

Il "continuum cardiovascolare"
nel genere femminile:
tappe di vita, malattia e cura



Le tre età della Donna - Gustav Klimt



8 marzo 2018, Cinquale (Ms)
Hotel Eden, Viale A. Gramsci, 26

La sindrome coronarica acuta al femminile: *malattia ostruttiva, dissezione, Tako-Tsubo*

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Cinquale, 8 marzo 2018



Quello che le donne non dicono...

- Coronaropatia ostruttiva
- Dissezione coronarica
- Sindrome di Tako-Tsubo



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Sex Differences in Mortality Following Acute Coronary Syndromes

11 RCT

From 1993 to 2006

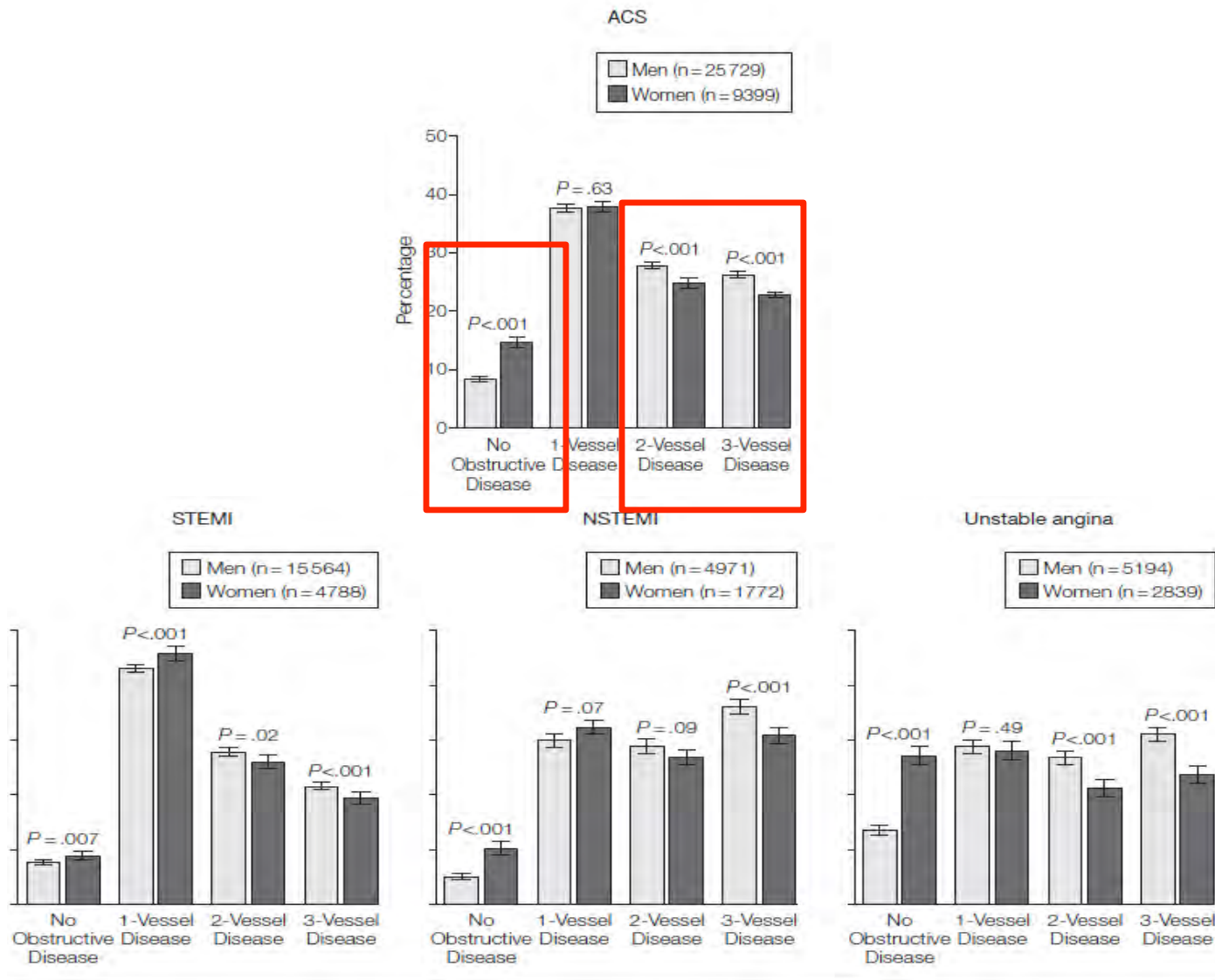
More than 136000 ptz

Women 28%

30 day mortality

F 9.6% vs M 5.3%
(OR 1.91, IC 1.83-2.00)

