arteries more commonly includes women and young people without dyslipidemia.⁹ An observational study in Sweden using data from the Swedeheart registry showed a mean age of 69.1 years and that 59.1% of the patients were women.¹⁰ A study conducted in China reported that patients diagnosed with MINOCA included a younger sample (aged 61.94 ± 13.07 years) and that 53%

were male, 52% had arterial hypertension, 40% had a history of smoking, 20% had dyslipidemia, and 11% had diabetes mellitus.¹¹ Dastidar et al.¹² studied a sample of MINOCA patients, of whom 52% were male. The present study sample included 52% male patients, and the mean patient age was 57.3 ± 15.5 years, corroborating the findings of Dastidar et al.¹² and Abdu et al.¹¹ Regarding risk factors, this study relatively corroborates the frequency of arterial hypertension as a comorbidity reported by Abdu et al.¹¹; however, the smoking rate was higher than that in the present study.

Although patients with MINOCA have a better prognosis than those with obstructive AMI⁶, the prognosis is not benign. Recent studies indicated that up to 24% of MINOCA patients present adverse events within approximately four years.¹³ A North American multicenter cohort study of data from the National Cardiovascular Data Registry[®] reported a 19% occurrence rate of adverse events beyond one year.¹⁴ The

Table 3 - Multivariate analysis using the Cox regression model to predict outcomes.

Variable	HR	95% CI	p value
Normal CMR	0.09	0.01-0.88	0.04
Ischemia on CMR	1.04	0.25-3.96	0.99
Cardiomyopathy on CMR	1.07	0.49-2.29	0.86
Diabetes	1.22	0.28-5.34	0.79
Age	1.03	0.98-1.05	0.07
SBP	1.01	0.99-1.03	0.08
Heart rate	1.02	0.98-1.04	0.29
Creatinine	1.19	0.76-1.87	0.43
LVEF	0.98	0.96-1.01	0.37
Dyslipidemia	1.62	0.72-3.67	0.24

CI, confidence interval; CMR, cardiac magnetic resonance; HR, hazard ratio; LVEF, left ventricular ejection fraction; SBP, systemic blood pressure.

Table 2 - Univariate analysis of adverse event determinants in the population with myocardial infarction with nonobstructive coronary artery.

Variable	Patients with events (n = 28)	Without events (n = 128)	Hazard ratio (95% CI)	p value
Age	61.7 ± 10.4	55.2 ± 15.9	1.02 (0.99-1.05)	0.16
Male sex	13 (54)	53 (49)	0.86 (0.38-1.93)	0.71
Smoking	3 (15)	15 (16)	1.02 (0.59-1.94)	0.79
SAH	13 (65)	59 (48)	1.19 (0.81-2.19)	0.64
Diabetes mellitus	5 (25)	17 (14)	1.49 (0.92-6.10)	0.08
Dyslipidemia	09 (40)	60 (32)	1.44 (0.94-2.20)	0.09
SBP, mmHg	129.8 ± 42.3	125.8 ± 25.5	1.01 (0.99-1.01)	0.09
HR, bpm	71.9 ± 21.7	74.3 ± 14.7	1.01 (0.99-1.02)	0.07
Creatinine, mg/dL	0.92 ± 0.23	0.89 ± 0.27	5.12 (0.84-31.37)	0.28
LVEF, %	52.1 ± 16.2	60.0 ± 12.5	0.98 (0.95-1.001)	0.06
Normal CMR	1 (4)	47 (37)	0.11 (0.01-0.82)	0.03
Ischemia on CMR	17 (61)	39 (30)	1.80 (0.83-3.91)	0.14
Cardiomyopathy on CMR	7 (25)	18 (14)	2.26 (0.94-5.43)	0.08
Myocarditis on CMR	3 (11)	24 (19)	1.24 (0.68-2.29)	0.48
Late highlighting	1.5±2.4	1.1± 1.6	1.15 (0.90-1.51)	0.24

Values are shown as n (%), mean ± standard deviation, or median (95% CI). CI, confidence interval; CMR, cardiac magnetic resonance; HR, heart rate; LVEF, left ventricular ejection fraction; SAH, systemic arterial hypertension; SBP, systemic blood pressure.

