CLINICAL RESEARCH STUDY

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Reinfarction in Patients with Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA): Coronary Findings and Prognosis

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ABSTRACT

BACKGROUND: Myocardial infarction (MI) with nonobstructive coronary arteries (MINOCA) is common. There are limited data on the mechanisms and prognosis for reinfarction in MINOCA patients.

METHODS: In this observational study of MINOCA patients hospitalized in Sweden and registered in the SWEDEHEART registry between July 2003 and June 2013 and followed until December 2013, we identified 9092 unique patients with MINOCA of 199,163 MI admissions in total. The 570 (6.3%) MINOCA patients who were hospitalized due to a recurrent MI constituted the study group.

RESULTS: The mean age was 69.1 years and 59.1% were women. The median time to readmission was 17 months. A total of 340 patients underwent a new coronary angiography and 180 (53%) had no obstructive coronary artery disease (CAD) and 160 (47%) had obstructive CAD; 123 had 1-vessel, 26 had 2-vessel, 9 had 3-vessel disease, and 2 had left main together with 1-vessel disease. Male sex, diabetes, peripheral vascular disease, higher levels of creatinine, and ST elevation at presentation were more common in patients with MI with obstructive CAD than in patients with a recurrent MINOCA. Mortality during a median follow-up of 38 months was similar whether the reinfarction event was MINOCA or MI with obstructive CAD 13.9% vs 11.9% ($P = .54$).

CONCLUSIONS: About half of patients with reinfarction after MINOCA who underwent coronary angiography had progression of coronary stenosis. Angiography should be strongly considered in patients with MI after MINOCA. Mortality associated with recurrent events was substantial, though there was no difference in mortality between those with or without significant CAD.

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KEYWORDS: Coronary angiography; Coronary artery disease; Predictors; SWEDEHEART

SEE RELATED EDITORIAL, page 267.

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INTRODUCTION

The large-scale use of acute coronary angiography in patients with acute myocardial infarction (MI) together with the use of sensitive cardiac troponin assays for diagnosis,[1] have revealed a significant proportion of MIs with nonobstructive coronary arteries (MINOCAs).[2–14] The reported prevalence of MINOCA is dependent on the definition used and the populations studied; it ranges between 1% and 15% in different studies,[3–16] with an overall prevalence of 6% in a recent meta-analysis.[13] Likewise, the prognosis differs between cohorts and is reported to be better,[3,6,12–14] similar,[4,10,11] and worse[4,15] than for patients with MI and obstructive coronary arteries.

MINOCA has varied underlying causes, including atherosclerotic plaque rupture/erosion, coronary artery spasm, coronary dissection, and others. Atherosclerosis is a progressive disease, particularly when not treated with statins. MINOCA patients are less likely than patients with MI and obstructive coronary artery disease (CAD) to receive statins and antiplatelet agents, despite our previous finding that statin therapy is associated with lower risk of major adverse cardiac event after MINOCA.[17] Therefore, we hypothesized that a substantial proportion of patients with recurrent MI after MINOCA may have progression to obstructive CAD on repeat angiography. Understanding of this subgroup could impact clinical care after MINOCA. No previous study has investigated coronary artery findings at readmission or assessed the prognosis after repeated episodes of MINOCA. Therefore, the purpose of the present study was to investigate the status of the coronary arteries at readmission for MI in patients with previous MINOCA, and secondly, to assess the prognosis after a reinfarction.

CLINICAL SIGNIFICANCE

- Almost half of the patients with reinfarction after myocardial infarction with nonobstructive coronary arteries (MINOCA) who underwent coronary angiography had progression of coronary stenosis.
- A review of risk factors for coronary artery disease should be considered for all patients with MINOCA.
- Angiography should be strongly considered in patients with new myocardial infarction after MINOCA.
- Mortality associated with recurrent events was substantial, though there was no difference in mortality between those with or without significant coronary artery disease.

METHODS

Study Population

The MINOCA population has been previously described.[16] In short, 9092 unique patients with MINOCA were identified among 199,163 acute MI admissions recorded in the Swedish Web-system for Enhancement and Development of Evidence-based care in heart disease Evaluated According to Recommended Therapy registry (SWEDEHEART) between July 1, 2003 and June 30, 2013. A total of 570 patients out of the MINOCA population were readmitted due to a new MI prior to December 31, 2013 (Figure 1).

Patients were identified as having MINOCA if the discharge diagnosis of the index event was acute MI (International Classification of Diseases, 10th Revision [ICD-10] code: I21-I22) and a coronary angiography performed during the index hospitalization did not show a diameter stenosis of 50% or more. Patients with a discharge diagnosis of takotsubo syndrome (ICD-10 code I42.8) were not included.

The SWEDEHEART registry contained the data on baseline characteristics, electrocardiography (ECG) changes, biochemical markers, coronary angiography results, left ventricular ejection fraction, medical and invasive treatment, and outcome (see http://www.swedeheart.se for details). To ensure the correctness of the data entered, there is routine in-person monitoring of the data entered into the SWEDEHEART, as compared with medical records at a rotating selection of participating centers, and agreement has been excellent. For example, agreement was 96.1% (range 92.6%-97.4%) when 637 randomly chosen computer forms from 21 hospitals containing 38,121 variables were reviewed in 2007,[18] and overall agreement

