

SUPPLEMENTAL MATERIAL

Table S1. Sex-specific comparison of sociodemographic and clinical profile of patients with MINOCA.

	MINOCA N= 299	
	Women N=269 (%)	Men N=30 (%)
Demographics		
Age, in years; Median (IQR)	46.0 (40.0 – 51.0)	47.0 (41.0 – 52.0)
White	179 (66.5%)	24 (80.0%)
Hispanic origin	26 (9.7%)	5 (16.7%)
Risk Factors – Conventional		
Hypertension	148 (55.0%)	16 (53.3%)
Diabetes	50 (18.6%)	2 (6.7%)
Dyslipidemia	147 (54.6%)	17 (56.7%)
Smoking in past 30 days	091 (33.8%)	12 (40.0%)
Obesity	114 (42.4%)	12 (40.0%)
Family history of CAD	168 (62.4%)	16 (53.3%)
Any of above cardiac risk factor	246 (91.4%)	27 (90.0%)
Stroke/TIA	9 (3.3%)	0 (0.0%)
Prior AMI	32 (11.9%)	5 (16.7%)
Congestive heart failure	12 (4.5%)	1 (3.3%)
Prior angina	59 (22.0%)	4 (13.3%)
Risk Factors - Unconventional		
Depression	77 (29.5%)	6 (20.7%)
Perceived Stress; Median (IQR)	26.0* (20.0 – 33.0)	21.0 (13.0 – 27.0)
Cocaine Use	17 (6.3%)	1 (3.3%)
Hypercoagulability Syndrome	9 (3.3%)	0 (0.0%)
Venous thromboembolism	10 (3.7%)	1 (3.3%)
Autoimmune disease	12 (4.5%)	0 (0.0%)
Renal dysfunction	25 (9.3%)	2 (6.7%)
Thyroid conditions	28 (10.4%)	1 (3.3%)
Diagnosis		
Pre-hospital ECG	60 (22.4%)	4 (13.3%)
Discharge diagnosis		
STEMI	58 (21.6%)	6 (20.0%)
NSTEMI	211 (78.4%)	24 (80.0%)
Length of Hospital Stay, in days; Median (IQR)	3.0 (2.0 – 4.0)	2.0 (2.0 – 4.0)
Severity of Disease		
Peak troponin; Median (IQR)	3.3 (1.1 – 11.0)	3.3 (1.1 – 10.3)
Ejection fraction <40%	27 (10.1%)	2 (6.7%)
Interventions		
PCI	29 (10.8%)	5 (16.7%)
CABG	5 (1.9%)	0 (0.0%)
AICD	4 (50.0%)	0 (0.0%)
Discharge Management (of eligible patients)		
Aspirin	238 (93.3%)	28 (96.5%)
Beta blockers	188 (84.7%)	25 (96.1%)
ACE inhibitors or ARB	120 (50.0%)	14 (51.8%)

Statin	180 (72.6%)	22 (81.5%)
Cardiac rehabilitation		
Referred on discharge	88 (32.7%)	9 (30.0%)
Reported referral at 1-month post-AMI follow-up	116 (47.4%)	11 (39.3%)

- p values not calculated given low numbers in this group

IQR: Interquartile Range; CAD: Coronary Artery Disease; AMI: Acute Myocardial Infarction; PAD: Peripheral Arterial Disease; TIA: Transient Ischemic Attack; PCI: Percutaneous Intervention; CABG: Coronary Artery Bypass Graft; AICD= automatic implantable cardioverter-defibrillator; ACE inhibitor: Angiotensin Converting Enzyme inhibitor; ARB: Angiotensin Receptor II Blocker; STEMI: ST-Elevation Myocardial Infarction; NSTEMI: Non-ST Elevation Myocardial Infarction; ECG: Electrocardiogram; MI-CAD: Myocardial Infarction due to Coronary Artery Disease; MINOCA: Myocardial Infarction with Non-Obstructive Coronary Arteries;

Table S2. Sequential Linear Regression Results for the Relationship Between Type of MI (MINOCA or MI-CAD) and Quality of life at 12-months.

Model Number	Quality of Life at 12-months (95% CI)	P values	Covariates Included in the Model
1	3.41 (0.29, 6.54)	0.0322 (unadjusted)	Type of AMI (MINOCA vs MICAD)
2	5.71 (2.62, 8.81)	0.0003 (above plus sociodemographics)	Type of AMI, age, sex, race, ethnicity, marital status
3	4.87 (1.85, 7.90)	0.0016 (above plus socioeconomics)	Type of AMI, age, sex, race, ethnicity, marital status, education level, employment status, insurance status
4	4.03 (0.90, 7.15)	0.0115 (above plus cardiac risk factors)	Type of AMI, age, sex, race, ethnicity, marital status, education level, employment status, insurance status, current smoking, hypertension, diabetes, dyslipidemia, obesity
5	3.81 (0.69, 6.93)	0.0167 (above plus other cardiovascular illnesses)	Type of AMI, age, sex, race, ethnicity, marital status, education level, employment status, insurance status, current smoking, hypertension, diabetes, dyslipidemia, obesity, prior AMI, prior stroke/TIA, prior angina, prior revascularization, peripheral arterial disease, congestive heart failure, renal dysfunction
6	4.05 (0.96, 7.13)	0.0102 (above plus noncardiac illnesses)	Type of AMI, age, sex, race, ethnicity, marital status, education level, employment status, insurance status, current smoking, hypertension, diabetes, dyslipidemia, obesity, prior AMI, prior stroke/TIA, prior angina, prior revascularization, peripheral arterial disease, congestive heart failure, renal dysfunction, COPD, autoimmune conditions, history of illicit drug use, history of depression or cancer.
7	4.06 (0.91, 7.21)	0.0115 (above plus severity of MI)	Type of AMI, age, sex, race, ethnicity, marital status, education level, employment status, insurance status, current smoking, hypertension, diabetes, dyslipidemia, obesity, prior AMI, prior stroke/TIA, prior angina, prior revascularization, peripheral arterial disease, congestive heart failure, renal dysfunction, COPD, autoimmune conditions, history of illicit drug use, history of depression or cancer, peak troponin, grace score, STEMI, reduced ejection fraction.
8	3.08 (0.11, 6.27)	0.0586 (above plus psychosocial factors)	Type of AMI, age, sex, race, ethnicity, marital status, education level, employment status, insurance status, current smoking, hypertension, diabetes, dyslipidemia, obesity, prior AMI, prior stroke/TIA, prior angina, prior revascularization, peripheral