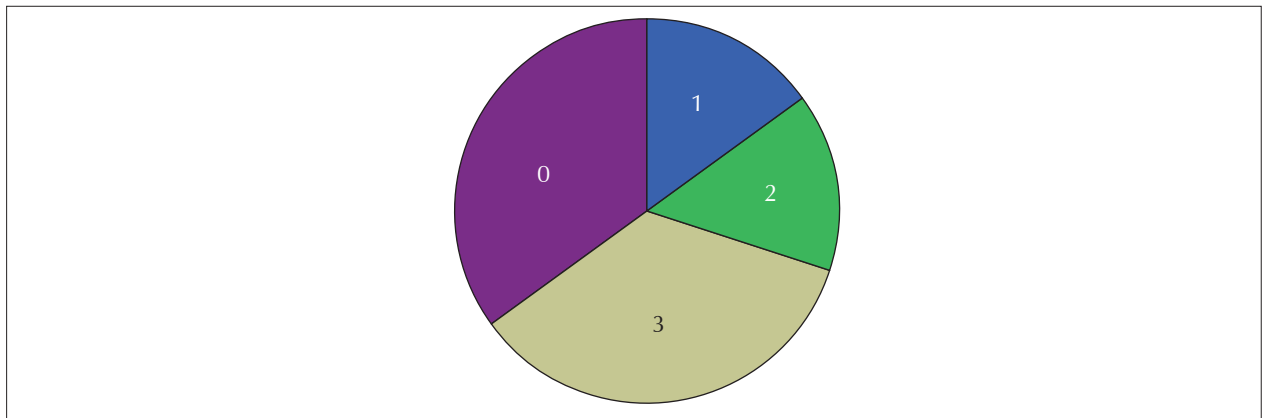


Figure 2 – Frequency of cardiac magnetic resonance diagnoses. Normal diagnosis (0: 35%), myocarditis (1: 16%), cardiomyopathy (2: 15%), and ischemia (3: 34%).

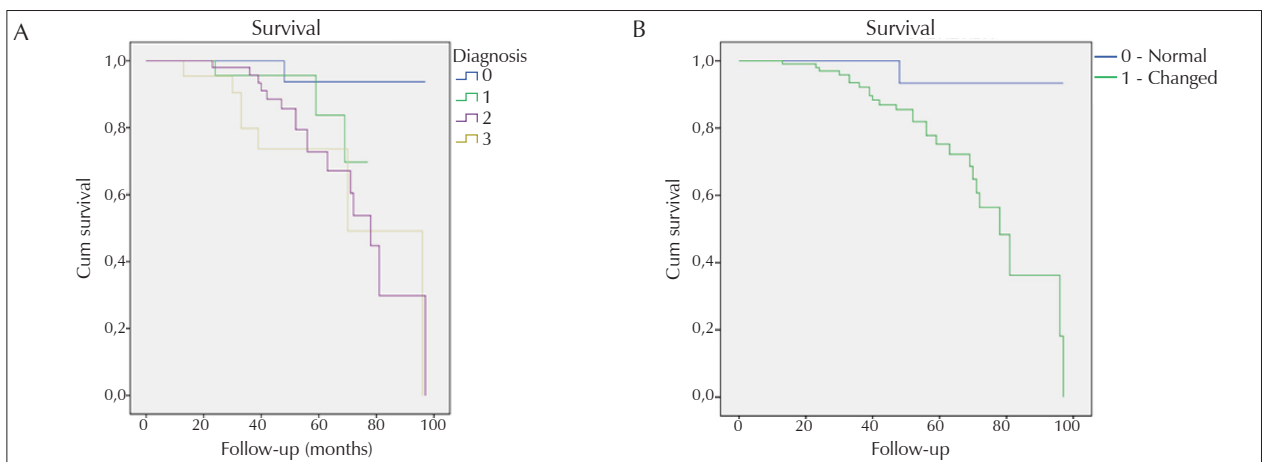


Figure 3 – Event-free survival of patients with normal diagnosis (0), myocarditis (1), cardiomyopathy (2), and ischemia (3) on cardiac magnetic resonance (log-rank $\chi^2 = 9.83$, $p = 0.02$) (A) and between patients with normal (0) and a changed diagnosis (1: ischemic and nonischemic) (log-rank $\chi^2 = 6.83$, $p = 0.009$) (B).

present study had a mean follow-up period of 3.8 years and a 17.9% occurrence rate of adverse events.

The present study had a mortality rate of 3.8% due to cardiovascular disease over a mean follow-up period of 3.8 years. A Canadian study conducted between 2002 and 2014 by Bainey et al.⁵ showed a five-year mortality of 11% for MINOCA and 16% for obstructive AMI-CAD. Choo et al.¹⁵ reported a 9.1% incidence of death in patients with MINOCA. Egger et al.¹⁶ obtained a 7% general mortality rate from all causes over a follow-up of 3.8 years. According to Nordenskjöld et al.,¹⁰ the mortality rate due to reinfarction in patients with MINOCA during a mean follow-up of 38 months was 13%. Dastidar et al.¹² reported a mortality rate of 5.7% in a mean follow-up of 3.5 years, with a worse prognosis in the group with cardiomyopathy. These data demonstrate that patients affected by MINOCA present greater morbidity and mortality rates than does the general population, showing the importance of a proper diagnosis, therapy, and follow-up.