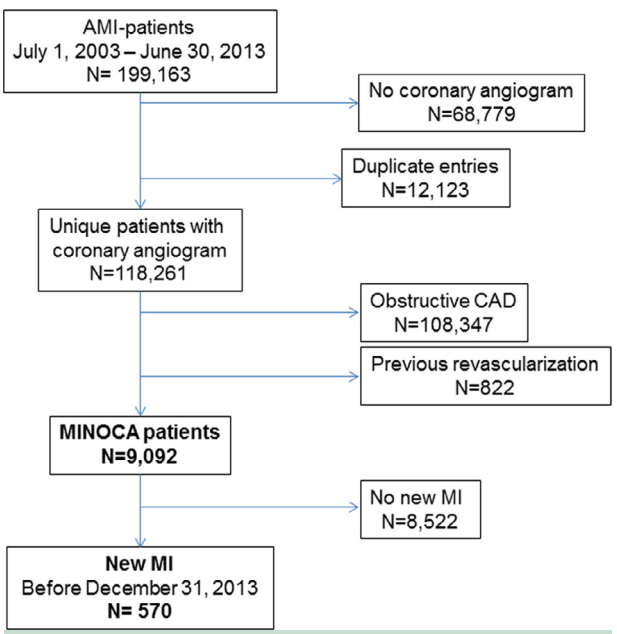

Figure 1 The cohort. AMI = acute myocardial infarction; CAD = coronary artery disease; MI = myocardial infarction; MINOCA = myocardial infarction with nonobstructive coronary arteries.

was 97% between entered data and electronic health records in 2015-2016.[19]

Coronary Angiography

Data about the coronary angiographies were extracted from the SWEDEHEART registry,[18] in which the angiograms are interpreted by the local interventionalist. The coronary vessels are divided into 19 segments, derived from the 16-segment model proposed by Austen et al.[20] The degrees of narrowing of diameter are categorized as <50%, 50%-69%, 70%-99%, or 100% (occlusion). Angiographic data are subject to routine monitoring as part of the SWEDEHEART standard operations. The classification of any stenosis is done according to the American College of Cardiology/American Heart Association Task Force.[21]

Outcome Definitions

Data on all-cause death are incorporated in the SWEDEHEART registry from the Swedish population register, which includes information on the vital status of all Swedish residents. Data on cause of death were obtained from the mandatory Cause-of-Death Register. Cardiovascular

Table 1 Clinical Characteristics of the MINOCA Patients With and Without a New MI During Follow-Up

	MINOCA Without New MI	MINOCA With New MI	*P*-Value
Total, n	8522	570	
Demographics			
Female (%)	62.2	59.1	.14
Age, y (±SD)	65.4 ± 11.5	67.0 ± 11.2	.001
Risk factors (%)			
Smoking			
Current	18.6	19.1	.37
Previous	30.0	32.6	
Diabetes	10.9	16.1	< .001
Hypertension	40.2	45.3	.04
Medical history, %			
Cancer	2.0	1.6	.47
COPD	8.2	10.4	.07
Dementia	0.2	0.2	.86
MI	6.	15.1	< .001
PVD	1.8	2.5	.29
Stroke	5.5	5.1	.70
ECG findings (%)			
ST-elevation	16.3	16.1	.20
ST-depression	15.7	19.1	
T wave abnormalities	12.9	12.1	
Laboratory findings			
Creatinine, μmol/L (±SD)	80.4 ± 35.9	87.0 ± 73.3	< .001
CRP mg/L (IQR)	5.0 (2.9-10.0)	5.0 (3.0-10.0)	.10
LDL cholesterol, mmol/L (±SD)	3.1 ± 1.0	3.0 ± 1.0	.10
Total cholesterol, mmol/L (±SD)	5.1 ± 1.2	5.1 ± 1.2	.41
LVEF (%)			
≥50%	55.5	46.7	.01
40%-49%	12.5	11.9	
30%-39%	6.8	7.5	
<30%	3.3	2.1	
Unknown	22.0	31.8	
Medication at discharge (%)			
Aspirin	89.0	91.2	.07
Other antiplatelets	68.1	67.0	.70
ACE-inhibitors or ARB	61.1	63.2	.04
Beta-blockers	82.3	83.5	.33
Statin	83.3	82.8	.89

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; ECG = electrocardiography, IQR = interquartile range; LDL = low-density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MINOCA = myocardial infarction with nonobstructive coronary arteries; PVD = peripheral vascular disease.

All data are from the first hospitalization.

The *P*-value describes the difference between MINOCA patients with and without new MI.

death was defined as ICD-10 codes I00-I78. Data on myocardial infarction (I21-I23) were obtained from the National Patient register, including all ICD codes from all hospital admissions in Sweden.

Follow-Up

Follow-up data became available by merging data from the Cause-of-Death Register and the National Patient Register with the SWEDEHEART registry. The merging was performed at the National Board of Health and Welfare based on the personal identification number that all permanent residents of Sweden have. Survival was monitored from the first MINOCA admission until December 31, 2013, with a mean follow-up of 52 months.

According to Swedish law, all patients must be informed about their participation in the registry and that they have the right to decline, but there is no oral or written consent. The study was approved by the Regional Ethical Review Board in Stockholm (2012/60-31/2).

