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ORIGINAL ARTICLE

Observational Study

Risk of ventricular arrhythmia in patients with myocardial infarction and non-obstructive coronary arteries and normal ejection fraction

Loïc Bière, Marjorie Niro, Hervé Pouliquen, Jean-Baptiste Gourraud, Fabrice Prunier, Alain Furber, Vincent Probst

Loïc Bière, Marjorie Niro, Fabrice Prunier, Alain Furber, Laboratoire Cardioprotection, Institut MITOVASC, Remodelage et Thrombose, Service de Cardiologie, CHU d'Angers, F-49045 Angers, France

Hervé Pouliquen, Jean-Baptiste Gourraud, Vincent Probst, L'institut du Thorax, Service de Cardiologie, CHU de Nantes, F-44000 Nantes, France

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Correspondence to: Dr. Loïc Bière, Laboratoire Cardioprotection, Institut MITOVASC, Remodelage et Thrombose, Service de Cardiologie, CHU d'Angers, Rue Haute de Reculée, F-49045 Angers, France. lobiere@chu-angers.fr
Telephone: +33-241-354858
Fax: +33-241-354004

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Abstract

AIM

To assess the arrhythmic determinants and prognosis of patients presenting with myocardial infarction and non-obstructive coronary arteries (MINOCA) with normal ejection fraction (EF).

METHODS

This is an observational analysis of 131 MINOCA patients with normal EF. Three cardiac magnetic resonance (CMR) diagnosis classes were recognized according to the late gadolinium enhancement (LGE) pattern: Myocardial infarction (MI) (n = 34), myocarditis (n = 47), and "no LGE" (n = 50). Ventricular events occurring during hospitalization were recorded and the entire population

was followed-up at 1 year.

RESULTS

Ventricular arrhythmia was observed in 18 (13.8%) patients during hospitalization. The "no LGE" patients experienced fewer ventricular events than the MI and myocarditis patients [4.0% *vs* 26.5% and 14.9%, respectively (P = 0.013)]. There was no significant difference between the MI and myocarditis groups. On multivariate analysis, LGE transmural extent [OR = 1.52 (1.08-2.15), P = 0.017] and ST-segment elevation [OR = 4.65 (1.61-13.40), P = 0.004] were independent predictors of ventricular arrhythmic events, irrespective of the diagnosis class. Finally, no patient experienced sudden cardiac death or ventricular arrhythmia recurrence at 1-year.

CONCLUSION

MINOCA patients with normal EF presented no 1-year cardiovascular events, irrespective of the CMR diagnosis class. LGE transmural extent and ST segment elevation at admission are risk markers of ventricular arrhythmia during hospitalization.

Key words: Ventricular tachycardia; Myocarditis; Myocardial infarction; Late gadolinium enhancement; Cardiac magnetic resonance; Myocardial infarction and non-obstructive coronary arteries

Core tip: Out of 131 myocardial infarction and non-obstructive coronary arteries patients, 18 experienced a ventricular arrhythmic event during hospitalization, consisting of 17 ventricular tachycardia and one ventricular fibrillation. No patient died during the 1-year follow-up. Cardiac magnetic resonance classified the underlying diagnosis in 61.8% of the cases, as a myocarditis or a myocardial infarction. Rather than the diagnosis itself, late gadolinium enhancement and ST-segment elevation were found as valuable tools to stratify the risk for arrhythmia of these patients. These findings may be useful to select patients who might be eligible for either arrhythmia prevention or secondary prevention therapy.

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INTRODUCTION

Sudden cardiac death is still the most common cause of death worldwide, accounting for over 50% of all deaths from cardiovascular disease. Coronary artery disease represents approximately 80% of all cases[1]. However, 1%-12% of patients with chest pain and cardiac troponin elevation present with normal coronary arteries on angiography analysis[2]. This pathological entity is called myocardial infarction and non-obstructive coronary arteries (MINOCA) and encompasses myocarditis, transient apical ballooning syndrome, and authentic ischemic injuries[2]. Cardiac magnetic resonance (CMR) imaging is helpful for providing detailed information on myocardial tissue characteristics, and has become the gold standard for *in vivo* detection of necrosis, notably in acute myocardial infarction (MI) and myocarditis[3].

Early-sustained ventricular arrhythmias complicate 2%-20% of acute MIs and are associated with increased hospital mortality rates[4,5]. While the arrhythmic prognosis of MI with abnormal coronary angiography is well known, there is little data concerning MINOCA, even when the arrhythmic prognosis seems to be relatively good[6,7]. As a result of the lack of data concerning this entity, there are no specific guidelines concerning hospitalization duration, follow-up, or treatment for this specific setting.

