

# Acute Coronary Syndromes in Premenopausal Women: Clinical and Angiographic Findings

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## Abstract

**Background:** Acute coronary syndromes in premenopausal women is uncommon and limited data is available regarding their risk factor profile and angiographic characteristics.

**Objectives:** To determine the clinical and angiographic findings in premenopausal women presented with acute coronary syndromes.

**Patients and methods:** Cross sectional study included 160 patients (68 premenopausal women and 92 age matched male controls) who were admitted in the coronary care unit of Ibn Al-Betar Center for Cardiac Disease and diagnosed as a cases of acute coronary syndromes between September, 2013 and June, 2014 . The clinical characteristics, angiographic findings for premenopausal women were compared to age matched males.

**Results:** Hypertension was the commonest risk factor for coronary artery disease in both premenopausal women (54.4%) and age matched males (43.5%). The prevalence of smoking was significantly lower in premenopausal women compared with age matched males (8.8% vs 63.0%,  $p=0.0001$ ). There was no clear risk factor for CAD in 32.4% of premenopausal women (32.4% vs 12.0%,  $p=0.0006$ ).

No significant difference was noted in the prevalence of hypertension (54.4% vs 43.5%,  $p=0.17$ ), diabetes mellitus (33.8% vs 27.2%,  $p=0.36$ ), dyslipidemia (27.9% vs 35.9%,  $p=0.29$ ) and family history of CAD (26.5% vs 20.7%,  $p=0.23$ ) between both groups . Typical chest pain was the presenting symptom in 57.4% of premenopausal women. There was more proximal left anterior descending artery involvement in the premenopausal group (25% vs 17.4%,  $p=0.02$ ). The rate of angiographically normal coronaries was more in premenopausal women (16.2% vs 9.8%,  $p=0.045$ ).

**Conclusion:** acute coronary syndrome could be considered in premenopausal women who present with chest pain and careful consideration, examination and diagnosis are essential workup steps in order to not miss this condition.

**Key words:** acute coronary syndrome, premenopause women, coronary angiography

## INTRODUCTION

During last 10 years the rise in coronary artery disease (CAD) prevalence in younger women is observed but in general, young women are poorly represented in clinical trials and this subgroup of patients' needs particular attention.

The incidence of CAD in women after menopause is about three times than that in women at the same age before menopause. Therefore, menopause is now accepted as a risk factor for CAD. The risk factors

profiles in women that are associated with CAD may be different from that in men and need reassessment.<sup>[1]</sup>

Women younger than 50 years of age with acute coronary syndrome (ACS) "have two fold higher mortality compared with age-matched men".<sup>[1]</sup>

Young women presenting with ACS have high rates of rehospitalization and less likely to receive evidence based medications and more likely to be readmitted within six-months after ACS.<sup>[2]</sup>

"The protective role of endogenous estrogens in young women is widely known and is directly connected with impact of these hormones to coagulation system".<sup>[3]</sup>

Increased levels of hemostatic factors, including fibrinogen, factor VIII, factor VII, tissue factor and von Willebrand factor have been related to increased cardiovascular disease risk in women.<sup>[4]</sup> In addition, Women with family history of premature CAD, have excessive platelet aggregation.<sup>[3]</sup>

Acute coronary syndrome in premenopausal women is uncommon and limited data is available regarding their risk factors for CAD and angiographic features. Studies in the 1970s and 1980s suggested that approximately 2 to 6% of acute myocardial infarction occur before the age of 45.<sup>[5]</sup> Series published in the 1990s report a prevalence of 4 to 10%.<sup>[6]</sup> In one 1998 study, women account for around 20 % of myocardial infarction before the age of 55.<sup>[7]</sup>

The diagnosis of ACS in younger women can be difficult. Pope et al. in his study concluded that among patients with ACS seen in the emergency room, those least likely to be hospitalized were women aged under 55.<sup>[8]</sup>

## **PATIENTS AND METHODS**

### **Data collection**

Cross sectional study includes premenopausal women and age- matched males controls who admitted in the coronary care unit (CCU) of Ibn Al-Betar Center for Cardiac Disease and diagnosed as a cases of acute coronary syndromes between September, 2013 and June, 2014.