Statistics

Normally distributed continuous variables are presented as mean ± standard deviation (SD). Not normally distributed continuous variables are presented as median and

Table 2 Clinical Characteristics of the 340 Patients Who Underwent Coronary Angiography and the 230 Who Did Not

	New MI Without Coronary Angiography	New MI With Coronary Angiography	*P*-Value
Total, n	230	340	
Demographics			
Female (%)	65.2	55.0	.02
Age, y (±SD)	71.9 ± 11.7	67.2 ± 10.6	< .001
Risk factors (%)			
Smoking			
Current	9.1	17.9	< .001
Previous	34.8	40.9	
Diabetes	22.2	21.5	.70
Hypertension*	46.1	44.7	.02
Medical history, %*			
Atrial fibrillation	25.2	15.0	.002
Cancer	1.7	1.5	.80
COPD	14.8	7.4	.004
Dementia	0	0.3	.41
MI	20.9	11.2	.003
PVD	2.6	2.4	.85
Stroke	5.2	5.0	.91
ECG findings (%)			
ST-elevation	6.5	20.0	< .001
ST-depression	23.5	13.5	
T-wave abnormalities	10.4	11.5	
Laboratory findings*			
Creatinine, μmol/L (±SD)	96.2 ± 112.6	80.8 ± 21.2	.02
CRP mg/L (IQR)	5.0 (3.0-10.0)	5.0 (3.0-9.0)	.41
LDL cholesterol, mmol/L (±SD)	2.9 ± 1.0	3.0 ± 1.0	.13
Total cholesterol, mmol/L (±SD)	4.9 ± 1.2	5.1 ± 1.2	.13
LVEF (%)*			
≥50%	46.1	47.1	.34
40%-49%	10.9	12.6	
30%-39%	5.2	9.1	
<30%	2.2	2.1	
Unknown	35.6	29.2	
Medication at discharge, %*			
Aspirin	89.6	92.4	.50
Other antiplatelets	62.2	70.3	.06
ACE-inhibitors or ARB	63.5	62.9	.72
Beta-blockers	80.4	85.6	.17
Statin	75.7	87.6	.001

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; ECG = electrocardiography; IQR = interquartile range; LDL = low-density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PVD = peripheral vascular disease.

*Data from the first hospitalization.

The *P*-value describes the difference between patients with and without new MI.

interquartile range (IQR). The Students' *t* test was used for comparison of normally distributed data, and the Mann-Whitney *U* test was used for not normally distributed data. The categorical variables are presented as frequency values, and comparisons were made using the chi-squared test.

In order to identify independent clinical characteristics associated with the presence of obstructive CAD, multivariable logistic regression analyses were performed. A model containing all factors associated in univariate analysis with the presence of CAD (sex, diabetes, peripheral vascular disease, previous MI, ST elevation, creatinine, and statin) was used. Odds ratios (OR) with corresponding 95% confidence intervals (CI) are reported. Log-rank test (Mantel-Cox) was used to identify differences in mortality between patients with and without a new coronary angiogram, as well as for patients with a new MINOCA and patients with MI and obstructive CAD.

Time to readmission was analyzed as both a continuous and categorical variable (0-12 months, 12-24 months, 24-48 months, 48-60 months, and >60 months) to identify potential nonlinear associations with the development of obstructive CAD.

All statistical tests are 2-tailed and $P < .05$ is regarded as statistically significant. Data analyses are performed using SAS Software Version 9.4 (SAS Institute, Cary, NC) and the Predictive Analytical SoftWare (PASW statistics 17.03) program (SPSS Inc, Chicago, Ill).

RESULTS

A total of 570 (6.3%) patients of 9092 MINOCA patients suffered a new MI during follow-up. The median time to readmission was 17 months (IQR 5-39 months). The median follow-up time after the readmission was 38 months (IQR 18-64 months).

The clinical characteristics at the index admission for MINOCA of the 570 patients with a new MI and the 8522 patients without a new MI during follow-up, are shown in Table 1. Patients with a recurrent MI were older, suffered more often of diabetes, hypertension, previous MI, and higher levels of creatinine. At admission for the recurrent MI, 14.6% of the patients had ST-segment elevation, 17.5% had ST-segment depression, 11.1% had T-wave changes, 35.3% had no ischemic ST-T changes, and 21.5% had other or unknown ECG changes.

Coronary Angiography

Of the 570 patients with a new MI, 340 (59.6%) patients underwent new coronary angiography. These patients were more likely to be younger, men, current smokers, presenting with ST elevation, statin users with lower levels of creatinine, and less likely to have atrial fibrillation, hypertension, repeated previous MIs, and chronic obstructive pulmonary disease compared with patients who did not have new coronary angiography performed (Table 2).

