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ORIGINAL RESEARCH

Characteristics of Young Women Presenting With Acute Myocardial Infarction: The Prospective, Multicenter, Observational Young Women Presenting Acute Myocardial Infarction in France Study

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BACKGROUND: The percentage of women <50 years of age hospitalized with myocardial infarction is increasing. We describe the clinical, morphological, and biological characteristics, as well as the clinical outcomes of this population.

METHODS AND RESULTS: This prospective, observational study included consecutive women <50 years of age admitted for myocardial infarction at 30 centers in France (May 2017–June 2019). The primary outcome was the composite of net adverse clinical events: all-cause death, cardiovascular death, recurrent myocardial infarction, stent thrombosis, any stroke, or major bleeding occurring during hospitalization with a 12-month follow up. Three hundred fourteen women were included. The mean age was 43.0 (±5.7) years, 60.8% presented with ST-segment–elevation myocardial infarction, 75.5% were current smokers, 31.2% had a history of complicated pregnancy, and 55.1% reported recent emotional stress. Most (91.6%) women presented with typical chest pain. Of patients on an estrogen-containing contraceptive, 86.0% had at least 1 contraindication. Of patients with ST-segment–elevation myocardial infarction, 17.8% had myocardial infarction with nonobstructive coronary arteries and 14.6% had spontaneous coronary artery dissection, whereas 29.3% presented with multivessel vessel disease. During hospitalization, 11 net adverse clinical events occurred in 9 (2.8%) women, but no deaths or stent thromboses occurred. By 12 months, 14 net adverse clinical events occurred in 10 (3.2%) women; 2 (0.6%) died (from progressive cancer) and 25 (7.9%) had an ischemia-driven repeat percutaneous coronary intervention.

CONCLUSIONS: Most young women with myocardial infarction reported typical chest pain and had modifiable cardiovascular risk factors. History of adverse pregnancy outcomes and prescription of combined oral contraceptive despite a contraindication were prevalent, emphasizing the need for comprehensive cardiological and gynecological evaluation and follow-up.

REGISTRATION: URL: <https://www.clinicaltrials.gov>; Unique identifier: NCT03073447.

Key Words: acute coronary syndrome ■ cardiovascular risk ■ coronary artery disease ■ myocardial infarction ■ women

See Editorial by Gaalema et al.

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*A complete list of the WAMIF investigators can be found in the Supplemental Material.

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CLINICAL PERSPECTIVE

What Is New?

- In young women, the most frequent risk factor was tobacco use.
- History of adverse pregnancy outcomes and use of combined oral contraception despite contraindications were highly prevalent.

What Are the Clinical Implications?

- Eighty-six percent of women presenting with myocardial infarction have at least 1 standard modifiable cardiovascular risk factor. The WAMIF (Young Women Presenting Acute Myocardial Infarction in France) study defined precisely the axes of communication for prevention campaigns, as well as the areas of development of multidisciplinary collaboration to reverse the increasing burden of premature myocardial infarction in women.

Nonstandard Abbreviations and Acronyms

NACE net adverse clinical events

Cardiovascular disease is the leading cause of death in women.¹ The rate of in-hospital death after myocardial infarction (MI), although decreasing, remains substantially higher in women than in men, especially in women <50 years of age.^{2–4} Thirty-day death from MI decreased for both sexes, but to a lesser extent among women, from 9.8% in 1995 to 2.6% in 2010 in men, but remains higher in women all ages combined (23.7% to 9.8%, respectively).⁵ Whereas the risk of MI increases with age and in the presence of traditional cardiovascular risk factors such as hypertension and diabetes, the occurrence of MI in premenopausal woman is not exceptional, and the incidence is rising, from <10% in 1995 to >20% of all MI in 2010.² Little is known about the effect of hormonal status and therapies, and of high-risk inflammatory and thrombophilia profiles, on the risk of MI in young women.

The WAMIF (Young Women Presenting Acute Myocardial Infarction in France) study was established to provide a comprehensive, systematic description of the clinical and biological characteristics of women <50 years of age hospitalized with an MI, and to assess their in-hospital and 12-month prognosis.

METHODS

Trial Design and Oversight

The prospective, multicenter, observational WAMIF study ([ClinicalTrials.gov](https://clinicaltrials.gov); Identifier: NCT03073447)

was conducted from May 2017 to June 2019 at 30 public and private interventional cardiology centers in France. The study involved all consecutive adult women ≤50 years of age admitted for ST-segment-elevation MI (STEMI) or non-ST-segment-elevation MI (NSTEMI). The data that support the findings of this study are available from the corresponding author upon reasonable request.

The WAMIF Steering Committee designed the protocol and statistical analysis plan, conducted and monitored the trial, and performed the statistical analyses. The French Society of Cardiology funded the study. The study was approved by the Committee for the Protection of Persons of Île de France VI. Ethics committee approval was obtained at all participating institutions. The study was performed in accordance with the principles of the Declaration of Helsinki and of Good Clinical Practices. All participants provided informed consent.