The following criteria had to be met for inclusion in the study:

1. Premenopausal women: age equal or less than 55 years.<sup>[9]</sup>
2. Satisfied the criteria for acute myocardial infarction (STEMI and NSTEMI) and unstable angina.<sup>[10]</sup>
3. Elevated troponin T or I in serial measurements on arrival at hospital and or 8-12 hours after the onset of chest pain.
4. Coronary angiography performed during admission.

Patients who previously underwent coronary angiography with or without coronary intervention were excluded from the study.

Coronary stenosis was classified into:

- Significant 50% luminal narrowing.
- Non-significant <50% luminal narrowing.<sup>[11]</sup>

The patient clinical characteristics included their medical history (diabetes mellitus, hypertension, smoking, dyslipidemia, previous MI or angina, and family history of CAD).

Diagnostic ECG (ST-segment elevation or depression, Q-wave, T-wave change and new left bundle branch block (LBBB)).

Blood samples were drawn for troponin test at time of presentation and 8-12 hour later on.

Blood samples were drawn during admission for fasting blood sugar, blood urea, serum creatinine.

Echocardiography was done for all patients with the following classification of LV systolic function: normal LV systolic function (ejection fraction (EF) 52-72% in male and 54-74% in female), mild LV systolic dysfunction (EF 41%-51% in male and 41%-53% in female), moderate LV systolic dysfunction (EF 30%-40%) and severe LV systolic dysfunction (EF<30%).<sup>[12]</sup>

Body mass index (BMI) was calculated for all patients.<sup>[13]</sup>

Appendix 1 show the patients questionnaire with clinical and angiographic findings.

### **Definitions**

Myocardial infarction: "detection of a rise or fall in cardiac biomarkers (troponin) with at least one value above the 99th percentile of the upper reference limit together with evidence of myocardial ischemia, ECG changes indicative of new ischemia (new ST-T changes or new LBBB), and development of new pathologic Q wave".<sup>[14]</sup>

Coronary stenosis "was considered significant if it is equal or exceeded 50% in one of main coronary arteries or the left main coronary artery".<sup>[11]</sup>

Hypertension: "history of hypertension with ongoing treatment or the blood pressure was equal to or greater than 140/90 mmHg during admission".<sup>[15]</sup>

Diabetes mellitus: "fasting blood sugar was greater than 125 mg/dl (7.0 mmol/l) or diabetes medication was actively used".<sup>[16]</sup>

Dyslipidemia: "history of dyslipidemia diagnosed and or treated by a physician or total cholesterol greater than 5.8 mmol/l (200 mg /dl, low density lipoprotein (LDL) greater than or equal to 3.37 mmol/l (130 mg/dl, or high density lipoprotein (HDL) less than 1.04 mmol/l (40 mg/dl)".<sup>[16]</sup>

Typical chest pain: "substernal chest discomfort with a characteristic quality and duration that is exacerbated by exertion or emotional stress and relieved by rest or

nitroglycerin". Atypical chest pain "meets two of these characteristics".<sup>[17]</sup>

### Coronary angiography

"Coronary angiography was performed in a standard manner. Left coronary angiography was performed at least at four projections and right coronary angiography was performed at least at two projections".

QCA (quantitative coronary analysis) and FFR (fractional flow reserve) techniques used for suspicious angiographic lesions. "Any luminal diameter narrowing equal or more than 50% in any of the major epicardial coronary arteries was diagnosed as CAD".<sup>[11]</sup>

### Statistical analysis

"Analysis of data was carried out using the statistical package of SPSS-22. Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different means (quantitative data) were tested using Students-t-test for difference between two independent means.

The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (X2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05".