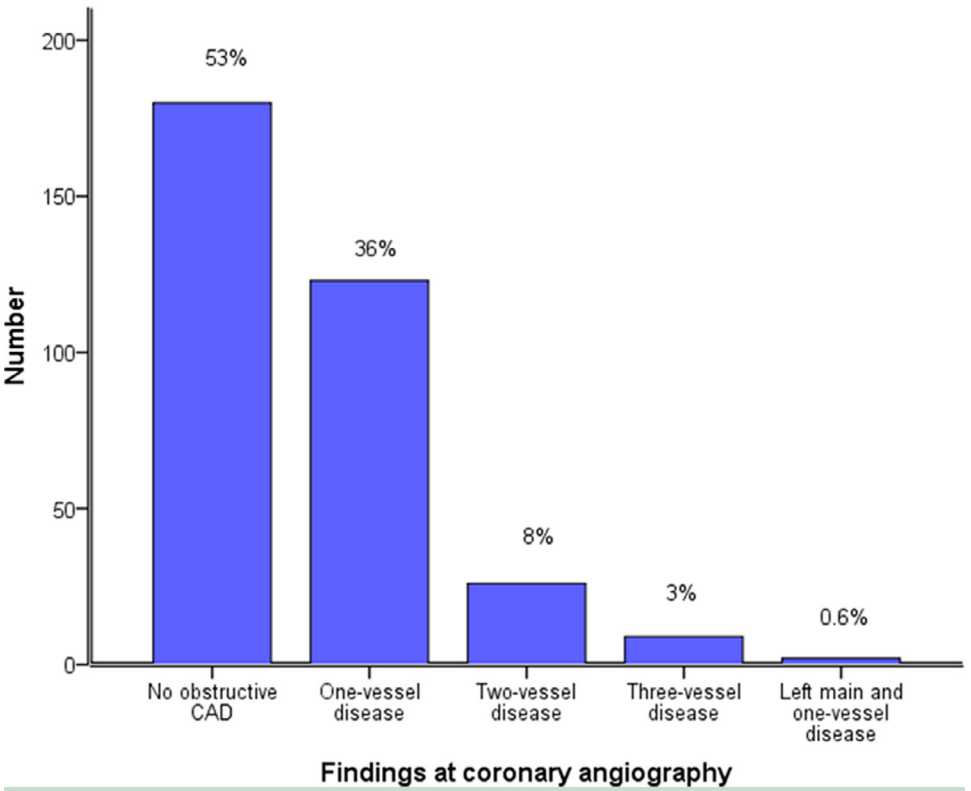

Figure 2 Findings at coronary angiography.

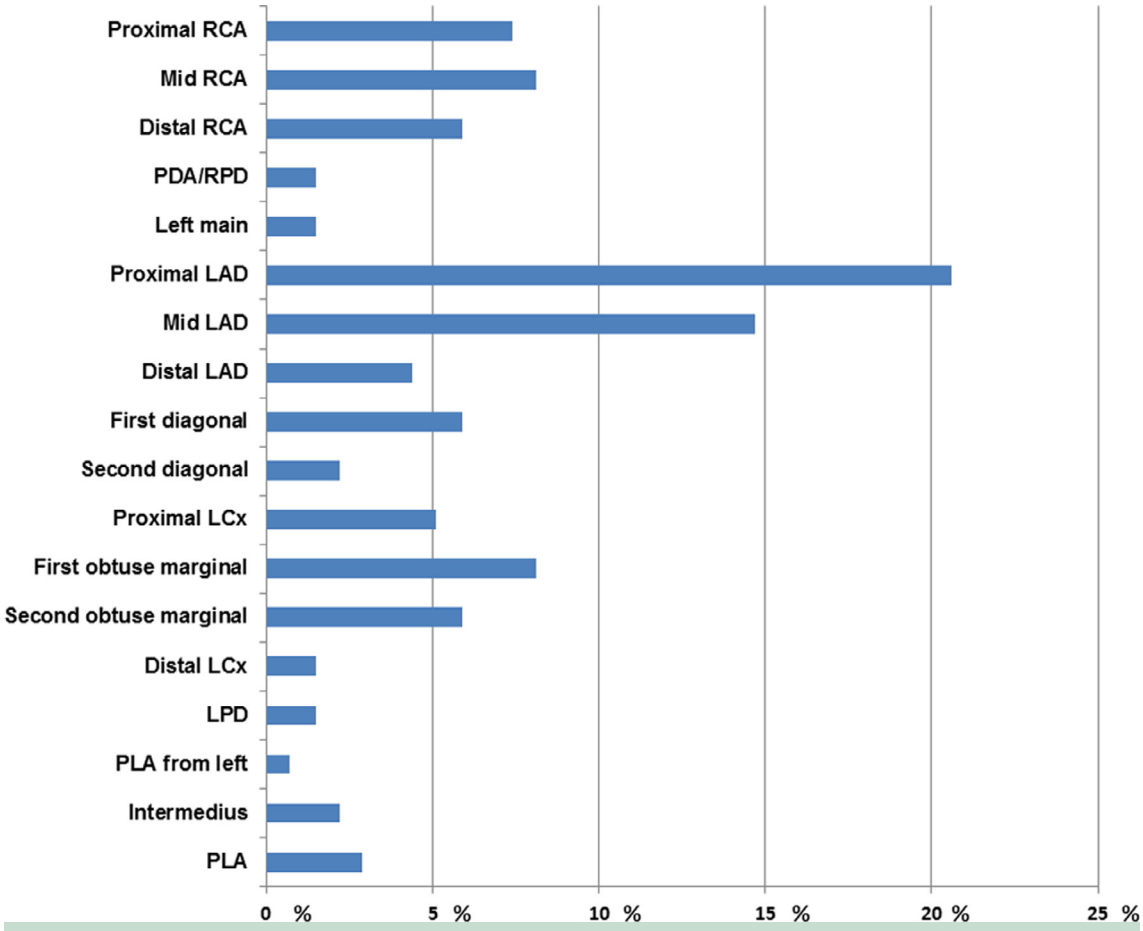

Figure 3 Coronary angiography findings of obstructive CAD at segment level. Numbers are in percent values. CAD = coronary artery disease; LAD = left anterior descending artery; LCx = left circumflex artery; PDA = posterior descending artery; RCA = right coronary artery; RPD = right posterior descending artery.

The median time to readmission for the new MI for patients with a new coronary angiogram was 23 months (IQR 11-43), compared with 10 months (IQR 1-26) for patients without a new coronary angiogram ($P < .001$).

Coronary angiography revealed that 160 of the patients (47%) had obstructive CAD with a diameter stenosis ≥50%, and the remaining 180 patients (53%) had nonobstructive coronary arteries, that is, a recurrent MINOCA.

Of the 160 patients with obstructive CAD, 123 had 1-vessel, 26 had 2-vessel, 9 had 3-vessel disease, and 2 had left main together with 1-vessel disease at the time for the new MI (Figure 2). Information about occlusions was available in 136 patients: 33.8% (46/136) patients had an occlusion and 66.2% (90/136) had not. Of 46 patients with an occluded coronary artery, 67.4% (31/46) had an initial ST-elevation on ECG.