Participants

Participants were women >18 and ≤50 years of age who were admitted for MI as a primary diagnosis, required coronary angiography, and were eligible to receive medical care. MI was defined according to the Third Universal Definition⁶ and completed by the Fourth.⁷ Exclusion criteria were iatrogenic infarction, namely type 4a and 5 myocardial infarction,⁷ death before hospitalization, other causes of thoracic pain syndrome with troponin elevation (eg, myocarditis, Takotsubo syndrome, sepsis), participation in another clinical study, and inability to understand the French language.

Data Collection

Management of MI, including the use of coronary angiography, complied with the European recommendations in place at the time.^{8,9} Routine biological samples were taken at admission, during hospitalization (≥24 hours after coronary angiography), and at discharge. A blood sample (60 mL) was taken during the index hospitalization to create a serum bank for immunological, genetic, and hormonal analyses.

Data were entered prospectively into an electronic case report form as original laboratory results. Information was collected on medical history according to the specified electronic Case Report Form including clinical and biological examinations, electrocardiograms, coronary angiography with or without percutaneous coronary intervention, coronary imaging, mammography, and arterial echo Doppler (carotid and lower limb). The results of invasive and noninvasive imaging (intravascular ultrasound, optical coherence tomography, cardiac and cerebral magnetic resonance imaging, echo Doppler) and coronary spasm provocation tests were collected at sites that routinely used these techniques. For

assessment of 12-month outcomes, a telephone interview with the patient or responsible medical team was conducted at 12 months to collect information on the occurrence of any net adverse clinical events (NACE). For any reported event, a medical report could have been obtained, and the event assessed.

Monitoring and audits, comprising checks on compliance with the research protocol and procedures, patient eligibility, and data accuracy and completeness, were performed by a clinical research associate appointed by the French Society of Cardiology. Monitoring took place at each site at least once during the study period.

Outcomes

The primary outcome was the composite of NACE, comprising all-cause death, cardiovascular death, recurrent MI, stent thrombosis, any stroke, or major bleeding occurring during hospitalization. Major bleeding was defined as a Bleeding Academic Research Consortium type 3 to 5 bleeding event.¹⁰

Other analyses included the frequency of the following nonatheromatous forms of MI: hematomas, spontaneous coronary dissections, and coronary spasms; the prevalence of cardiovascular risk factors, pathologies linked to inflammation or thrombophilia, systemic disease, and hereditary disorders; the influence of hormonal variables; and the occurrence of NACE during the period from hospital discharge to 12 months.

High-risk thrombophilic profile was defined as at least 1 positive result for double heterozygosity for factor V Leiden mutation G1691A and factor II/prothrombin gene mutations G20210A, or homozygosity for factor V Leiden mutation G1691A, or homozygosity for factor II/prothrombin gene mutations G20210A or confirmed deficiency in antithrombin or protein C, or protein S, or confirmed positive anticardiolipin antibody immunoglobulin G or immunoglobulin M or confirmed anti-beta 2 glycoprotein 1 immunoglobulin G or immunoglobulin M, or confirmed positive lupus anticoagulant (Rosner or Dilute Russell's viper venom time) or high level of homocysteine.

Statistical Analysis

Continuous variables are described as mean±SD or median with quartiles. Categorical variables are expressed as frequency with 95% CI. The population was categorized according to final diagnosis (STEMI or NSTEMI). Comparisons between STEMI and NSTEMI populations were performed using the Student *t* test. Pearson χ^2 or Fisher tests (when expected value <5 in cell count) were used for categorical variables.

A *P*<0.05 was considered statistically significant. The statistical analysis was performed using SPSS software (version 26.0; IBM, Armonk, NY).

RESULTS

Participants

Between May 2017 and June 2019, 324 women were enrolled in the study, 10 of whom were excluded (Figure 1). Because completeness of prospective inclusion was the cornerstone of this observational study, the acceptance rate by women was high in all participating centers, which were regularly monitored. The study population therefore comprised 314 women with a mean age of 43.0 (±5.7) years.

The final diagnosis was STEMI in 191 (60.8%) women and NSTEMI in 123 (39.2%) women. Overall, 75.5% were current smokers, 40.1% were sedentary, 28.0% were obese, 14.6% had diabetes, 35.0% had a family history of premature cardiovascular disease, 26.4% had dyslipidemia, 26.4% had hypertension, but a minority were on antihypertension therapy (15.3%) or were taking a statin (8.2%) before admission. Depression was reported in 27.7%, 31.2% had an adverse pregnancy outcome (gestational diabetes, pre-eclampsia, preterm delivery, fetal hypotrophy, macrosomia, or stillbirth), and 55.1% reported recent emotional stress. Almost half (46.2%) had an Évaluation de la Précarité et des Inégalités de santé dans les Centres d'Examen de Santé: Assessment of Deprivation and Health Inequalities for Health Examination Centers score >30, indicating significant social deprivation.¹¹ Patient characteristics according to final diagnosis and age group are detailed in Table 1.¹²