## RESULTS

We evaluate 160 patients (68 premenopausal women and 92 age-matched men) with a mean age  $46 \pm 7$  and  $46 \pm 1$  years, respectively.

The demographic and baseline clinical characteristics of studied groups were summarized in table-1. Hypertension was the commonest risk factor in both premenopausal women (54.4%) and age-matched men (43.5%).

**Table 1: The baseline clinical characteristics of studied groups**

Variable	*PW (n=68)	Men (n=92)	P value
Age (years) Mean $\pm$ SD	46 $\pm$ 7	46 $\pm$ 1	
DM	23 (33.8%)	25 (27.2%)	0.364
Hypertension	37 (54.4%)	40 (43.5%)	0.171
Dyslipidemia	19 (27.9%)	33 (35.9%)	0.290
Smoking	6 (8.8%)	58 (63.0%)	0.0001*
Family history of CAD	18 (26.5%)	19 (20.7%)	0.234
BMI	28 $\pm$ 1	27 $\pm$ 1	
No risk factor	22 (32.4%)	11 (12.0%)	0.0006*
Three or more risk factors	11 (16.2%)	22 (23.9%)	0.232
Chest pain Typical	39 (57.4%)	59 (64.1%)	0.384
Atypical	29 (42.6%)	33 (35.9%)	

\*"P value < 0.05 is considered statistically significant".

\*PW: premenopausal women.

The prevalence of smoking was significantly lower in premenopausal women compared with age matched-men (8.8% vs. 63.0%, p=0.0001). There was no clear risk factor for CAD in 32.4% of premenopausal women (32.4% vs. 12.0%, p=0.0006). No significant difference was noted in the prevalence of hypertension (54.4% vs. 43.5%, p=0.17), diabetes mellitus (33.8% vs. 27.2%, p=0.36), dyslipidemia (27.9% vs. 35.9%, p=0.29) and family history of CAD (26.5% vs. 20.7%, p=0.23) between both groups.

Typical chest pain was the presented symptom in 57.4% of premenopausal women compared with age-matched men (64.1%).

**Table 2: ECG changes at time of presentation in studied groups**

ECG changes	*PW			Men			P value
	Normal (n=11)	Nonsignificant lesion (n=5)	Significant lesion (n=52)	Normal (n=9)	Nonsignificant lesion (n=8)	Significant lesion (n=75)	
ST elevation	2(18.2%)	0	13 (25.0%)	1 (11.1%)	0	53 (70.7%)	0.05*
ST depression	4 (36.4%)	2 (40%)	34 (65.4%)	6 (66.7%)	4 (50.0%)	17 (22.7%)	0.11
LBBB	1 (9.1%)	0	2 (3.8%)	1 (11.1%)	1(12.5%)	3 (4.0%)	0.68
Normal	4 (36.3%)	3 (60%)	3 (5.8%)	1 (11.1%)	3 (37.5%)	2 (2.6%)	0.58

\*"P value <0.05 is considered statistically significant".

\*PW: premenopausal women.

Normal coronary angiography: no evidence of stenosis. Non significant lesion :<50% stenosis. Significant lesion :>50% stenosis.

Table-2 show the ECG changes in our patients at time of admission. Premenopausal women had a significantly lower ST segment elevation ( $p=0.05$ ). No significant difference in the presence of ST segment depression, LBBB and normal ECG at time of presentation between both groups. In our study 22.1% of premenopausal women presented with STEMI (22.1% vs. 58.7%,  $p=0.0001$ ) (table-3).

**Table 3: Types of acute coronary syndromes in studied groups**

ACS	*PW (n=68)	Men (n=92)	P value
STEMI	15 (22.1%)	54 (58.7%)	0.0001*
UN/NSTEMI	53 (77.9%)	38 (41.3%)	

\*"P value <0.05 is considered statistically significant".

\*PW: premenopausal women, STEMI: ST elevation myocardial infarction, UA/NSTEMI: unstable angina/non ST elevation myocardial infarction.