Prevalence of multivessel CAD

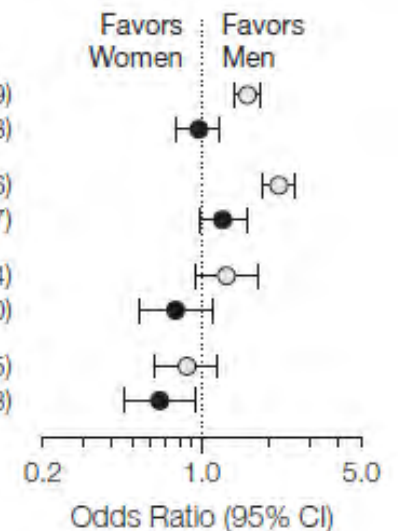


Clinical characteristics

Characteristics		Any ACS	
		Women (n = 38 048)	Men (n = 98 199)
Demographics			
Age, median (IQR), y		68 (60-75)	60 (51-69)
White race		30 083 (92)	77 215 (92)
BMI, median (IQR)		26.6 (24-30)	26.6 (24-29)
Smoker		9845 (26)	38 482 (40)
Geographic region			
North America			
Western Europe			
Eastern Europe			
Other ^a			
	All ACS		
		Sample Size, No.	30-d Mortality, No. (%)
		WomenMen	WomenMen
		937525 653	354 (3.8)625 (2.4)
			Odds Ratio (95% CI)
			Unadjusted 1.57 (1.38-1.79)
			Adjusted 0.96 (0.77-1.18)
Clinical history			
Hypertension	STEMI	477115 506	230 (4.8)355 (2.3)
Diabetes			Unadjusted 2.16 (1.83-2.56)
			Adjusted 1.23 (0.96-1.57)
Hyperlipidemia	NSTEMI	17704966	61 (3.5)135 (2.7)
Prior MI			Unadjusted 1.28 (0.94-1.74)
			Adjusted 0.76 (0.53-1.10)
Prior CABG surgery	Unstable angina	28345181	63 (2.2)135 (2.6)
Heart failure			Unadjusted 0.85 (0.62-1.15)
			Adjusted 0.65 (0.46-0.93)
Clinical presentation			
Heart rate, median (IQR), beats/min			
Systolic BP, median (IQR), mm Hg		132.0 (117-150)	130.0 (118-150)

Favors Women Favors Men

Odds Ratio (95% CI)



Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction

Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients)

Interview to

- 2009 women
- 976 men

Age 18-55 yrs

Recent ACS

	Overall		
	Women (n=2009)	Men (n=976)	P
Medical history, %			
Prior MI, PCI, or CABG	20.6	23.1	0.119
Prior angina	27.4	26.1	0.470
Congestive heart failure	5.8	2.5	<0.001
Hypertension	67.1	64.7	0.176
Diabetes mellitus	34.8	21.1	<0.001
Hypercholesterolemia	66.4	72.2	0.001
Smoked within past 30 days	57.7	56.6	0.578
Obesity (BMI ≥ 30 kg/m ²)	55.3	47.7	<0.001
Family history of CAD	73.8	73.1	0.657
Prior stroke/TIA	5.7	2.8	<0.001
Chronic kidney disease	12.7	8.6	0.001
Chronic lung disease	14.2	6.4	<0.001

Lichtman et al, Circulation 2018

Clinical presentation

	Women (n=2009)	Men (n=976)	<i>p</i> *
Patient did not perceive cause of symptoms to be heart-related, %	54.7	52.3	0.379