The locations of the stenosis at segment level were known in 136 patients; 47.8% of the stenoses affected left anterior descending coronary artery segments, 25.8% right coronary artery segments, and 22.8% left circumflex artery segments (Figure 3). The classification of the stenosis, available in 134 patients, is presented in Figure 4.

The median time to readmission was 23 months (IQR 9-43) for patients with MI and obstructive CAD and 24 months (IQR 11-43) for patients with a new MINOCA. When the time to readmission was categorized into 6 different time periods, the proportion of coronary angiographies revealing obstructive CAD and recurrent MINOCA was similar regardless of the time passed ($P = .94$) (Figure 5).

The majority (67%) of the patients with a new MINOCA were women, whereas the majority (58%) of patients with MI and obstructive CAD was men (Table 3). Diabetes, peripheral vascular disease, higher levels of creatinine, and ST elevation at presentation were more common in patients with MI and obstructive CAD than in patients with new MINOCA. Patients with a new MINOCA were more likely to have had repeated previous MIs. In a multivariate logistic regression model, male sex (OR 2.1; 95% CI, 1.2-3.5), diabetes (OR 2.0; 95% CI, 1.1-3.7), and ST elevation at presentation (OR 8.0; 95% CI, 3.6-17.8) remained associated with the presence of obstructive CAD, while repeated previous MIs were associated with lower likelihood of obstructive CAD at the time of the new MI (OR 0.29; 95% CI, 0.1-0.8).

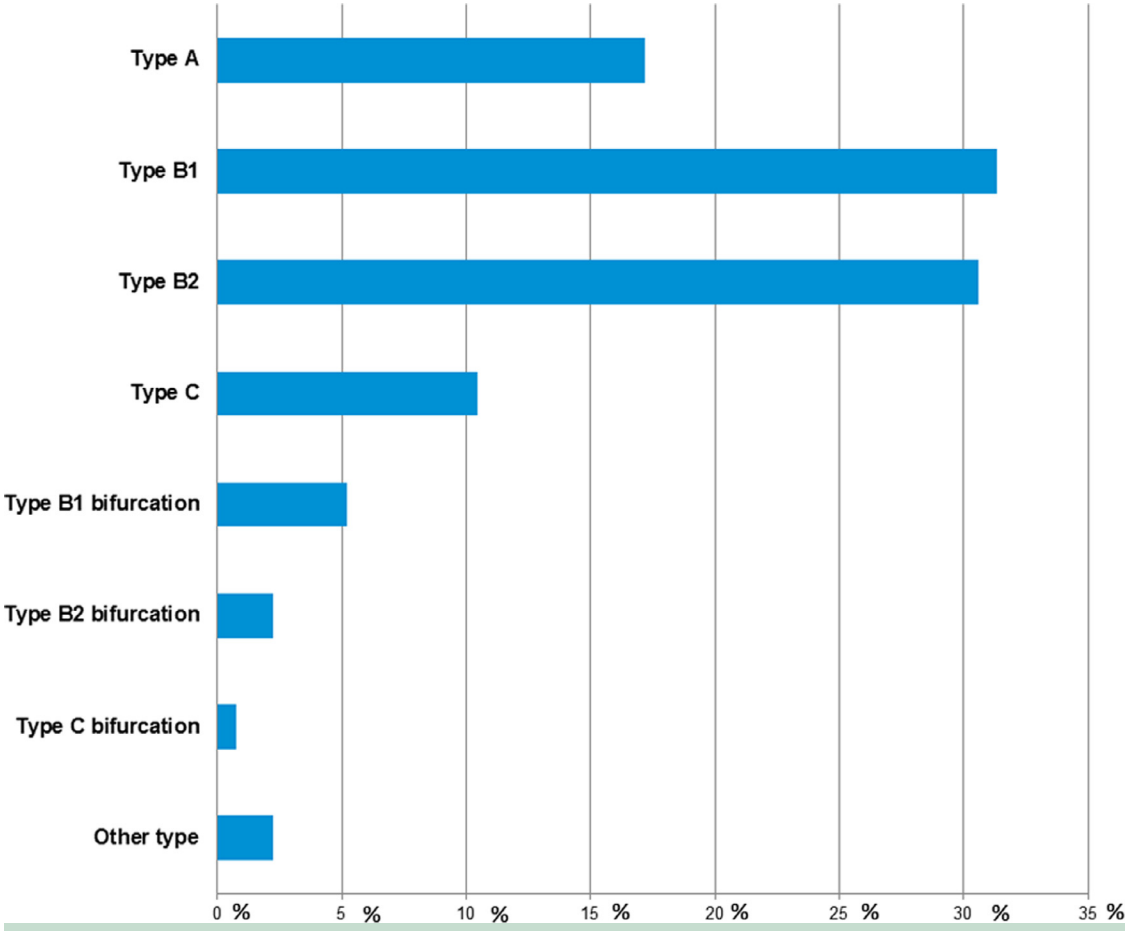

Figure 4 Classification of stenoses.

Prognosis

A total of 21.6% (123/570) of the MINOCA patients with a new MI died during follow-up, and 49.6% (61/123) of the deaths were cardiovascular. The all-cause mortality rate was 34.3% (79/230) among patients without a new coronary angiography and 12.9% (44/340) among patients with a new coronary angiography ($P < .001$) (Figure 6A).

A total of 13.9% (25/180) of patients with a new MINOCA and 11.9% (19/160) of patients with MI and obstructive CAD died ($P3 = .74$) (Figure 6B). Cardiovascular death affected 5.6% (10/180) of MINOCA patients and 7.5% (12/160) of patients with MI and obstructive CAD ($P = .39$).