Left ventricular (LV) dysfunction by echocardiography or LV angiography was noted to be non significantly higher in age-matched men control group (41.2% vs. 53.3%,  $p=0.13$ ) (table-4).

**Table 4: Echocardiography finding during admission.**

Echo data		*PW (n=68)	Men (n=92)	P value
RWMA		29 (43%)	57 (62%)	0.11
LV dysfunction	mild	13 (19.2%)	23 (25%)	0.13
	moderate	9 (13.2%)	15 (16.3%)	
	sever	6 (8.8%)	11 (12%)	

\*"P value <0.05 is considered statistically significant".

\*PW: premenopausal women, RWMA: regional wall motion abnormalities.

Proximal left anterior descending artery (LAD) involvement in the premenopausal women was significantly higher than age-matched men (25% vs. 17.4%,  $p=0.02$ ) (table-5). No significant difference in the involvement of other vessels between both groups. The rate of angiographically normal coronaries was significantly more in premenopausal women (16.2% vs. 9.8%,  $p=0.045$ ) (table-5).

Table-6 demonstrated no statistically significant difference in the number of diseased vessels between both groups. Left main coronary artery involvement also was not statistically different between both groups (5.9% vs. 6.5%,  $p=0.5$ ).

Left ventricular (LV) dysfunction by echocardiography or LV angiography was noted to be non significantly higher in age-matched men control group (41.2% vs. 53.3%,  $p=0.13$ ) (table-4).

**Table 5: Distribution of coronary angiography data of studied groups according to coronary lesion severity.**

Lesion severity		*PW (n=68)	Men (n=92)	P value
Left main artery	significant	4 (5.9%)	6 (6.5%)	0.503
	Non-significant	0	1 (1.1%)	
LAD proximal	significant	17 (25%)	16 (17.4%)	0.027*
	Non-significant	0	2 (2.2%)	
Mid	significant	14 (20.6%)	29 (31.5%)	0.42
	Non-significant	2 (2.9%)	4 (4.3%)	
Distal	significant	1 (1.5%)	10 (10.9%)	0.12
	Non-significant	0	0	
Diagonal	significant	0	3 (3.3%)	-
	Non-significant	0	0	
LCX proximal	significant	8 (11.8%)	19 (20.6%)	0.33
	Non-significant	2 (2.9%)	2 (2.2%)	
Distal	significant	3 (3.3%)	5 (5.4%)	0.47
	Non-significant	0	7 (7.6%)	
OM	significant	6 (8.8%)	12 (13.0%)	0.045*
	Non-significant	0	1 (1.1%)	
Normal		11 (16.2%)	9 (9.8%)	0.045*

\*"P value <0.05 is considered statistically significant".

\*PW: premenopausal women. "LAD: left anterior descending artery, LCX: left circumflex artery, OM: obtuse marginal artery, RCA: right coronary artery".

Proximal left anterior descending artery (LAD) involvement in the premenopausal women was significantly higher than age-matched men (25% vs. 17.4%,  $p=0.02$ ) (table-5). No significant difference in the involvement of other vessels between both groups. The rate of angiographically normal coronaries was significantly more in premenopausal women (16.2% vs. 9.8%,  $p=0.045$ ) (table-5).

Table-6 demonstrated no statistically significant difference in the number of diseased vessels between both groups. Left main coronary artery involvement also was not statistically different between both groups (5.9% vs. 6.5%,  $p=0.5$ ).

**Table 6: Distribution of coronary angiography data of studied groups according to number of diseased vessels (with significant lesions).**

Stenosed coronary artery	*PW (n=68)	Men (n=92)	P value
Single vessel	25 (36.8%)	33 (35.9%)	0.946
Two vessels	17 (25%)	28 (30.4%)	0.745
Multiple vessel	9 (13.2%)	16 (17.4%)	0.866
Left main artery	4 (5.9%)	6 (6.5%)	0.503

\*"P value <0.05 is considered statistically significant".