Our study sought to evaluate the risk of ventricular arrhythmias of presumed low-risk MINOCA patients at both early-stage consultation and 1-year follow-up, based on the diagnosis class established by CMR imaging.

MATERIALS AND METHODS

One hundred and sixty-seven patients were retrospectively enrolled between 2007 and 2012 in the French university hospitals of Nantes and Angers. The inclusion criteria were: (1) hospitalization for acute anginal chest pain; (2) increase in troponin rates superior to the normal range; (3) left ventricular ejection fraction (LVEF) $\geqslant$ 45%; and (4) absence of coronary artery stenosis or thrombosis (stenosis < 50% of the diameter of the epicardial vessel).

All patients underwent CMR and the arrhythmic evaluation included at least 48 h of electrocardiography (ECG) monitoring after admission.

In order to avoid overestimating the arrhythmic risk in this population, patients hospitalized for sustained ventricular tachycardia (n = 8) or cardiopulmonary arrest were not included in the study. Patients presenting with Tako-Tsubo (n = 21) were therefore also from the study due to this syndrome's specific pathophysiology. Seven more patients could not be included due to poor CMR quality so that the study was performed on 131 patients (Figure 1). The study complies with the Declaration of Helsinki and local ethics committee has approved the research protocol.

Ventricular tachycardia (VT) was defined as at least three consecutive ventricular beats with a rate > 100 bpm[8]. Prolonged VT was defined as at least eight consecutive ventricular beats[9]. Ventricular fibrillation

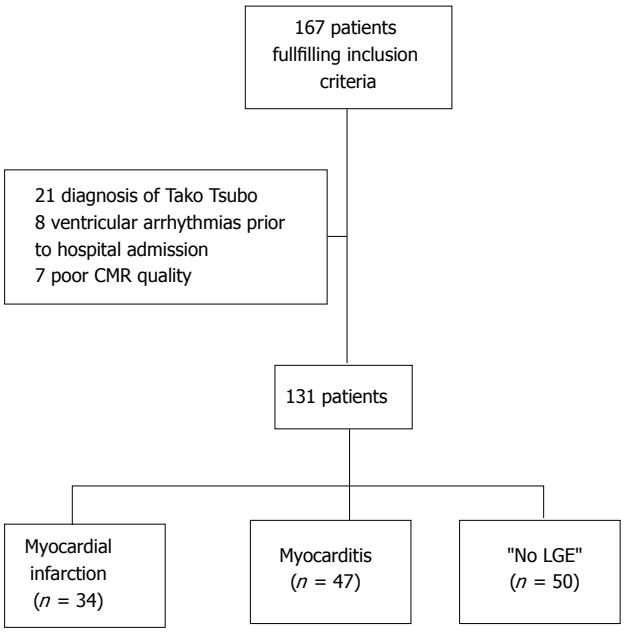

Figure 1 Flow chart of the study population. CMR: Cardiac magnetic resonance; LGE: Late gadolinium enhancement.

was defined as an irregular ventricular rhythm with marked variability in the QRS cycle length, morphology, and rapid amplitude, usually over 300 bpm/200 ms (cycle length: 180 ms or less)[8].

All data concerning the initial hospitalization were recorded from the patient medical files. Repolarization abnormalities were defined as ST-segment depression $\geqslant$ 0.1 mV at 0.08 s from the junction (J point) (STD), asymmetrical T wave inversion $\geqslant$ 0.1 mV deep in two or more leads except lead aVR, and ST-segment elevation $\geqslant$ 0.2 mV (STE). Q waves > 0.3 mV in depth or > 0.04 s in duration in at least two leads, except lead aVR, were considered abnormal.

At the 1-year follow-up, the following outcomes were collected: Ventricular arrhythmia, death from any cause, cardiovascular (CV) death, and particularly sudden cardiac death. The chosen treatments were evaluated on hospital discharge and at 1 year. If necessary, the referring cardiologists or general practitioners were contacted to obtain information concerning the patients at 1-year follow-up. Data on 1-year survival was completed for every patient.

CMR was performed using 1.5T scanners (Avanto, Siemens, Erlangen, Germany) with 8-element phased-array cardiac receiver coils. The median time from presentation of MINOCA to CMR was 7 d (interquartile range: 4; 13).

LV function was determined by means of cine imaging, in multiple short-axis views covering the entire LV. The typical in-plane resolution was 1.6 mm × 1.9 mm and 7.0-mm thickness sections were used. Temporal resolution was around 35-45 ms.

Late gadolinium enhancement (LGE) was performed 10 min after administering the gadolinium-based contrast agent, at a cumulative dose of 0.2 mmol/kg, by means of a two-dimensional segmented inversion recovery gradient-echo pulse sequence. The inversion time was set to null the signal of the viable myocardium, typically ranging from 240 to 300 ms.