	Overall		
	Women (n=2009)	Men (n=976)	<i>p</i> *
Individual symptoms, %			
Chest pain, pressure, tightness, or discomfort	87.0	89.5	0.185
Dizziness	28.0	26.3	0.774
Epigastric: indigestion, nausea, or stomach pain, pressure, burning	61.5	50.2	<0.001

comfort. Women presented with a greater number of non-chest pain symptoms, and although the total number of additional symptoms may not be noteworthy, the presentation of chest pain within the context of multiple symptoms may influence the prompt recognition of heart disease and initial actions on the part of providers. Our results highlight the challenge

	Women (n=2009)	Men (n=976)	<i>p</i> *
Pain too bad to ignore	59.8	56.3	0.290
Worried about heart problem	41.6	49.8	<0.001

Mean (SD)	3.4 (2.0)	3.0 (1.9)	<0.001
0 symptoms, %	5.6	6.7	<0.001
1-2 symptoms, %	32.5	38.5	
3-4 symptoms, %	33.0	33.4	
>4 symptoms, %	29.0	21.4	

Quello che le donne non dicono...

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- **Dissezione coronarica**
- Sindrome di Tako-Tsubo



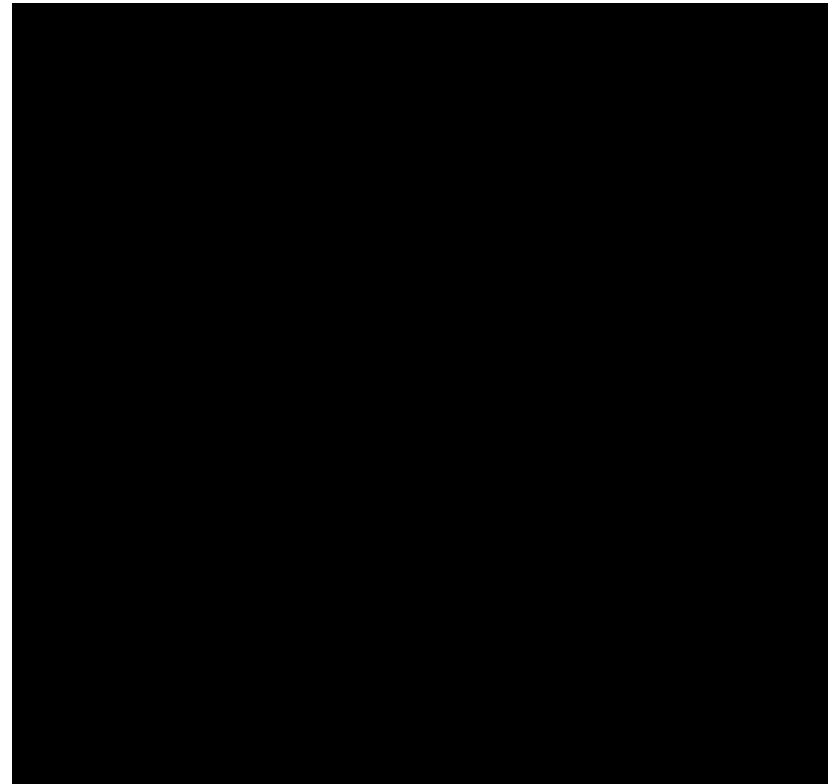
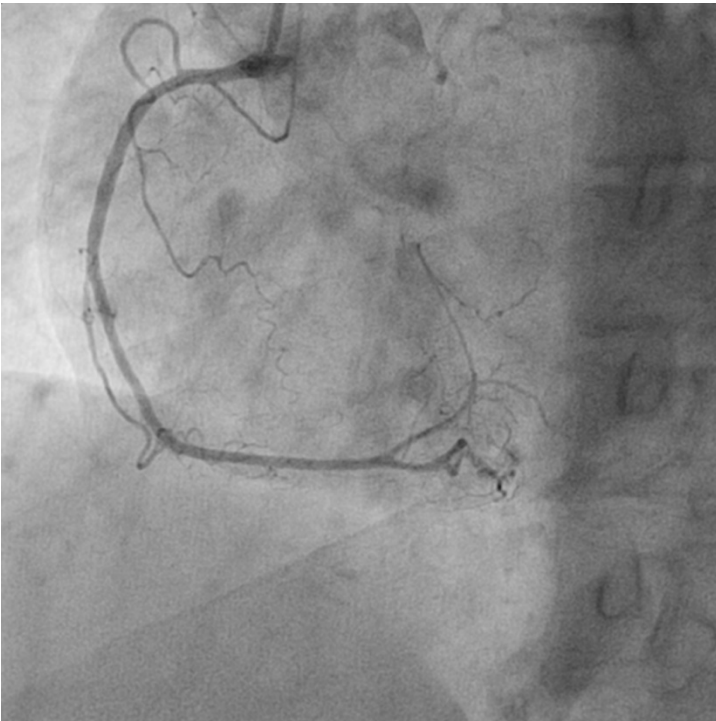
Clinical case