\*PW: premenopausal women.

## DISCUSSION

We Cardiovascular risk factors have a high predictive value of the presence and severity of CAD in young women.<sup>[18,19]</sup> In most of the Western literature consulted, smoking is reported as the most prevalent risk factor for CAD.<sup>[20,21]</sup> In the current study, smoking was significantly less prevalent in premenopausal women compared with age matched men control (8.8% vs. 63.0%,  $p=0.0001$ ), this may be related to our cultural and social environment.

Smoking may accelerate the menopausal transition by 2 years<sup>[23]</sup> and it is considered an important risk factor for acute myocardial infarction in both genders, but studies pointed out the harmful effect of the relative estrogen deficiency that female smokers appear to have and suggested more metabolic effects among women, predisposing them to acute myocardial infarction at a relatively younger age".<sup>[24]</sup> An interaction between oral contraceptive pill and smoking was also observed.<sup>[25]</sup>

In the current study hypertension was the commonest risk factor for CAD in both premenopausal women (54.4%) and age matched men (43.5%). There was no

significant difference in the prevalence of diabetes mellitus (33.8% vs. 27.2%,  $p=0.36$ ) in both groups.

Hatim A. et al study<sup>[22]</sup> reported a non significant trend in premenopausal women for more hypertension (50% vs. 39%,  $p=0.34$ ) and diabetes mellitus (21% vs. 14%  $p=0.45$ ). In Luis A. et al study,<sup>[20]</sup> 48.5% of premenopausal women was hypertensive but only 12.1% was diabetic. However, it is known that the risk of CAD in premenopausal diabetic women is similar to that of young non-diabetic men; in other words, "diabetes mellitus appears to lessen the cardioprotective effect associated with female gender".<sup>[26]</sup>

The presence of diabetes is relatively greater risk factor for CAD in women compared with men, "increasing a woman's risk for CAD by three-to sevenfold with only a two-to threefold increase in diabetic men".<sup>[27]</sup>

There was no significant difference in the prevalence of dyslipidemia (27.9% vs. 35.9%,  $p=0.29$ ) in both group.

Hatim A. et al,<sup>[22]</sup> reported a non significant lower prevalence of dyslipidemia in premenopausal women (38% vs. 50%,  $p=0.25$ ) compared with males. In Luis A. et al study,<sup>[21]</sup> prevalence of dyslipidemia in young women was 39.6%.

There was no significant difference in family history of CAD (26.5% vs. 20.7% respectively between both groups,  $p=0.23$ ). In La Charity LA, et al study<sup>[28]</sup> all participants had strong family histories of CAD, other previous studies found no significant difference in family history of CAD between both groups.

In the current study, 32.4% of the premenopausal women did not had even one of the classical cardiovascular risk factors (compared with age-matched control men (12.0%),  $p=0.0006$ ) and this may suggest the need to look for other non traditional risk factors of CAD such as hyperhomocysteinemia, lipoprotein abnormalities and hypercoagulation states.

In this study, 57.4% of premenopausal women presented with typical chest pain which is non significantly lower than the prevalence of chest pain in age-matched

control men (64.1%). Luis A. et al study<sup>[21]</sup> reported a higher percentage (78.7%) of premenopausal women presented with typical chest pain.

Despite the low specificity of chest pain, it is the most common presenting symptom in women with CAD. Women with ACS are also more likely than men to have middle or upper back pain, neck pain, jaw pain, shortness of breath, paroxysmal nocturnal dyspnea, nausea or vomiting, abdominal pain, weakness or fatigue, cough, dizziness, and palpitations.<sup>[6]</sup>



Women who present with chest pain are more likely than men to have a non cardiac cause or other non atherosclerotic causes, such as vasospastic angina and coronary microvascular dysfunction.<sup>[29]</sup>