Overall, 100 (31.8%) women were using a contraceptive for the purpose of contraception; 43 (13.7%) were on combined contraception and 34 (10.8%) on oral progestin (Table S1). Among the 314 women, 49 (15.6%) were postmenopausal and 8 (2.5%) were on hormone-replacement therapy. Of the 43 women on a combined contraceptive, 37 (86.0%) had at least 1 contraindication for a combined contraceptive; 84.4% of these women >35 to ≤50 years of age were active smokers. The STEMI and NSTEMI populations were similar except in 4 particular risk factors. Patients with STEMI reported higher rates of insulin-treated diabetes at 9.4% versus 2.4%, risk difference of 7.0% (95% CI, 1.4–12.2; *P*=0.019) and previous assisted reproduction therapy at 8.4% versus 2.4%, risk difference of 6.0% (95% CI, 0.5–11.0; *P*=0.005). Conversely, patients with NSTEMI were more often obese at 35% versus 24.6%, risk difference of 10.4% (95% CI, 0.1–20.7; *P*=0.048) and with previous neoplasia at 7.3% versus 2.1%, risk difference of 5.2% (95% CI, 0.6–11.4; *P*=0.038).

Maximum concentrations of creatine phosphokinase were higher in women with STEMI versus NSTEMI (*P*=0.004) (Table S2). One-fifth (18.8%) of women presented with a high homocysteine concentration, and 56 (17.8%) had a thrombophilic risk factor (Table S3). Thirty of 314 (9.4%) women had

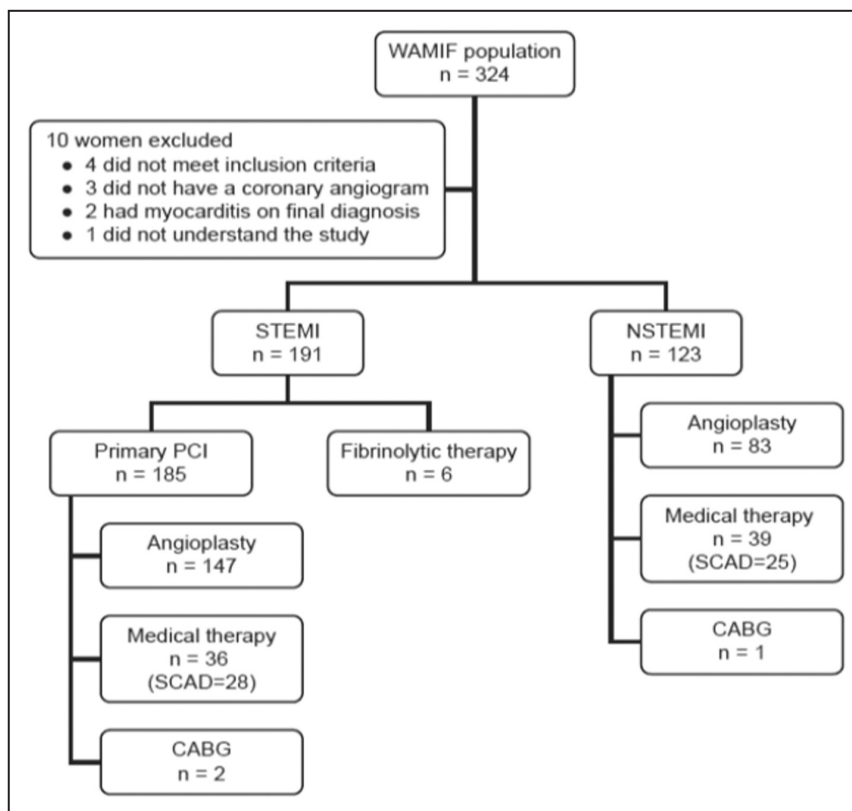


Figure 1. Flowchart.

CABG indicates coronary artery bypass graft; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; SCAD, spontaneous coronary artery dissection; STEMI, ST-segment–elevation myocardial infarction; and WAMIF, Young Women Presenting Acute Myocardial Infarction in France

an inherited high-risk thrombophilic profile, with the highest prevalence among the patients with STEMI (Table 2). Hyperhomocysteinemia was the most frequent (18.7%) thrombophilic risk factor (Table S3).

Characteristics of patients without standard modifiable risk factors such as current smoker, hypertension, dyslipidemia, and diabetes are detailed in Table S4.¹²

Presentation and Management

The presentation and early treatment (≤ 24 hours of presentation) for women are detailed in Table 3. Out of 191 women with STEMI, 175 women (91.6%) presented with chest pain, 59.7% had associated symptoms (nausea, vomiting, left arm pain, asthenia, sweats, dizziness, or palpitations), 10.5% had experienced symptoms for >1 week, and 13.6% presented with cardiac arrest.