A post-hoc core analysis was specifically performed for this study, using a dedicated software package (Medis 7.1, Mass, Leiden, The Netherlands). For all qualitative assessments, the recommended 17-segment system was applied, requiring the consensus of two blinded observers.

On all the short-axis cine slices, the endocardial and epicardial borders were outlined manually on the end-diastolic and end-systolic images, with the exclusion of the trabeculae and papillary muscles. The reproducibility of the LVEF and LV volumes assessments was good, the details of which are published elsewhere[10].

The cine imaging was assessed visually by analyzing the LV wall thickening using a three-grade scale: 0 = normal, 1 = hypokinesia, 2 = akinesia. We counted the number of segments affected in order to determine the extent of hypokinesis. Furthermore, pericardial effusion was noted when considered exceeding trivial effusion[3].

LGE was evaluated by means of visual analysis. We estimated the maximal transmural extent of LGE within each segment as a percentage of the LV using a five-grade scale: 0% = 0, 0%-25% = 1, 25%-50% = 2, 50%-75% = 3, and > 75% = 4 (Figure 2). The number of segments with LGE defined the LGE transversal extent.

Following analysis by means of CMR, the patients were classified according to LGE pattern, as described: Subendocardial LGE was revealed in the MI group, subepicardial or medioventricular LGE in the myocarditis group, and absence of LGE in the "no LGE" group[11].

When the extent of LGE was transmural (> 75%), the border zones were analyzed to more precisely determine the CMR diagnosis, for example, if the signal of LGE borders was subendocardial, myocardial infarction was diagnosed.

Statistical analysis

Statistical analyses were performed using SPSS Version 15.0 software for Windows (SPSS Inc., Chicago, Illinois, United States). The data was presented as mean ± standard deviation (SD) or median (25^{th}; 75^{th} percentiles) in cases of non-normal distribution, with categorical data expressed as frequencies and percentages. Continuous variables were compared by means of the unpaired *t* test or Wilcoxon rank-sum test, when necessary. Non-continuous variables were compared using the χ^2 test. Differences were considered significant with a $P < 0.05$. For the multivariate analysis of ventricular events during hospitalization, clinical and CMR data were tested by means of an ascending step-by-step binomial logistic regression analysis, including variables with *P* values < 0.05 in univariate analysis. The Hosmer-Lemeshow goodness-of-fit test was used to assess the applied models.

Table 1 Patient characteristics

	All patients (n = 131)	MI (n = 34)	Myocarditis (n = 47)	"No LGE" (n = 50)	P
Age, yr	48.5 ± 16.1	52.4 ± 14.2	40.5 ± 13.5[1]	53.4 ± 16.9[3]	< 0.001
Risk factors, n (%)					
Male gender	87 (66.4)	22 (64.7)	39 (83.0)	26 (52.0)[2,3]	0.005
Hypertension	39 (29.8)	13 (38.2)	8 (17.0)	18 (36.0)	0.06
Diabetes	11 (8.4)	4 (11.8)	2 (4.3)	5 (10.0)	0.42
Dyslipidemia	38 (29.0)	9 (26.5)	10 (21.3)	19 (38.0)	0.18
Current smoker	45 (34.4)	14 (41.4)	12 (25.5)	19 (38.0)	0.27
Family history of premature CHD	25 (19.1)	11 (34.2)	5 (10.6)	9 (18.0)	0.05
Time from symptom onset to admission, h	9 [2; 24]	3.5 [2; 13.5]	13 [4; 48][1]	9.5 [2; 24]	0.01
Hospitalization duration, d	6 [4; 7]	5.5 [4; 7]	6 [5; 7]	5 [4; 7]	0.42
ECG monitoring duration, d	5 [4; 6]	5 [4; 6]	5 [4; 7]	4 [3; 6]	0.12
Primary ECG abnormality, n (%)	91 (69.5)	26 (76.5)	34 (72.3)	31 (62.0)	0.32
ST-segment elevation	46 (35.1)	9 (26.5)	22 (46.8)	15 (30.0)	0.10
ST-segment depression	8 (6.1)	2 (5.9)	4 (8.5)	2 (4.0)	0.65
T-wave inversion	31 (23.7)	11 (32.4)	8 (17.0)	12 (24.0)	0.27
Q wave	2 (1.5)	2 (5.9)	0	0	0.06
Atrioventricular block	1 (0.8)	0	0	1 (2.0)	0.28
Laboratory measurements					
Peak troponin, μg/L	2.1 ± 5	3.6 ± 6.1	2.9 ± 6.3	0.5 ± 0.6[2,3]	0.013
Leucocytes on admission, G/L	9.3 ± 3.6	9.3 ± 3.9	9.2 ± 3.5	9.2 ± 3.4	0.99
CRP on admission, mg/L	28.2 ± 41.1	8.8 ± 18.9	39.5 ± 38.4[1]	31.0 ± 50.4[2]	0.004
Coronary atheroma, n (%)	45 (34.6)	15 (45.5)	14 (29.8)	16 (32.0)	0.31
β-blocker use, n (%)					
During hospitalization	91 (69.5)	27 (79.4)	31 (66.0)	33 (66.0)	0.34
At 1 yr	16 (12.2)	10 (29.4)	1 (2.1)	5 (10.0)	0.05
ACEI use, n (%)					
During hospitalization	56 (43.1)	16 (48.5)	16 (34.0)	24 (48.0)	0.29
At 1 yr	17 (13.0)	10 (29.4)	1 (2.1)[1]	6 (12.0)	0.042