In National Registry of Myocardial Infarction (NRMI) "women were more likely than men to present without chest pain (atypical angina) specifically, younger women (aged <45 years)".<sup>[30]</sup> At present, there is no clear explanation for this, but one of hypotheses is that "Neurobiologic features of atypical angina are suggested by evidence that links anxiety, disruption of brain stem cardiovascular control, dysregulation of the brain-gut axis, subclinical impairment of lung airways, and vasospasm with dopamine abnormalities lateralized to the right hemisphere for which the metabolic rate is higher in women".<sup>[31]</sup>

The National Institutes of Health-sponsored Women's Ischemia Syndrome Evaluation (WISE) study confirmed a marked discordance between observed rates of obstructive CAD and the predicted probability of coronary disease. "This discordance was pervasive across age groups, regardless of whether angina was classified as typical or atypical".<sup>[32]</sup>

ECG was of major importance since in 85.3% of premenopausal women group it showed abnormalities compatible with acute ischemia (ST segment deviation or LBBB) and premenopausal women presented more with unstable angina or NSTEMI (77.9% vs. 41.3%,  $p=0.0001$ ).

GENESIS-PRAXY female study subjects "were less likely than men to have received a diagnosis of STEMI and were more likely to have received a diagnosis of unstable angina or NSTEMI".<sup>[33]</sup>

Women suffer more plaque erosions compared to plaque rupture in men, therefore, women present more often with unstable angina, representing 30% to 45% of patients with this condition, compared with 25% to 30% of patients with NSTEMI and only 20% of patients with STEMI.<sup>[34]</sup> "Autopsy research has demonstrated that coronary artery lesions in young women contain less calcium and dense fibrous tissue than those of men and older women".<sup>[35]</sup>

Coronary atherosclerotic plaque of young patients was comprised mainly of fatty deposits, which was extremely easy to rupture and caused acute coronary thrombosis that led to acute cardiovascular disease.<sup>[36]</sup> In addition, the use of newer invasive and noninvasive imaging techniques such as IVUS (intravascular ultrasound), OCT (optical coherence tomography) showed some of these differences in acute coronary events between men and women.<sup>[37]</sup>

The presence of left ventricular dysfunction (by echocardiography or by LV angiography) was non significantly lower in premenopausal women (41.2% vs. 53.3%,  $p=0.13$ ).

Most of the literatures has demonstrated that women are at increased risk of heart failure complicating acute myocardial infarction. However, as more men than women have ACS, the absolute number of patients with heart failure may still be greater in men. In addition, only the premenopausal women were involved in our study and this is may be the cause of the different results. In the NRMI, women (regardless the age) were more likely to have heart failure at time of acute myocardial infarction.<sup>[38]</sup> A similar increased risk of heart failure was found in the Global Registry of Acute Coronary Events (GRACE).<sup>[39]</sup>

In this study, 16.2% of premenopausal women had normal coronary angiography compared with age-matched males control (9.8%) which was statistically significant ( $p=0.045$ ). Hatim A. et al,<sup>[22]</sup> reported a non significant difference of normal coronary angiography between premenopausal women with ACS and age-matched males (7.4% vs. 6.9%,  $p=0.94$ ). In Luis A. et al study (21), 9.1% of premenopausal women had normal coronary angiography. Dou KF, et al<sup>(18)</sup>, reported that 9.6% of premenopausal women had normal coronary angiography.

In Gehrie ER et al study,<sup>[40]</sup> absence of obstructive CAD was more common in women than men (15.1% vs. 6.8%,  $p=0.0001$ ) among unstable angina and NSTEMI patients.

"A significant number of women with normal coronary angiography actually show biochemical or imaging evidence of myocardial ischemia. These women may have coronary circulation dysfunction that could lead to vascular constriction and subsequent ACS".<sup>[41]</sup> Additionally, "over one-third of women with MI have plaque rupture and ulceration, despite having no angiographically demonstrable CAD".<sup>[42]</sup>

There was no significant difference noted in the involvement of left main artery (5.9% vs. 6.5%,  $p=0.5$ ) between both groups.