Out of 191 women with STEMI, 185 women underwent primary percutaneous coronary intervention (Figure 1). The median time from symptom onset to first medical contact was >1 hour, and the median time from the first medical contact to coronary angiography exceeded 2 hours.

Angiographic data according to type of MI are given in Table 4. Nineteen women underwent intravascular imaging (Intravascular ultrasound or Optical coherence tomography). Among women with STEMI, 1.0% had normal coronary arteries, 17.8% had nonobstructive atheroma, and 14.6% had spontaneous coronary artery dissection. Multivessel disease was found in 29.3%.

Among 123 women with NSTEMI, 83 (67.5%) had percutaneous coronary intervention and 39 (31.7%) received medical therapy (Figure 1). Eight women (6.5%) had normal coronary arteries, 12.2% had nonobstructive atheroma, and 16.3% had spontaneous coronary artery dissection. Multivessel disease was present in 30.1% (Table 4).

Cardiovascular Events in the Hospital and at 12 Months

Eleven NACE occurred in 9 women during hospitalization (Table 5) but no deaths or stent thromboses. Recurrent MI occurred in 5 women, all of whom had

Table 1. Baseline Characteristics of Women With STEMI or NSTEMI

Variable	Overall (N=314)	STEMI (n=191)	NSTEMI (n=123)	P value
Age minimum, y	19	19	25	
Age, y, mean±SD	42.9±5.7	42.6±6.2	43.6±4.9	0.17
Cardiovascular risk factors				
Smoker (≤3 mo)	237 (75.5)	148 (77.5)	89 (72.4)	0.30
Diabetes	46 (14.6)	32 (16.8)	14 (11.4)	0.19
Insulin treated	21 (6.7)	18 (9.4)	3 (2.4)	0.019
Dyslipidemia	83 (26.4)	46 (24.1)	34 (27.6)	0.48
Hypertension	83 (26.4)	50 (26.2)	33 (26.8)	0.89
Family history of premature cardiovascular disease*	110 (35.0)	66 (34.6)	44 (35.8)	0.83
Obese (BMI ≥30 kg/m ²)	88 (28.0)	47 (24.6)	43 (35.0)	0.048
Sedentary (<30 min/d)	126 (40.1)	76 (39.8)	49 (39.8)	0.99
No SMURF	44 (14.0)	25 (13.1)	19 (15.4)	0.61
Cardiovascular history				
Previous myocardial infarction	19 (6.1)	11 (5.8)	8 (6.5)	0.79
PCI or CABG	16 (5.1)	9 (4.7)	7 (5.7)	0.70
Cardiac failure	1 (0.3)	0	1 (0.8)	0.39
Other cardiac surgery	0			
Stroke or transient ischemic attack	6 (1.9)	4 (2.1)	2 (1.6)	0.99
Pulmonary embolism	18 (5.7)	12 (6.3)	6 (4.9)	0.80
Arrhythmia	8 (2.5)	7 (3.7)	1 (0.8)	0.16
Other				
Creatine clearance <60 mL/min per 1.73 m ²	9 (2.9)	6 (3.1)	3 (2.4)	0.99
Depression (patient reported)	87 (27.7)	58 (30.4)	29 (23.6)	0.19
Excessive alcohol consumption†	18 (5.7)	12 (6.3)	6 (4.9)	0.60
Cannabis use	32 (10.2)	21 (11.0)	11 (8.9)	0.56
Systemic disease‡	9 (2.9)	5 (2.6)	4 (3.3)	0.74
Neoplasia	13 (4.1)	4 (2.1)	9 (7.3)	0.038
Migraine	105 (33.4)	60 (31.4)	45 (36.6)	0.34
Gynecological and obstetric history				
No. of pregnancies, mean±SD	2.8±2.2	2.8±2.5	2.7±1.8	0.86
Pregnancy with adverse outcome§	98 (31.2)	65 (40.1)	33 (29.5)	0.07
Menopause¶	49 (15.6)	30 (15.7)	19 (15.4)	0.85
Hormonal contraception	115 (36.6)	75 (46.9)	40 (39.2)	0.22
Assisted reproduction	19 (6.1)	16 (8.4)	3 (2.4)	0.05
Recent emotional stress	174 (55.6)	98 (51.3)	76 (62.3)	0.056
EPICES score >30¶¶	145 (46.2)	84 (44.0)	57 (46.3)	0.73
Treatment before admission				
Aspirin	24 (7.6)	13 (6.8)	11 (0.08)	0.60
Statin	26 (8.2)	16 (8.4)	10 (8.1)	0.94
P2Y12 inhibitor	4 (1.3)	1 (0.5)	3 (2.4)	0.30
Oral anticoagulation	9 (2.9)	3 (1.6)	6 (4.9)	0.16
Antihypertensive therapy	48 (15.3)	28 (14.7)	20 (16.3)	0.70
Steroids	12 (3.8)	5 (2.6)	7 (5.7)	0.23
Nonsteroidal anti-inflammatory drugs	15 (4.8)	9 (4.7)	6 (4.9)	0.99
Antidepressant drugs	39 (12.4)	26 (13.6)	13 (10.6)	0.43

Results are shown as n (%) or mean±SD. BMI indicates body mass index; CABG, coronary artery bypass grafting; EPICES, Évaluation de la Précarité et des Inégalités de santé dans les Centres d'Examen de Santé: Assessment of Deprivation and Health Inequalities for Health Examination Centers; NSTEMI, non-ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; SMURF, standard modifiable risk factor: current smoker, hypertension, dyslipidemia, diabetes¹²; and STEMI, ST-segment–elevation myocardial infarction.