[1]P significant between MI and myocarditis groups; [2]P significant between MI and "no LGE" groups; [3]P significant between myocarditis and "no LGE" groups. MI: Myocardial infarction; LGE: Late gadolinium enhancement; ACEI: Angiotensin converting enzyme inhibitor; CHD: Coronary heart disease; CRP: C-reactive protein.

RESULTS

A total of 131 patients (87 men, median age: 48.5 ± 16 years) fulfilled our criteria. LGE was present in 81 of the 131 patients (61.8%). There were 34 (25.9%) patients classified in the MI group, 47 (35.9%) in the myocarditis group, and 50 (38.2%) in the "no LGE" group (Table 1). The myocarditis group exhibited a specific pattern of myocarditic lesions, located predominantly in the free lateral wall (42/47 cases) and in the subepicardial layers (45/47 cases). The ischemic lesions were distributed homogeneously (Figure 2).

Patients classed in the myocarditis group were younger (P < 0.001) and more frequently male (P < 0.005) than the others. No differences in cardiovascular risk factor were noted.

The median time between symptom onset and hospital admission was 9 h (2; 24). Patients from the MI group were admitted to the hospital more quickly than those in the myocarditis group (P = 0.002).

The prevalence of ECG abnormalities was 69.5%, predominantly consisting of STE (35.7%) and T-wave inversion (23.1%). There were no differences in the frequency of ECG abnormalities between the groups.

Troponin rates were lower in the "no LGE" group compared to those of the MI and myocarditis groups (P = 0.001 and P = 0.013, respectively).

The MI patients presented with lower C-reactive protein (CRP) rates than the myocarditis and "no LGE" patients (P < 0.001 and P = 0.020, respectively). Elevated CRP was observed in 42 (93.3%), 22 (66.7%), and 37 (82.2%) patients from the myocarditis, MI, and "no LGE" groups, respectively.

During hospitalization, 69% of patients were treated with β-blockers and 43% received angiotensin-converting enzyme inhibitors (ACEIs), with no difference observed between the different groups. At 1 year, only 13% of the patients were receiving either β-blockers or ACEIs, with a trend for higher rates of treatment seen in the MI group, though this difference was not statistically significant. Notably, no other antiarrhythmic drug than β-blockers was given at any time of the study.

The mean LVEF was 58.6% ± 8.2%. No significant differences were observed in either LVEF or LV end-diastolic volume between the groups. The "no LGE" group exhibited smaller LV end-systolic volumes than those of the MI and myocarditis patients. LV wall thickening was more often altered in the MI group. Moreover, the MI patients presented with higher rates of akinesia compared to the myocarditis and "no LGE" patients (58.8% *vs* 4.3% and 2.0%, P < 0.001). Pericardial effusion was detected nonspecifically in 20 patients (15.4%) (Table 2).