DISCUSSION

This is the first study investigating the status of the coronary arteries in recurrent MI in patients with previous MINOCA and providing information about the prognosis after a new episode of MINOCA. This nationwide study of >9000 patients with MINOCA contains, therefore, several novel and important findings relevant to clinical practice. A new MI occurred in 6% of the original MINOCA patients during a mean follow-up of 4.3 years. Almost half of the patients had developed significant CAD at the time of the new MI, most often 1-vessel disease. The mortality during follow-up was not statistically different between those with a new episode of MINOCA and those with significant CAD at the time of new MI.

Recurrent MI

Recurrent MI occurred in 6.3% of the patients during follow-up. The new MI occurred after a mean of approximately 1.5 years from the index event. Previous studies have demonstrated a 1-year re-infarction rate in MINOCA patients of 1.2%-3.6%[7,11,15] and a 2-year re-infarction rate of 4.3%.[6] The 2.4% 1-year incidence of recurrent MI in the present study is twice as high as in a pooled analysis of 3 Thrombolysis in Myocardial Infarction (TIMI) trials[7] and one-third lower than the 3.6% in the ACUITY trial.[15] The differences may be due to our nationwide inclusion of consecutive MINOCA patients and our reliable system for event capture, whereas both the comparing cohorts may be influenced by selection due to predetermined inclusion and exclusion criteria as well as biased by the knowledge that the first event was MINOCA.

Unfortunately, our data did not permit subdivision of the MINOCA patients into those with normal coronary arteries

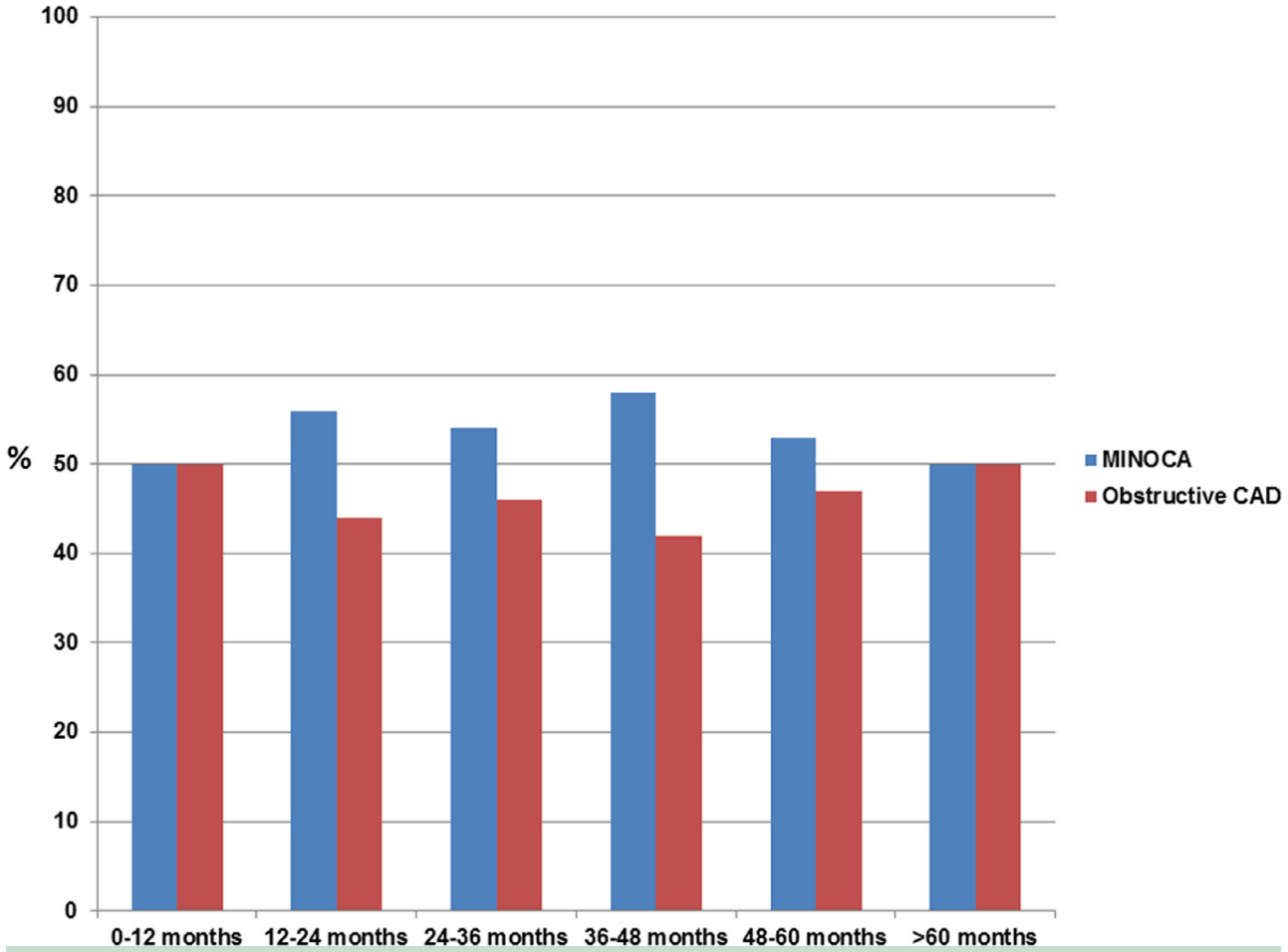

Figure 5 Findings at coronary angiography stratified according to time between the index MINOCA event and the reinfarction. CAD = coronary artery disease; MINOCA = myocardial infarction with nonobstructive coronary arteries.