*Father's age <55 y, mother's age <65 y.

†>2 drinks per d.

‡Lupus, Behçet's disease, antiphospholipid syndrome, vasculitis, chronic rheumatismal inflammation.

§Gestational diabetes, pre-eclampsia, preterm delivery, fetal hypotrophy, macrosomia, or stillbirth.

¶Reported by patient as amenorrhea for 12 mo without any other obvious pathological or physiological cause.

¶¶Deprivation score, measure of precariousness, a score of >30 indicates more deprived.¹¹

Table 2. Thrombophilia Profile According to STEMI or NSTEMI Diagnosis

Variable	Overall (N=314)	STEMI (n=191)	NSTEMI (n=123)	P value
High-risk thrombophilic profile				
Inherited	30 (9.4)	24 (12.6)	6 (4.9)	0.029
Acquired (antiphospholipid antibodies)	18 (5.7)	9 (4.7)	9 (7.3)	0.33
Hyperhomocysteinemia	59 (18.8)	36 (18.8)	23 (18.7)	0.99
Anti-nuclear factor	34 (10.8)	21 (11.0)	13 (10.6)	0.99

Results are shown as n (%). NSTEMI indicates non-ST-segment-elevation myocardial infarction; and STEMI, ST-segment-elevation myocardial infarction.

spontaneous coronary artery dissection that had initially been medically treated with extension of the dissection.

Complete follow-up was obtained for all of the women included. At 12 months, 90.4% (284 out of 314) of the patients were well and event free, 58.0% (n=182) had followed the rehabilitation program, 72.6% (n=228) were asymptomatic, and 74.0% (n=232) had returned to their normal professional activities. Fourteen NACE

occurred in 10 women after discharge from the hospital (Table 5). Figure 2 shows the time course of a first NACE according to age group and STEMI or NSTEMI. Two deaths occurred, 1 linked to pulmonary cancer and 1 to ovarian cancer. In addition to NACE, 38 patients (12.1%) had been admitted to the emergency department for recurrent chest pain, none of whom showed electrocardiographic changes or troponin elevation consistent with MI.

Table 3. MI Presentation, Treatment, and Medications Within 24H

Variable	STEMI (n=191)	NSTEMI (n=123)	P value
MI presentation			
Chest pain	175 (91.6)	106 (86.2)	0.125
Symptoms lasting >1 wk	20 (10.5)	16 (13)	
Associated symptoms*	114 (59.7)	79 (64.2)	0.42
Linked to effort	27 (14.1)	21 (17.1)	0.48
Linked to emotional stress	27 (14.1)	19 (15.1)	0.75
Syncope	10 (5.2)	3 (2.4)	0.26
Cardiac arrest	26 (13.6)	2 (1.6)	<0.001
Acute heart failure	5 (2.62)	0	0.16
Heart rate at admission, bpm	80.0 (68.0–89.0)	77 (70–90)	0.79
Systolic blood pressure at admission, mmHg	122.5 (110.0–144.0)	135.0 (122.0–151.0)	<0.001 [†]
Time from symptom onset to first medical contact, min	90.0 (55.0–300.0) [1 h 50 min]	139.0 (60.0–600.0)	0.048
Delay to hospital presentation >12 h	20 (12.0)	18 (20.0)	0.084
Time from first medical contact to coronary angiography, min	127.0 (72.0–292.0) [2 h 12 min]	1232 (745–1579.0)	<0.001 [†]
Total ischemic time (from pain to TIMI 3 flow), min	264.0 (165.0–619.0) [4 h 24 min]	1416.0 (924.0–2992.0)	<0.001 [†]
Troponin level at admission, ng/mL	23.0 (1.0–292.0)	14 (0.54–62.0)	0.019 [†]
Cardiac medications within 24 h of admission			
Fibrinolysis	6 (3.1)	0	0.085
Unfractionated heparin	82 (42.9)	28 (30.1)	0.005
Low-molecular-weight heparin (enoxaparin)	86 (45.0)	41 (44.1)	0.34
Glycoprotein IIb/IIIa inhibitor	11 (5.8)	3 (2.4)	0.26
Aspirin	182 (95.3)	110 (89.4)	0.047
Ticagrelor	126 (65.9)	61 (49.6)	0.004
Prasugrel	29 (15.2)	5 (4.1)	0.001
Clopidogrel	12 (6.3)	9 (7.3)	0.72

Results are shown as n (%) or median (quartile 1–quartile 3). MI indicates myocardial infarction; NSTEMI, non-ST-segment-elevation myocardial infarction; STEMI, ST-segment-elevation myocardial infarction; and TIMI, Thrombolysis In Myocardial Infarction.