Hatim et al,<sup>[21]</sup> reported that there was no statistically significant difference in mean SYNTAX score between premenopausal women and age-matched men control.

The LAD was the culprit vessel in 42.5% of premenopausal women and proximal LAD involvement was significantly higher in premenopausal women (25% vs. 17.4%,  $p=0.02$ ). Hatim A. et al reported that LAD was the culprit vessel in 40% of premenopausal women compared to 32% in men. Luis A. et al, reported a

prevalence of 57.6%. Dou KF et al, reported more prevalence of proximal LAD involvement in premenopausal group (28.2 %).

Another recent study found that LAD stenosis was more common in young people; 63.9% of patients in the 35 years old age group, 41.7% in the 35 to 55 age group, and 33.7% in the older than 55 age group exhibited atherosclerosis in the left anterior descending artery ( $P < 0.01$ ).<sup>[43]</sup>

The mechanism of this phenomenon is still uncertain and need a further study but one of the explanations is that "it was most likely because premenopausal women are more active, and the left ventricle needs to consume more oxygen and nutrients and the LAD artery is more involved as it is the main artery of the left ventricle".<sup>[44]</sup>

"Many studies showed that severe lesion at proximal LAD and left main artery were associated with higher early mortality, more in-hospital adverse cardiac events, poorer long term survival and lower residual left ventricle ejection fraction compared with those at non-proximal LAD and non-left main artery lesions".<sup>[45-47]</sup>

#### Study limitations

We evaluated the classical coronary risk factors. Other newer risk factors like lipoprotein abnormalities, hypercoagulation states and elevated homocysteine levels were not studied.

Non-atherosclerotic coronary diseases which should be considered in young patients with ACS such as vasospastic angina and microvascular angina, were not evaluated.

#### Conclusions and recommendations

- ) Acute coronary syndromes could be considered in premenopausal women who present with chest pain.
- ) No statistically significant difference in traditional risk factors for coronary artery disease in premenopausal women compared with men.
- ) Many premenopausal women presented with acute coronary syndromes have no traditional risk factors for coronary artery disease and this may suggest the need to look for other non traditional risk factors such as hyperhomocysteinemia, lipoprotein abnormalities and hypercoagulation states.
- ) Premenopausal women more frequently have acute coronary syndromes with angiographically "normal" coronary arteries compared with men.

- ) In premenopausal women with coronary artery disease, the lesion frequently located at proximal left anterior descending artery.
- ) Careful consideration, examination and diagnosis are essential workup steps in order not to miss this condition.

### Appendix 1

Patients questionnaire with clinical and angiographic finding.

<b>Name</b>	<b>cath. Serial No.:</b>
<b>Age</b>	<b>body weight</b>
	<b>hight</b>
<b>Risk factors:</b>	HTN DM dyslipidemia smoking family history
<b>Previous coronary intervention:</b>	PCI CABG
<b>Comorbidity:</b>	anemia renal impairment other comorbidity
<b>Obstetrical history:</b>	married unmarried pregnant parity recurrent abortion contraception (device, pills, tubal ligations) gynecological problems:
<b>Medications before admission:</b>	Aspirin B-Blockers ACEIs Thrombolytic therapy statins CCBs
<b>Symptoms:</b>	chest pain dyspnea fatigue nausea palpitation others
<b>ECG:</b>	ST depression T-inversion ST elevation LBBB normal
<b>Troponin:</b>	positive negative
<b>Echo-study:</b>	hypokinesia others normal Ejection fraction:

#### Coronary. Angiography:

<b>LMS</b>	critical	intermediate	non critical	normal
<b>LAD</b>	total	critical	intermediate	non critical normal
<b>LCX</b>	total	critical	intermediate	non critical normal
<b>RCA</b>	total	critical	intermediate	non critical normal

#### LV angiography:

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