During hospitalization, 18 patients experienced

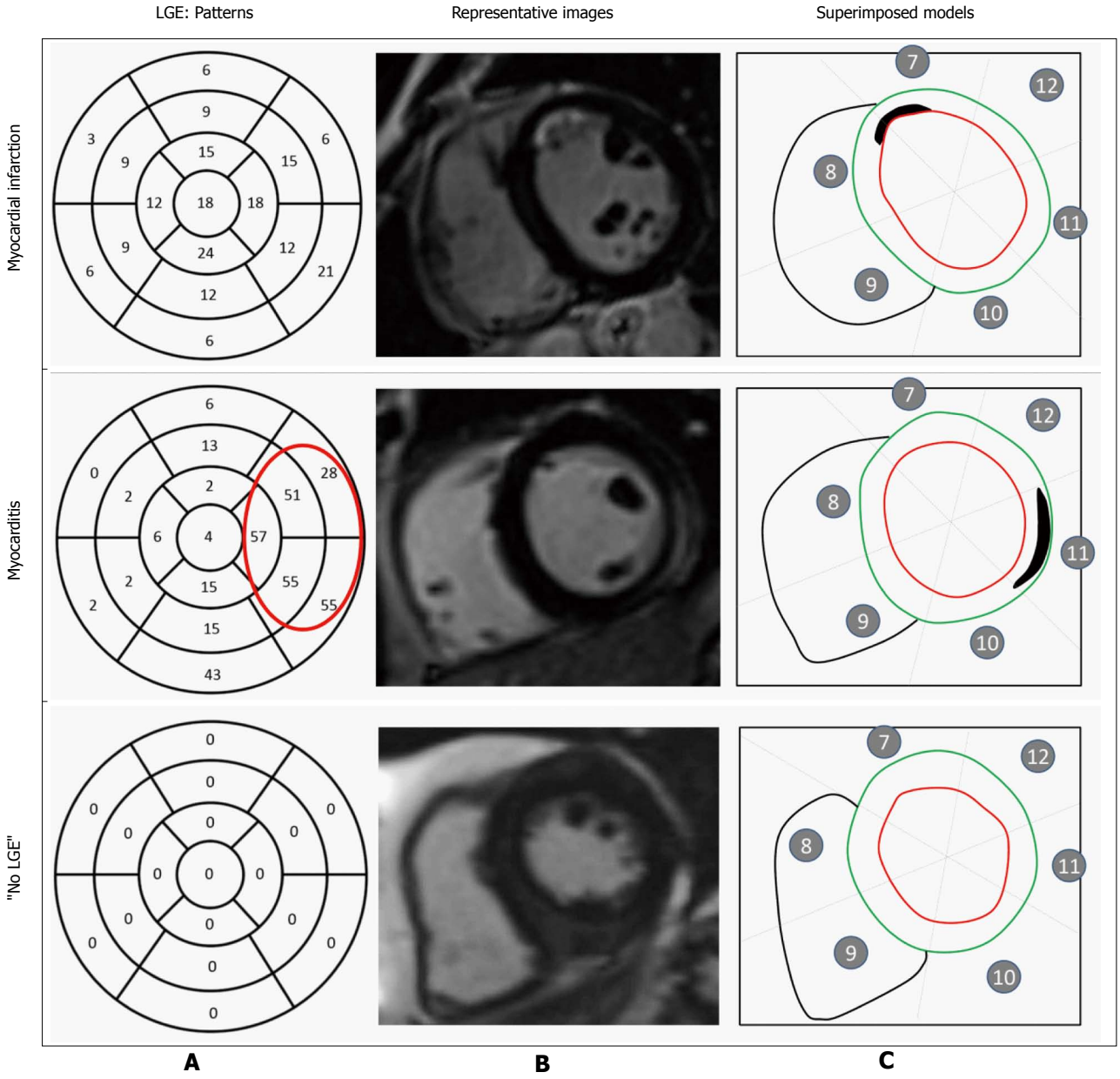

Figure 2 Pattern of late gadolinium enhancement. A: Incidence of late gadolinium enhancement (LGE) within each segment (percentage) of all patients, including those with and without LGE. In myocarditis cases, LGE was predominantly on the lateral wall. In myocardial infarction, no specific pattern of LGE could be identified; B: Representative short-axis slice images showing LGE location; C: Superimposed segmental models showing location and spatial extent of LGE (outlined).

a ventricular arrhythmic event, consisting of 17 VTs and one ventricular fibrillation (Tables 3 and 4). No differences were observed between the MI and the myocarditis groups (n = 9, 26.5% *vs* n = 6, 12.8%, P = 0.10), whereas the MI patients exhibited higher rates of VT than the "no LGE" group (n = 2, 4.0%, P = 0.001). All these events occurred in the early stages of hospitalization, with a median onset of 1 (0-1) d. One episode of ventricular fibrillation occurred in a myocarditis patient on day 3, who was successfully defibrillated. We found no differences in cardiovascular risk factor, CRP, coronary atheroma, or use of β-blockers and ACEIs in correlation with the ventricular events.

The transmural extent of LGE was more marked in the MI group (P < 0.001). An LGE transmural extent > 50% was observed in 32 patients (94.1%) in the MI group, in contrast to 16 patients (34.0%) in the myocarditis group (P < 0.001). LGE was more contained in the MI group, exhibiting lower transversal extents than the myocarditis group. Only eight patients (23.5%) were found to have more than two segments with LGE presence in the MI group, *vs* 27 (57.4%) in the myocarditis group (P = 0.002).

Of note, the concordance among Cine and LGE data was higher in the MI group compared to the myocarditis group (88.2% *vs* 41.3%, P < 0.001).