*Nausea 43 (22.5%), asthenia 6 (3%), sweats 15 (7.9%), dizziness 17 (8.9%), palpitations 3 (1%).

[†]Student *t* test for comparison.

Table 4. Angiographic Data According to STEMI or NSTEMI Diagnosis

Variable	STEMI (n=191)	NSTEMI (n=123)	P value
Radial approach	162 (84.8)	116 (94.3)	0.01
Normal coronary arteries	2 (1.0)	8 (6.5)	0.016
MINOCA	34 (17.8)	15 (12.2)	0.18
Coronary spasm	4 (2.1)	5 (4.1)	0.32
Culprit artery identified	185 (96.9)	110 (89.3)	0.015
Left main	3 (1.6)	1 (0.8)	
Left anterior descending	94 (49.2)	67 (54.5)	
Circumflex	20 (10.5)	15 (12.2)	
Right coronary artery	68 (35.6)	27 (21.9)	
Left main disease	22 (11.5)	7 (5.7)	0.08
Single-vessel disease	133 (69.6)	78 (63.4)	0.06
Multivessel disease	56 (29.3)	37 (30.1)	0.78
Spontaneous coronary artery dissection*	28 (14.6)	20 (16.3)	0.36
Iatrogenic dissection	5 (2.6)	3 (3.6)	0.40
TIMI 0 flow	88 (46.1)	22 (17.9)	<0.001
Left ventricular ejection fraction, %	51.0 (11.3)	56.2 (8.6)	<0.001
Percutaneous coronary intervention	155 (81.1)	83 (67.5)	0.003
Thromboaspiration [†]	38 (24.5)	6 (7.2)	0.001
Direct stenting [†]	83 (53.5)	39 (46.9)	0.34
Drug-eluting stent [†]	135 (87.1)	74 (89.2)	0.49
Bioresorbable scaffold [†]	3 (1.9)	0	0.55
Balloon only [†]	12 (7.7)	5 (6.0)	0.62
Procedural complication [‡]	7 (4.5)	5 (6.0)	0.55

Results are shown as n (%). MINOCA indicates myocardial infarction with nonobstructive coronary arteries; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; and TIMI, Thrombolysis In Myocardial Infarction.

*Possible or definite.

[†]Percentage calculated among patients treated by percutaneous coronary intervention.

[‡]Any complication (eg, embolism, rupture, slow flow).

DISCUSSION

In this prospective observational study, all women <50 years of age admitted for MI were prospectively and exhaustively included. The cutoff of 50 years of age was chosen to focus on premenopausal women.¹³ The overall prognosis for these young women was good despite the high rate of emergency consultations in the year following the MI (Figure 3).

Cardiovascular Disease Risk Factors

Awareness of cardiovascular disease in women has risen over the past decade, yet cardiovascular risk still tends to be underestimated by both the public and health care practitioners,¹ especially among younger women,^{14–30} highlighting the need to develop

sex-specific approaches to optimize treatment of cardiovascular disease in women.¹ Also of concern is the rise in the incidence of acute MI among younger women.³¹

Three-quarters of the women were current smokers, 40.1% were sedentary, and 28.0% were obese, indicating key opportunities for prevention through the implementation of programs for smoking cessation and adoption of a healthy lifestyle.³² Furthermore, 26.4% of the women had dyslipidemia, yet only 8.2% of the overall population were taking a statin before admission. Similarly, 26.4% had hypertension, but only 15.3% of the overall population were on antihypertension therapy. In comparison, a high-risk thrombophilic profile accounted for a much lower proportion of patients. Over 10% of the participants reported that their symptoms had lasted >1 week. These findings indicate a failure of patients to recognize the severity of their symptoms and the need to seek medical attention. They also highlight the need for cooperation between medical specialties to ensure appropriate management of this young, at-risk population and the early instigation of recommended treatments and lifestyle changes.³² In particular, it was striking to observe that among women using combined contraception, 37 of 43 had at least 1 contraindication according to the World Health Organization recommendations, most commonly age and smoking. A recent systematic review involving women from various countries³³ also reported prevalence rates ranging from 5.9% to 41.9% for the use of contraceptives in women with contraindications; the most prevalent risk factor was hypertension followed by smoking and age, as in our study.