The data from the present study showed that CMR provided the etiological diagnosis in two-thirds of patients. Dastidar et al.¹² identified the cause of MINOCA in 74% of patients

(25% due to myocarditis, 25% due to AMI, and 25% due to cardiomyopathy), while the other 26% of patients had normal CMR findings. A study conducted in Stockholm by Collste et al.¹⁷ revealed that 45% of patients had normal CMR findings, with 22% presenting with Takotsubo cardiomyopathy, 19% with myocardial infarction, 7% with evidence of myocarditis, and the remaining (7%) with hypertrophic cardiomyopathy or no classification. Gerbaud et al.¹⁸ determined a diagnosis in 100 of 130 patients (76.9%) with MINOCA using CMR, with 23.1% presenting with normal study findings, 28.5% with AMI, 26.1% with myocarditis, 21.5% with Takotsubo cardiomyopathy, and 0.8% with hypertrophic cardiomyopathy. Pasupathy et al.⁶ observed an infarction pattern in 24% of patients, myocarditis in 33%, Takotsubo cardiomyopathy in 18%, and normal examination findings in 26% in a meta-analysis of 26 studies using CMR.

Interstudy differences can be predominantly related to the sample characteristics such as age, number of cases, and time to perform CMR. However, all studies demonstrated the diagnostic capacity of the method and its importance in the management of these patients, with some showing that the

initial diagnosis and management can be modified in 65% and 32% of cases, respectively.¹⁷⁻¹⁹ These findings reinforce the idea of using CMR as a standard propaedeutic in patients with MINOCA.

The limiting factors of the present study include its single-center design and small sample size. In addition, since it is a prospective study, the vulnerability of the methodology to follow-up bias should be considered. Obtaining information by telephone may also have influenced survival and adverse event data due to potential bias in the information provided by the patient or their relatives as well as the possibility of unknown deaths.

Conclusion

The present study demonstrated that patients with MINOCA can present with different diagnoses and have a heterogeneous but non-benign progression (adverse events and mortality) in a mean follow-up of four years, demonstrating the importance of the etiological definition

in the management of these patients. Normal CMR imaging findings was a predictor of a good prognosis in this cohort, showing the value of this test in the diagnostic evaluation and risk stratification of patients with MINOCA.

Authors' contributions

Research conception and design: Barros MVL, Ornelas CE, Siqueira MHA, Melo Júnior MA, Costa SMF, Rabello WA, and Pena HPM; data collection: Barros MVL, Siqueira MHA, Militão RC, Melo Júnior MA, Costa SMF, and Rabello WA; data analysis and interpretation: Barros MVL; statistical analysis: Barros MVL; manuscript writing: Barros MVL; and critical review of the manuscript for important intellectual content: Barros MVL, Ornelas CE, Siqueira MHA, Militão RC, and Pena HPM.

Conflict of interest

The authors have declared that they have no conflict of interest.