The multivariate analysis demonstrated that STE [OR = 5.72 (1.77-18.46), P = 0.004] and LGE transmural extent [OR = 1.50 (1.02-2.20), P = 0.039] were both independently related to ventricular events during hospitalization (Table 5). STE presented high sensitivity for the diagnosis of prolonged VT (83%), achieving a

Table 2 Cardiac magnetic resonance parameters

	Total (n = 131)	MI (n = 34)	Myocarditis (n = 47)	"no LGE" (n = 50)	P
LVEF (%)	58.6 ± 8.2	57.1 ± 7.8	57.9 ± 8.6	60.2 ± 7.8	0.18
LVEDV (mL)	154.7 ± 37.7	158.8 ± 41	159.6 ± 28.6	147.3 ± 42.1	0.21
LVESV (mL)	64.5 ± 22.1	69.5 ± 25.5	67.1 ± 16.9	58.6 ± 22.9[2,3]	0.048
LV wall thickening abnormality, n (%)	62 (47.3)	30 (88.2)	22 (46.8)[1]	10 (20.0)[2,3]	< 0.001
Hypokinetic extent, segments	1.1 ± 1.5	2 ± 1.6	1.2 ± 1.6[1]	0.4 ± 1.1[2,3]	< 0.001
0 segment, n (%)	69 (52.7)	4 (11.8)	25 (53.2)	40 (80.0)	
1-2 segments, n (%)	43 (32.9)	20 (58.8)	14 (29.8)	9 (18.0)	
> 2 segments, n (%)	19 (14.5)	10 (29.4)	8 (17.0)	1 (2.0)	
LGE transmural extent, segments	0.9 ± 0.8	3.6 ± 0.6	2.1 ± 0.9[1]	0	< 0.001
< 50%, n (%)	83 (73.4)	2 (5.9)	31 (66.0)	0	
> 50%, n (%)	48 (36.6)	32 (94.1)	16 (34.0)	0	
LGE transversal extent, segments	1.9 ± 2.2	1.9 ± 1.3	3.5 ± 2.4	0[2,3]	< 0.001
0 segment, n (%)	50 (38.2)	0	0	50 (100.0)	
1-2 segments, n (%)	46 (35.1)	26 (76.5)	20 (42.6)	0	
> 2 segments, n (%)	35 (26.7)	8 (23.5)	27 (57.4)	0	
LGE/CINE concordance, n (%)	49 (37.4)	30 (88.2)	19 (41.3)[1]	0	< 0.001
Pericardial effusion, n (%)	20 (15.3)	4 (11.8)	8 (17.4)	8 (16)	0.8

[1]P significant between MI and myocarditis groups; [2]P significant between MI and "no LGE" groups; [3]P significant between myocarditis and "no LGE" groups. MI: Myocardial infarction; LGE: Late gadolinium enhancement; LV: Left ventricle; LVEDV: Left ventricular end diastolic volume; LVESV: Left ventricular end systolic volume; LVEF: Left ventricular ejection fraction.

Table 3 Acute event rates

	All patients (n = 131)	MI (n = 34)	Myocarditis (n = 47)	"No LGE" (n = 50)	P
Ventricular event, n (%)	18 (13.8)	9 (26.5)	7 (14.9)	2 (4.0)[1]	0.013
VT, n (%)	17 (13.0)	9 (26.5)	6 (12.8)	2 (4.0)[1]	0.011
Prolonged VT or VF, n (%)	8 (6.1)	4 (11.8)	4 (8.5)	0[1]	0.06
VF, n (%)	1 (0.8)	0	1 (2.1)	0	0.41

[1]P significant between MI and "no LGE" groups. MI: Myocardial infarction; LGE: Late gadolinium enhancement; VF: Ventricular fibrillation; VT: Ventricular tachycardia.

specificity of 77% and negative predictive value of 92%. At 1 year, no patients presented with sudden cardiac death or recurrence of symptomatic ventricular event. One patient died of cancer.

DISCUSSION

The key point of the study is to demonstrate that none of the patients presenting with MINOCA and normal LVEF died of cardiovascular death or sudden cardiac death following the initial phase of hospitalization. ST segment elevation and LGE extent were the best predictors of in-hospital ventricular arrhythmic events, irrespective of the etiology.

During hospitalization, 13.8% of the patients experienced a ventricular arrhythmic event, primarily consisting of VT, with one case of ventricular fibrillation. Most of these events occurred during the first 48 h following symptom onset. These results are consistent with the literature, with previous reports of similar rates of early arrhythmic outcomes among patients with MINOCA[7,12-14] or in cases of myocarditis[15]. Our study demonstrated that, in the absence of decreased LVEF, MI and myocarditis patients are affected by the same arrhythmic risks. Following the initial phase of the disease, where the risk of ventricular arrhythmia is present, the arrhythmic risk appears very low.

The initial arrhythmic risk of myocarditis is well known and studies have shown that in patients < 35 years, myocarditis was the second most common identified cause of sudden cardiac death after coronary artery disease[16].