Alongside established cardiovascular risk factors, several other factors appear to contribute to cardiovascular risk among women. These include psychosocial, economic, social, and cultural factors, as well as obstetric and gynecological history. Our study showed a high rate of adverse pregnancy outcomes (31.2%), which exceeds that in the general female population (25%)³⁴ but is lower than that in the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study in the United States (45.3%).²⁰ History of adverse pregnancy outcomes has been shown to increase the risk of accelerated atherosclerosis and premature coronary artery diseases.³⁵

Over half of the participants reported recent emotional stress, with 14.1% being linked to the MI, and 46.2% had an Évaluation de la Précarité et des Inégalités de santé dans les Centres d'Examen de Santé: Assessment of Deprivation and Health Inequalities for Health Examination score >30, both of which are regarded as important risk factors for the development of cardiovascular disease. Of note,

Table 5. Number of NACE During Hospitalization and From Discharge to 12 Mo

Event	During hospitalization	Discharge to 12 mo
No. of women with at least 1 event	9	10
NACE	11	14
Recurrent myocardial infarction	5	7
Stroke	3	0
Major bleed	3	3
Stent thrombosis	0	2
Death	0	2*

NACE indicates net adverse clinical events.
 *Both were due to cancer.

the prevalence of cigarette and cannabis smoking in our cohort was more common than in women in the YOUNG-MI study (retrospective study examining a cohort of young adults age ≤ 50 years with a first-time myocardial infarction) in the United States³⁶: cigarettes (75.5% versus 55.5%) and cannabis (10.5% versus 3.7%). None of the participants reported the use of illicit drugs other than cannabis.

Of note, our cohort included 44 patients (14.0%) with no standard modifiable risk factors³⁷ similar to the proportion reported in an analysis from the Swedish myocardial infarction registry.³⁸ Nevertheless, we found some recent or specific risk factors among this subgroup (Table S4). Spontaneous coronary artery dissection was definite or possible in 23 women, and 12 presented with a thrombolysis in myocardial infarction (TIMI) flow of 0. Their prognosis was good, with no NACE at 12 months and only 3 emergency department consultations for chest pain without ischemia.

The potential effect of such factors, along with social deprivation, should be investigated further in the management of young women.

Presentation and Angiographic Features

The most frequent symptom of acute MI, regardless of age, is chest pain.³⁹ Despite the preconceived rate of atypical presentations among women, 9 in 10 participants in our study presented with typical chest pain, similar to the rates reported in men and women in the YOUNG-MI study.³⁶ A further 59.7% reported associated symptoms, consistent with the VIRGO study, in which young women presented with chest pain as frequently as men but with a higher number of associated symptoms.²⁴

Most of the women had obstructive coronary artery disease, with the remaining 15.6% having myocardial infarction with nonobstructive coronary arteries (34 STEMI and 15 NSTEMI). In the YOUNG-MI study in the United States,³⁶ the rate of myocardial infarction with nonobstructive coronary arteries among similarly aged women (mean 44 [±5.1] years) was 10.2%, which was significantly higher than that among young men with MI (4.2%, *P*<0.001). The rate of spontaneous coronary artery dissection in the present study was 15.3% (14.6% of STEMI and 16.3% of NSTEMI), which compares with 7.2% in women and 0.2% in men in the YOUNG-MI study,³⁶ probably linked to high-volume investigative centers that are particularly aware of this entity.

Outcomes and Follow-Up

The overall prognosis for these young women was better than previously reported.⁴⁰ Interestingly, in the WAMIF study, performed in high-volume centers

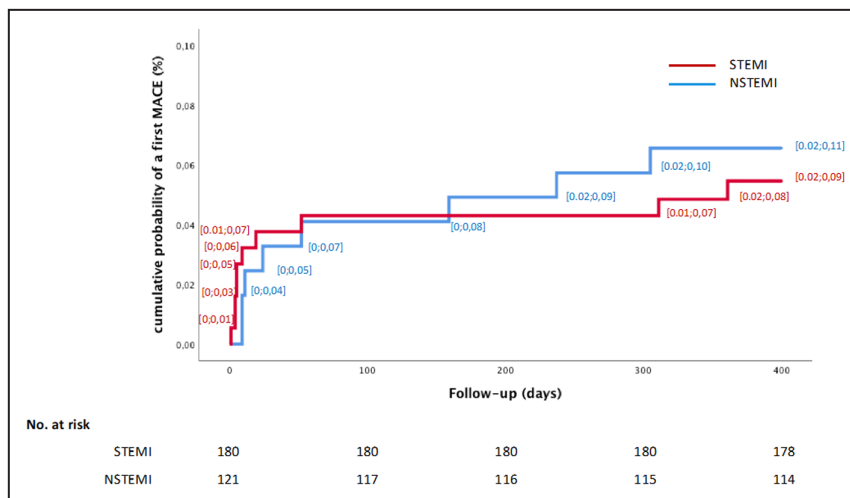


Figure 2. Cumulative incidence of first NACE in women. Between the brackets are reported pointwise 95% CIs. NACE indicates net adverse clinical events; NSTEMI, non-ST-segment elevation myocardial infarction; and STEMI, ST-segment elevation myocardial infarction.