Woman, 68 yrs

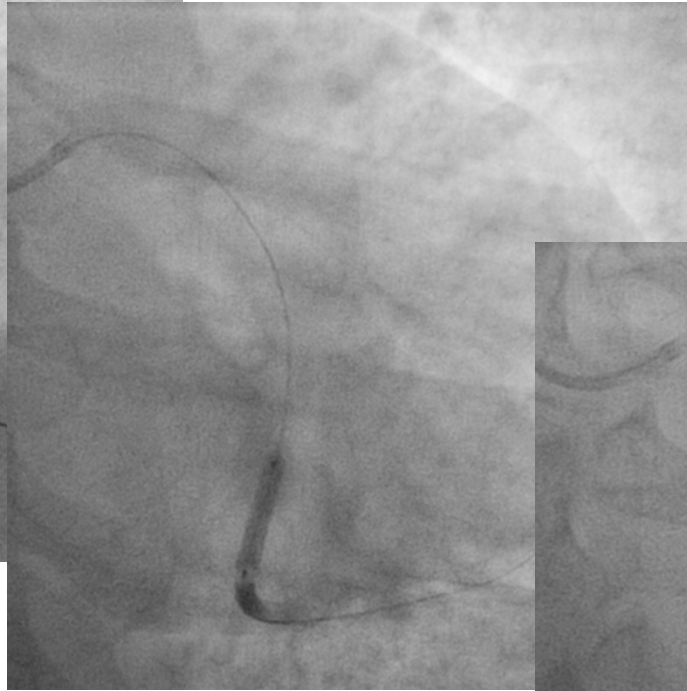
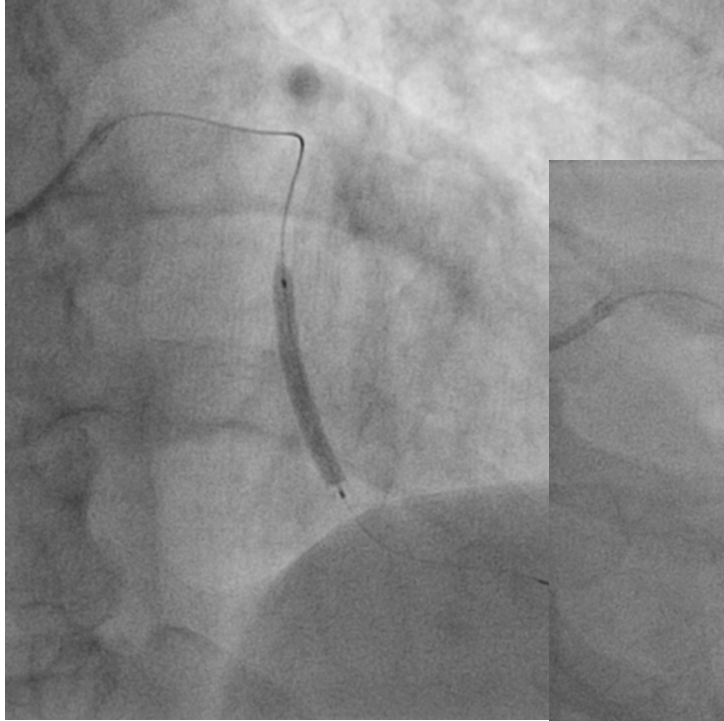
Hypertension