Our study demonstrated that STE is an independent predictor of ventricular arrhythmia at early-stage disease, achieving a good negative predictive value of 92% for prolonged VT. Data on the prognostic role of ECG abnormalities are currently scarce. This finding was assumed to be in relation to the transient character of the ST changes in myocarditis[17], as well as the weak relationship between STE and LGE localization[17,18].

The adverse prognostic value of LGE-CMR in ischemic and non-ischemic cardiomyopathy has been proven in patients with reduced LVEF[19]. Conversely, Grün *et al*[20] demonstrated a relevant cardiac mortality of 15% in 203 patients with myocarditis, which was primarily driven by the presence of LGE. Nevertheless, a large proportion of their patients presented with heart failure and decreased LVEF. In another report of fewer selected patients with suspected myocarditis, LGE was found in only 28% of cases, and LGE and LVEF were defined as predictors for a composite of cardiac death and heart failure[15]. In our study, considering the

Table 4 Acute event characteristics

Patient	Gender	Age (yr)	ECG	Troponin (μg/L)	LVEF (%)	Diagnosis	LGE transmural extent[1]	β-blocker use	ACEI use	VT	VF	CMR delay (d)	Ventricular arrhythmia length
13	Male	39	STE	0.3	51.7	MI	4	1	0	1	0	1	10 VPBs
52	Male	45	Normal	0.4	57.7	MI	3	0	0	1	0	1	10 VPBs
53	Female	30	STE	17.3	45.5	MI	4	1	1	1	0	0	30 VPBs
63	Male	51	Normal	0.3	57.8	MI	3	1	1	1	0	1	6 VPBs
64	Male	56	STE	1.6	61.2	MI	4	1	1	1	0	1	15 VPBs
75	Male	32	STE	0.8	63.2	MI	4	1	0	1	0	0	7 VPBs
92	Male	57	STD	0.4	48.1	MI	3	1	0	1	0	0	6 VPBs
128	Female	55	STD	0.6	49.8	MI	4	1	1	1	0	1	5 VPBs
97	Male	83	STD	0.2	46.5	MI	2	1	1	1	0	0	6 VPBs
3	Male	45	STE	0.1	66.9	Myocarditis	3	1	0	1	0	2	9 VPBs
37	Male	40	STE	4.8	56.1	Myocarditis	2	0	1	1	0	2	5 VPBs
44	Male	25	STE	36.6	65.7	Myocarditis	3	0	0	0	1	3	VF
94	Male	28	STE	1.4	57.1	Myocarditis	2	1	0	1	0	0	4 VPBs
76	Male	53	STE	1.4	69.6	Myocarditis	2	1	1	1	0	0	7 VPBs
104	Female	42	STE	21.2	57.1	Myocarditis	4	1	0	1	0	1	13 VPBs
131	Female	31	STD	0.6	51.7	Myocarditis	1	1	0	1	0	1	8 VPBs
80	Male	34	STE	0.4	53.1	No LGE	0	0	1	1	0	0	7 VPBs
125	Male	56	Normal	0.1	62.4	No LGE	0	1	1	1	0	4	3 VPBs

[1]LGE transmural extent: 0 = 0%, 1 = 0%-25%, 2 = 25%-50%, 3 = 50%-75%, and 4 > 75%. LGE: Late gadolinium enhancement; ECG: Electrocardiography; LVEF: Left ventricular ejection fraction; STD: ST-segment depression; STE: ST-segment elevation; VT: Ventricular tachycardia; VF: Ventricular fibrillation; VPBs: Ventricular premature beats; MI: Myocardial infarction; ACEI: Angiotensin-converting enzyme inhibitor.

Table 5 Univariate and multivariate analysis for ventricular arrhythmia

	Univariate analysis		Multivariate analysis	
	Odds ratio (95%CI)	*P*	Odds ratio (95%CI)	*P*
STE	4.65 (1.61-13.40)	0.004	5.72 (1.77-18.46)	0.004
STD	-	0.06		
T-wave inversion	-	0.99		
Troponin	1.10 (1.02-1.20)	0.02	-	0.27
Hypokinetic extent	-	0.09		
LGE transmural extent	1.52 (1.08-2.15)	0.017	1.50 (1.02-2.20)	0.039
LVEF	-	0.31		
LVEDV	-	0.3		
LVESV	-	0.17		
Pericardial effusion	-	0.24		
Coronary atheroma	-	0.68		
CMR diagnosis	-	0.12		
MI or myocarditis	0.17 (0.04-0.77)	0.022		

LVEDV: Left ventricular end-diastolic volume; LVESV: Left ventricular end-systolic volume; LVEF: Left ventricular ejection fraction; STD: ST-segment depression; STE: ST-segment elevation; MI: Myocardial infarction; CMR: Cardiac magnetic resonance.

excellent prognosis of the population, we have found that LGE is not useful for evaluating cardiac outcomes.