			arterial disease, congestive heart failure, renal dysfunction, COPD, autoimmune conditions, history of illicit drug use, history of depression or cancer, peak troponin, grace score, STEMI, reduced ejection fraction, baseline SAQ angina frequency, baseline perceived stress score.
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Abbreviations: CI, Confidence Interval; AMI, Acute Myocardial Infarction; MINOCA, Myocardial infarction with no obstructive coronary artery; MI-CAD, myocardial infarction with coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; STEMI, ST-elevation myocardial infarction; SAQ, Seattle Angina Questionnaire; STEMI, ST-elevation myocardial infarction

Table S3. Risk Factor Profile and Clinical Characteristics in Patients with MINOCA and a) history of heart failure and b) low ejection fraction (<40%).

	History of congestive heart failure		Reduced Ejection Fraction during Index Hospitalization	
	N (N = 283)	Y (N = 13)	No (N = 266)	Yes (N = 29)
Median age in years (IQR)	46.0 (40.0 – 51.0)	50.0 (41.0 – 52.0)	46.0 (40.0 – 51.0)	50.0 (41.0 – 54.0)
Women	255 (90.11%)	12 (92.31%)	239 (89.85%)	27 (93.10%)
Race				
Black / African American	62 (21.91%)	7 (53.85%)	61 (22.93%)	7 (24.14%)
White / Caucasian	195 (68.90%)	5 (38.46%)	179 (67.29%)	21 (72.41%)
Other	14 (9.19%)	1 (7.69%)	26 (8.78%)	1 (3.45%)
Hispanic	29 (10.25%)	2 (15.38%)	29 (10.90%)	2 (6.90%)
Hypertension	149 (52.65%)	13 (100.00%)	143 (53.76%)	18 (62.07%)
Diabetes	41 (14.49%)	10 (76.92%)	42 (15.79%)	8 (27.59%)
Dyslipidemia	151 (53.36%)	11 (84.62%)	142 (53.38%)	19 (65.52%)
Current smoker	99 (34.98%)	4 (30.77%)	92 (34.59%)	11 (37.93%)
Obese	115 (40.64%)	9 (69.23%)	114 (42.86%)	10 (34.48%)
Troponin maximum Median (IQR)	3.5 (1.3 – 11.1)	1.0 (0.2 – 1.2)	3.4 (1.2 – 10.5)	1.7 (1.0 – 31.5)

IQR: Interquartile range

Table S4. Clinical Characteristics and Outcomes in patients with MI-CAD versus indeterminate cause (Class V).

	Obstructive CAD N=2,411 (89.8%)	Indeterminate Cause N=17 (0.6%)
Demographics		
Age, in years; Median (IQR)	48 (44, 52)	50 (44, 52)
Women	1,574 (65.3)	15 (88.2)
White	1,853 (76.9)	9 (52.9)
Hispanic origin	175 (7.3)	1 (5.9)
Risk Factors – Conventional		
Hypertension	1,608 (66.7)	12 (70.6)
Diabetes	752 (31.2)	3 (17.7)
Dyslipidemia	1,676 (69.5)	13 (76.5)
Smoking in past 30 days	1,440 (59.8)	9 (52.9)
Obesity	1,296 (53.8)	7 (41.2)
Family history of CAD	1,804 (74.9)	12 (70.6)
Stroke/TIA	112 (4.7)	3 (17.7)
Prior AMI	523 (21.7)	8 (47.1)
Congestive heart failure	107 (4.4)	1 (5.9)
Severity of Disease		
Peak troponin; Median (IQR)	7.7 (1.6, 29.7)	3.4 (1.0, 12.7)
Ejection fraction <40%	273 (11.7)	0 (0)
Discharge diagnosis		
STEMI	1,257 (52.1)	3 (17.7)
NSTEMI	1,154 (47.9)	14 (82.4)
Interventions		
PCI (of patients eligible n=1,139)	1,050 (93.3)	0 (0)
CABG	253 (10.6)	0 (0)
Pacemaker (of patients eligible n=50)	26 (63.4)	0 (0)
Defibrillator (of patients eligible n=47)	14 (36.8)	1 (100)
Discharge Management		
Aspirin	2,351 (98.7)	17 (100)
Beta blockers	2,253 (98.3)	13 (92.9)
ACE inhibitors or ARB	1,594 (73.2)	9 (52.9)
Statin	2,284 (96.7)	16 (100)
Cardiac rehab		
Referred on discharge	1,171 (48.6)	4 (23.5)
Reported referral at 1-month post-AMI follow-up	1,438 (65.3)	5 (33.3)
Outcomes		
Mortality; N(%)		
In-hospital mortality	4 (0.2)	0 (0)
1-month mortality	14 (0.6)	0 (0)
12-months mortality	53 (2.3)	0 (0)

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Figure S1. Flow of patients through the VIRGO study.