References

1. Writing Group Member, Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics- update: a report from the American Heart Association. *Circulation*. 2012;125(1):e2-e220. doi: <https://doi.org/10.1161/CIR.0b013e31823ac046>
2. Agewall S, Beltrame JF, Reynolds HR, Niessner A, Rosano G, Caforio AL, De Caterina R, Zimarino M, Roffi M, Kjeldsen K, Atar D, Kaski JC, Sechtem U, Tornvall P; WG on Cardiovascular Pharmacotherapy. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. *Eur Heart J*. 2017;38(3):143-153. doi: 10.1093/eurheartj/ehw149
3. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39(2):119-177. doi: 10.1093/eurheartj/ehx393
4. Tamis-Holland JE, Jneid H, Reynolds HR, Agewall S, Brilakis ES, Brown TM, Lerman A, Cushman M, Kumbhani DJ, Arslanian-Engoren C, Bolger AF, Beltrame JF; American Heart Association Interventional Cardiovascular Care Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Epidemiology and Prevention; and Council on Quality of Care and Outcomes Research. Contemporary Diagnosis and Management of Patients With Myocardial Infarction in the Absence of Obstructive Coronary Artery Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2019;139(18):e891-e908. doi: 10.1161/CIR.0000000000000670
5. Baine KR, Welsh RC, Alemayehu W, Westerhout CM, Traboulsi D, Anderson T, Brass N, Armstrong PW, Kaul P. 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*. 2018;264:12-17. doi: 10.1016/j.ijcard.2018.04.004
6. Pasupathy S, Air T, Dreyer RP, Tavella R, Beltrame JF. Systematic review of patients presenting with suspected myocardial infarction and nonobstructive coronary arteries. *Circulation*. 2015;131(10):861-70. doi: 10.1161/CIRCULATIONAHA.114.011201. Erratum in: *Circulation*. 2015;131(19):e475.
7. Vignisson ST, Gudmundsdottir JJ, Gudnason T, Danielsen R, Gardarsdottir M, Andersen K. [MINOCA in Iceland. Acute coronary syndrome in patients with normal or nonobstructive coronary arteries]. *Laeknabladid*. 2018 Mai;104(5):237-242. doi: 10.17992/lbl.2018.05.185. Icelandic.
8. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, White JA, Abdel-Aty H, Gutberlet M, Prasad S, Aletras A, Laissy JP, Paterson I, Filipchuk NG, Kumar A, Pauschinger M, Liu P; International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis. Cardiovascular magnetic resonance in myocarditis: A JACC White Paper. *J Am Coll Cardiol*. 2009;53(17):1475-87. doi: 10.1016/j.jacc.2009.02.007
9. Da Costa A, Isaaz K, Faure E, Mourot S, Cerisier A, Lamaud M. Clinical characteristics, aetiological factors and long-term prognosis of myocardial infarction with an absolutely normal coronary angiogram; a 3-year follow-up study of 91 patients. *Eur Heart J*. 2001;22(16):1459-65. doi: 10.1053/ehhj.2000.2553
10. Nordenskjöld AM, Lagerqvist B, Baron T, Jernberg T, Hadziosmanovic N, Reynolds HR, et al. Reinfarction in Patients with Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA): Coronary Findings and Prognosis. *Am J Med*. 2019 Mar;132(3):335-346. doi: 10.1016/j.amjmed.2018.10.007
11. Abdu FA, Liu L, Mohammed AQ, Luo Y, Xu S, Auckle R, et al. Myocardial infarction with non-obstructive coronary arteries (MINOCA) in Chinese patients: Clinical features, treatment and 1 year follow-up. *Int J Cardiol*. 2019 Jul 15;287:27-31. doi: 10.1016/j.ijcard.2019.02.036
12. Dastidar AG, Baritussio A, De Garate E, Drobni Z, Biglino G, Singhal P, et al. Prognostic Role of CMR and Conventional Risk Factors in Myocardial Infarction With Nonobstructed Coronary Arteries. *JACC Cardiovasc Imaging*. 2019;12(10):1973-1982. doi: 10.1016/j.jcmg.2018.12.023
13. Nordenskjöld AM, Baron T, Eggers KM, Jernberg T, Lindahl B. Predictors of adverse outcome in patients with myocardial infarction with non-obstructive coronary artery (MINOCA) disease. *Int J Cardiol*. 2018;261:18-23. doi: 10.1016/j.ijcard.2018.03.056
14. Dreyer RP, Tavella R, Curtis JP, Wang Y, Pauspathy S, Messenger J, et al. Myocardial infarction with non-obstructive coronary arteries as compared with myocardial infarction and obstructive coronary disease: outcomes in a Medicare population. *Eur Heart J*. 2020;41(7):870-8. doi: 10.1093/eurheartj/ehz403
15. Choo EH, Chang K, Lee KY, Lee D, Kim JG, Ahn Y, Kim YJ, Chae SC, Cho

- MC, Kim CJ, Kim HS, Jeong MH; KAMIR-NIH Investigators. Prognosis and Predictors of Mortality in Patients Suffering Myocardial Infarction With Non-Obstructive Coronary Arteries. *J Am Heart Assoc.* 2019;8(14):e011990. doi: 10.1161/JAHA.119.011990
16. Eggers KM, Hjort M, Baron T, Jernberg T, Nordenskjöld AM, Tornvall P, et al. Morbidity and cause-specific mortality in first-time myocardial infarction with nonobstructive coronary arteries. *J Intern Med.* 2019 Apr;285(4):419-428. doi: 10.1111/joim.12857
 17. Collste O, Sörensson P, Frick M, Agewall S, Daniel M, Henareh L, 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.* 2013 Feb;273(2):189-96. doi: 10.1111/j.1365-2796.2012.02567.x
 18. Gerbaud E, Harcaut E, Coste P, Erickson M, Lederlin M, Labèque JN, et al. Cardiac magnetic resonance imaging for the diagnosis of patients presenting with chest pain, raised troponin, and unobstructed coronary arteries. *Int J Cardiovasc Imaging.* 2012;28(4):783-94. doi: 10.1007/s10554-011-9879-1.
 19. Assomull RG, Lyne JC, Keenan N, Gulati A, Bunce NH, Davies SW, et al. The role of cardiovascular magnetic resonance in patients presenting with chest pain, raised troponin, and unobstructed coronary arteries. *Eur Heart J.* 2007;28(10):1242-9. doi: 10.1093/eurheartj/ehm113