Despite this, however, the transmural extent of LGE was identified as an independent predictor for ventricular arrhythmia during the acute phase of the disease. This could therefore be of great value, if performed very early after the hospitalization, to identify at-risk patients requiring special attention and perhaps more prolonged rhythmic monitoring.

In our study, CMR imaging provided etiological diagnosis in 81 patients (61.8%), which is consistent with previous reports[21,22]. Clinical evaluations including biopsy have demonstrated that myocarditis could be present in patients with normal CMR results in 32% to 47% of cases[20,23]. It is likely that the frequency of myocarditis was underestimated in our study, especially in the "no LGE" group, as suggested by the CRP levels that were similar to those with myocarditis. It has been suggested that global LV involvement in myocarditis may be the cause of LGE absence[24].

The choice of medical management strategy for these patients remains controversial. There is little data, which is also conflicted, on the use of a secondary prevention treatment involving at least β-blockers in patients affected by myocarditis mimicking acute MI[25]. In our cohort, 69.5% of the patients received β-blockers during hospitalization, reflecting the management of a recent MI. Regarding the relatively-high percentage of patients who experienced ventricular arrhythmia, there is no doubt that this treatment is of interest during this period of time.

In our study, the absence of sudden cardiac death at 1 year suggests that β-blockers should not be continued over the long term, even if the β-blocker treatment had already been stopped in most of the population, with only one myocarditis patient still undergoing treatment. The need to prolong the treatment immediately after the hospital discharge is, however, a more controversial topic. LGE and ST segment elevation may represent valuable tools to stratify the risk of these patients and select those eligible for secondary prevention therapy.

The first limitation of our study was the sample size, which was too small to detect any statistical difference between the myocarditis group and the MI group. Secondly, the retrospective study design also, evidently, posed a limit. Finally, no systematic rhythm

monitoring was organized to screen the last recurrence of ventricular events after discharge. Similarly, the therapeutic management that may be chosen based on such preclinical events was left to the discretion of the referring cardiologist, and the use of β-blockers or ACEIs was extremely low at follow-up (12.2% and 13.0%, respectively). Nevertheless, none of our patients presented with sudden cardiac death or severe arrhythmia during follow-up. We must also admit that prognosis may differ by ethnicity but are not stressed in our study.

In conclusion, our study indicated that patients with MINOCA and normal LVEF did not present any 1-year CV events, particularly no sudden cardiac death, after hospital discharge. Most of them had even stopped treatment at 1-year follow-up.

STE on admission and LGE transmural extent appear to be good markers for identifying patients at risk of ventricular events in the early stages of disease.

COMMENTS

Background

About 1%-12% of patients with chest pain and cardiac troponin elevation present with normal coronary arteries on angiography analysis. While the arrhythmic prognosis of myocardial infarction with abnormal coronary angiography is well known, there is little data concerning myocardial infarction with non-obstructive coronary arteries (MINOCA). This study sought to evaluate the risk of ventricular arrhythmias of presumed low-risk MINOCA patients, based on the diagnosis class established by cardiac magnetic resonance (CMR) imaging.

Research frontiers

Numerous patients are affected by MINOCA, and yet prognosis is expected to be favorable as soon as left-ventricular ejection fraction (LVEF) is good. Nevertheless, the mere presence of a myocardial injury/scar/fibrosis, let us empirically dare for the occurrence of ventricular arrhythmia.

Innovations and breakthroughs

CMR was used systematically to identify MINOCA's aetiology, but also to assess myocardial injury and its extent. Continuous electrocardiography was also systematically performed to solve the question of arrhythmic risk during the first days after symptoms onset. It was continued by a one-year clinical follow-up. Nevertheless, this study does not focus on medical therapy, including the effect of β-blockers on ventricular arrhythmia.

Applications

This study provides evidence on the good prognosis (including arrhythmic events) presented by patients with MINOCA and preserved LVEF. When ventricular arrhythmias occurred, they correlated with myocardial injury, as assessed by transmural late gadolinium enhancement (LGE) by CMR. Therefore, this study provides reassuring data about survival but also point out the need to stress the effect of antiarrhythmic therapies on the newly-identified risk markers that are LGE and ST segment elevation.

Terminology

MINOCA is a recent terminology that relates to ischemic injuries, myocarditis, tako-tsubo cardiomyopathy, hypertrophic cardiomyopathy, dilated cardiomyopathy, and other causes such as pericarditis and amyloidosis.

Peer-review

This paper is interesting, novel, and an overall well-conducted study. It provides a timely study on this field.

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