(0% stenosis) and mild CAD (>0% to <50%). The study by Bainey et al[22] comparing MINOCA patients with normal coronary arteries with MINOCA patients with mild CAD, however, showed significantly higher rates of 1-year death and recurrent MI among the latter group.

An unexpected finding was that patients who had MINOCA at the time of the new MI, compared with those that had developed obstructive CAD, had a history of previous MI at the time of the index MI 3 times as often (Table 2). One may contemplate whether the lack of a specific underlying diagnosis in the MINOCA patients may have led to underutilization of secondary prevention medications for MI.

Coronary Angiography

Only 60% of the patients with a new MI underwent a new coronary angiography. Use of coronary angiography at the time of the recurrent event was associated with clinical characteristics such as younger age, male sex, and ST elevation. Patients who had a longer time to recurrent MI were more likely to undergo angiography, but among those undergoing angiography, the time passed between the index MINOCA event and the new MI did not seem to influence the occurrence of CAD to any great extent.

Coronary angiography at the time of the new MI revealed obstructive CAD (ie, ≥50% diameter stenosis or occlusive) in approximately half of the patients. One-vessel disease, with uncomplicated stenoses of type A or type B1 and B2 affecting the segments of the left anterior descending artery proved to be most common. Most likely this finding represents atherosclerotic progression, but it might also in some cases be due to recurrent spasm where the spasm may have resolved by the time of the first angiography in the first MINOCA event and not by the time of the second angiogram. Meticulous comparisons of changes in the grade of stenosis between the 2 admissions are, unfortunately, not possible. This finding merits further study.

Prognosis

Approximately 22% of the MINOCA patients with a reinfarction died during follow-up, and half of the deaths were

Table 3 Clinical Characteristics of the Patients With and Without Obstructive CAD at Coronary Angiography

	New MINOCA with <50% Stenosis	New MI with ≥50% Stenosis	*P*-Value
Total, n	180	160	
Demographics			
Female (%)	66.7	41.9	< .001
Age, y (±SD)	67.4 ± 10.1	67.0 ± 11.2	.38
Risk factors (%)			
Smoking			
Current	18.3	17.5	.92
Previous	42.2	39.4	
Diabetes	15.6	28.1	.01
Hypertension*	46.7	42.5	.44
Medical history,% *			
Cancer	0.6	2.5	.14
COPD	8.9	5.6	.25
Dementia	0	0.6	.29
MI	12.2	4.4	.006
PVD	0.6	4.4	.02
Stroke	4.4	5.6	.62
ECG findings (%)			
ST-elevation	7.8	33.8	< .001
ST-depression	15.0	11.9	
T-wave abnormalities	12.8	10.8	
Laboratory findings*			
Creatinine, μmol/L (±SD)	78.2±19.6	83.8±22.6	.02
CRP mg/L (IQR)	5.0 (2.3-9.0)	5.0 (3.0-10.0)	.34
LDL cholesterol, mmol/L (±SD)	2.7 ± 1.0	3.0 ± 1.0	.30
Total cholesterol, mmol/L (±SD)	5.1 ± 1.2	5.1 ± 1.2	.93
LVEF (%)			
≥50%	53.9	46.3	.26
40%-49%	10.6	15.6	
30%-39%	6.7	6.9	
<30%	1.7	3.8	
Unknown	27.3	27.5	
Medication at discharge* (%)			
Aspirin	91.7	93.1	.61
Other antiplatelets	63.9	77.5	.005
ACE-inhibitors or ARB	62.8	63.1	.58
Beta-blockers	85.0	86.3	.64
Statin	82.8	93.1	.004

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; ECG = electrocardiography; IQR = interquartile range; LDL = low-density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PVD = peripheral vascular disease.

*At the first hospitalization.

cardiovascular. Both the all-cause mortality and the cardiovascular mortality were considerably higher among patients who did not undergo a new coronary angiography compared with patients who did. The higher mortality rate may partly be explained by older age and more comorbidities in the conservatively managed group.

Surprisingly, mortality was equally high after recurrent MINOCA, as compared with MI and obstructive CAD after an initial MINOCA event. Our previous SWEDEHEART-based study, as well as other studies, have demonstrated a significantly higher mortality rate in MI and obstructive CAD patients compared with MINOCA patients.[5] However, in contrast to the previous studies, the present work studied the prognosis of MINOCA patients only after a reinfarction. The results strengthen the understanding that MINOCA, and especially repeated episodes of MINOCA, is in no way a harmless disease.[4,6,7,10–12,15]

Limitations

Our study has some limitations that need to be considered. MINOCA patients form a heterogeneous group, consisting of subgroups with different underlying pathophysiological mechanisms such as plaque rupture, coronary artery spasm, coronary dissection, thrombosis with spontaneous induced thrombolysis, type 2 MI, and clinically unrecognized