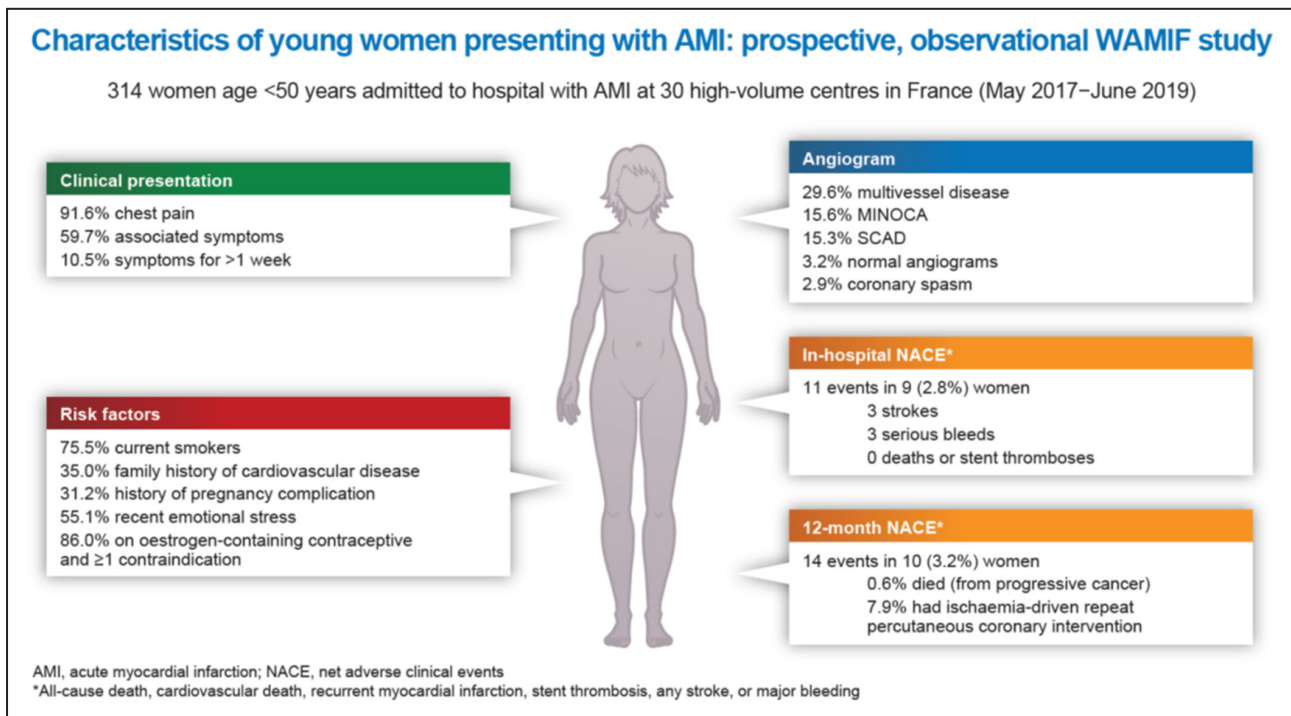


Figure 3. WAMIF study main results.

AMI indicates acute myocardial infarction; MINOCA, myocardial infarction with nonobstructive coronary arteries; NACE, net adverse clinical events; SCAD, spontaneous coronary artery dissection; and WAMIF, Young Women Presenting Acute Myocardial Infarction in France

sensitized and mobilized on the specificities of the management of coronary disease for women, the in-hospital mortality rate was null and was low in the year following the event, without cardiovascular deaths. During the 12 months of follow-up, a sizable percentage of our population presented to the emergency department for chest pain unrelated to unstable angina, emphasizing the high levels of stress reported and the need for a better network of follow-up among in these young women.

Limitations

Women who died before hospitalization were not eligible to participate and may have had higher risk characteristics than those who were enrolled.

Our aim was to focus on young premenopausal women, yet 16% of the women included reported being postmenopausal. We decided to use an age-inclusion criterion, because 50 years of age is the mean age of menopause, instead of menopause as an exclusion criterion, which could be difficult for the patient to clearly report.

Lastly, it is important to underline that the use of multiple statistical tests increased the α risk. Among the 89 statistical tests performed for this analysis, we would expect 4 statistically significant results. We observed 24 statistically significant results so that ≈ 20 may have been observed by chance. However, given

the design and the exploratory purpose of this cohort study, no adjustment nor hierarchical hypothesis was performed.

CONCLUSIONS

To our knowledge, WAMIF is the first study specifically analyzing the specificity of women-related characteristics in MI. History of adverse pregnancy outcomes and use of combined contraception in women despite contraindication(s) were highly prevalent, emphasizing the need for better cardiological and gynecological evaluation and follow-up. This study, focusing on young women with MI, highlights the effect of sex-specific risk factors. The overall prognosis for this female population was better than previously reported despite the high rate of emergency consultations in the year following the index MI, highlighting the need for more comprehensive follow-up.

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Disclosures

None.

Supplemental Material

WAMIF Investigators and Steering Committee
Tables S1–S4

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