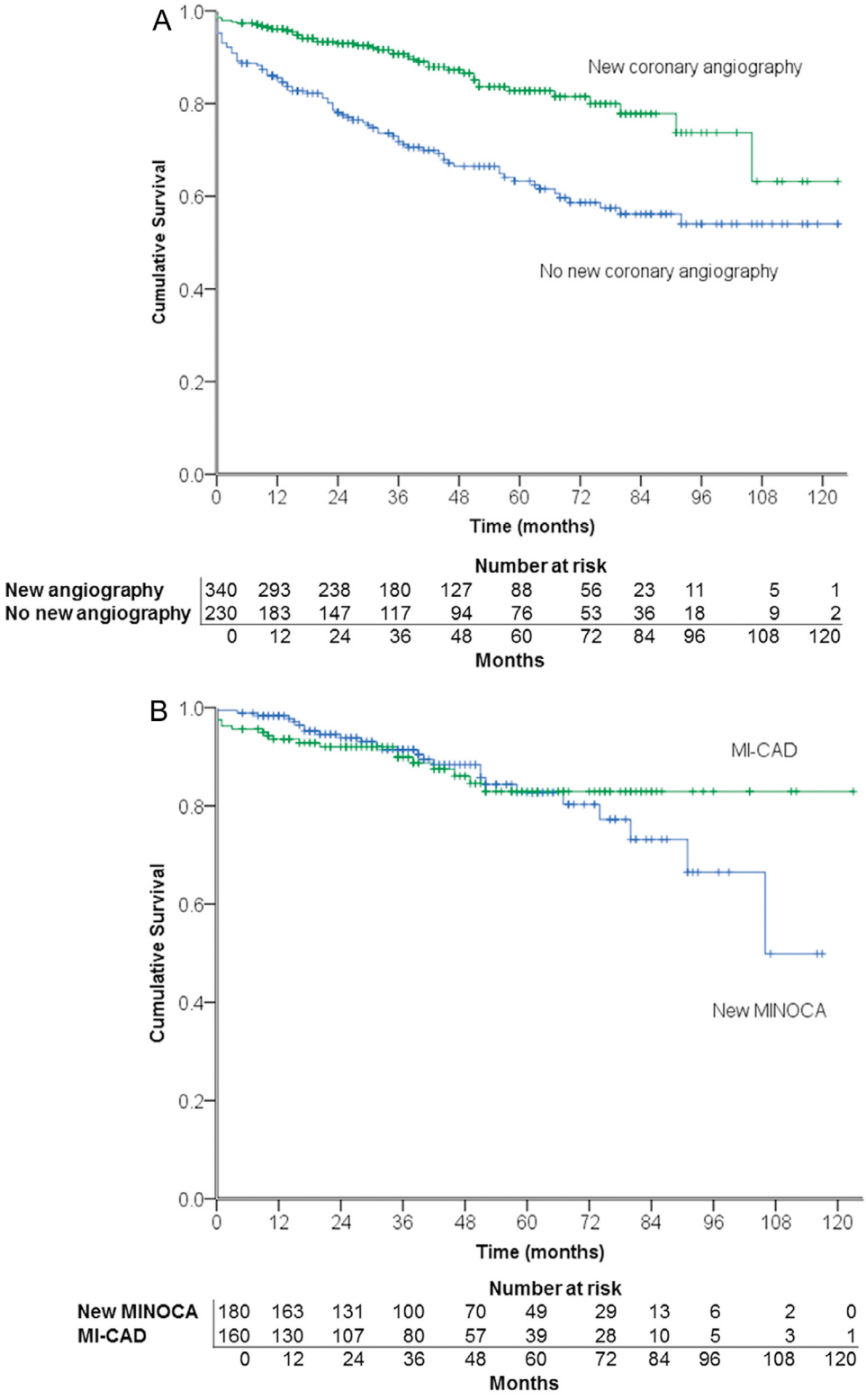

Figure 6 Cumulative survival. **(A)** Cumulative survival for patients with and without a new coronary angiography illustrated with Kaplan-Meier curves, $P < .001$. **(B)** Cumulative survival for patients with MI-CAD and patients with a new MINOCA illustrated with Kaplan-Meier curves, $P = .74$. MI-CAD = myocardial infarction with coronary artery disease; MINOCA = myocardial infarction with nonobstructive coronary arteries.

myocarditis or takotsubo syndrome.[23] Any results of investigations scheduled or performed after the initial hospitalization that may have changed the initial MINOCA diagnosis (eg, cardiac magnetic resonance imaging) are not registered in SWEDEHEART and thus, unknown. There might be some cases of takotsubo syndrome in the cohort, wrongly given the diagnosis of MI, especially during the first years of the study period where the awareness of this condition was limited.

All data concerning findings at coronary angiography emerges from the SWEDEHEART registry, in which all data about the coronary angiography are entered by the local operator. The coronary angiograms were thus evaluated locally at each hospital and not at a core laboratory. Unfortunately, the data available do not permit separation of patients into those with normal coronary arteries without any signs of atherosclerosis and those with signs of minor atherosclerotic lesions but no stenosis of ≥50%. We also lack sufficient information on the results of any additional examinations such as fractional flow reserve, optical coherence tomography, intravascular ultrasound, provocative testing for coronary reactivity and spasm, and left ventricular angiography.

The study was unable to demonstrate a difference in mortality during follow-up between those with a new episode of MINOCA and MI and obstructive CAD. However, the power to detect a significant difference was low due to the limited number of events. This finding must therefore be interpreted with caution.

Clinical Implications

Because almost half of the patients with reinfarction after MINOCA who underwent coronary angiography had progression of coronary stenosis, a review of risk factors for CAD should be considered for all patients with MINOCA. In addition, coronary angiography should be strongly considered in patients readmitted with MI after MINOCA.

The prognosis, in terms of all-cause death, in patients with previous MINOCA readmitted due to new MI, is poor. The adverse prognosis was most pronounced in the patients selected for a conservative, noninvasive, strategy. Additionally, the prognosis after the new MI did not differ between patients with MI and obstructive CAD and a new MINOCA. There are currently no published randomized trials of treatments aiming at improving the prognosis for patients with MINOCA. Hence, randomized trials of secondary prevention after MINOCA are urgently needed. However, in the meantime, intense treatment for traditional risk factors seems reasonable because the predictors for adverse outcome are mostly similar after MINOCA as for MI, with obstructive CAD[16] and an observational study has suggested beneficial effects of statins and renin-angiotensin system receptor blockers.[17]

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