No previous CV history

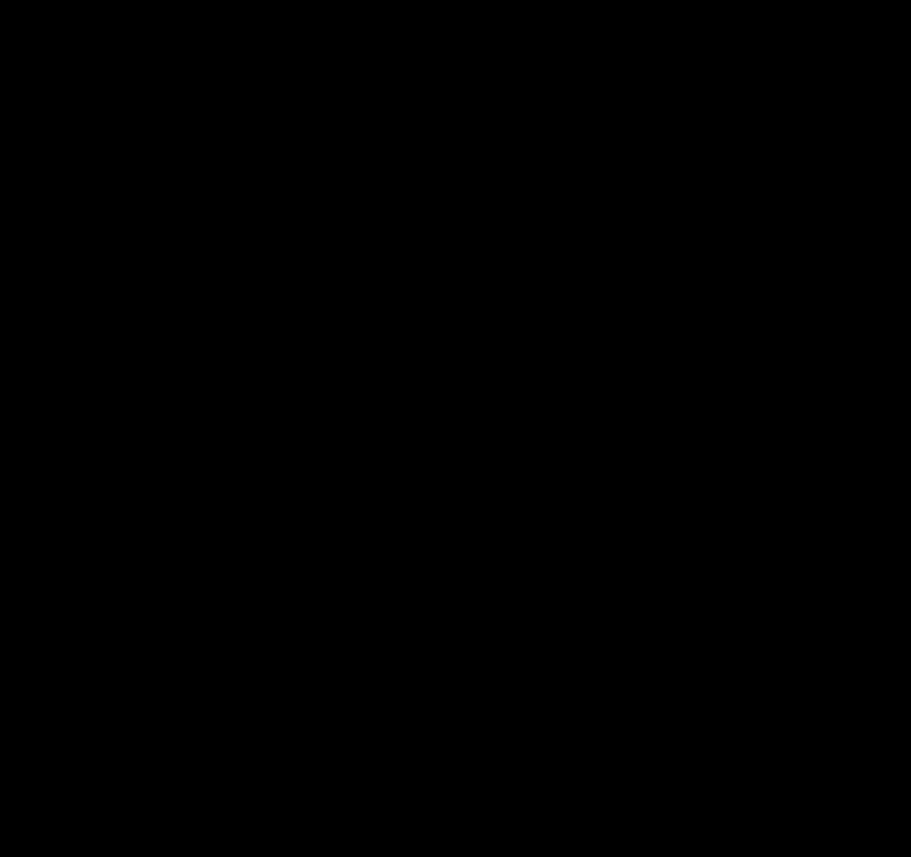
NSTE-ACS



Progressive retrograde stenting

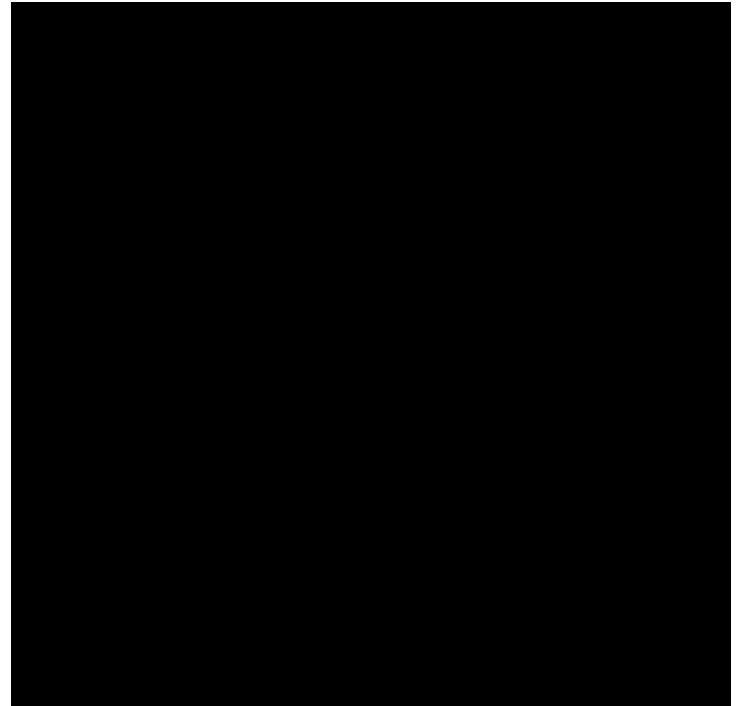
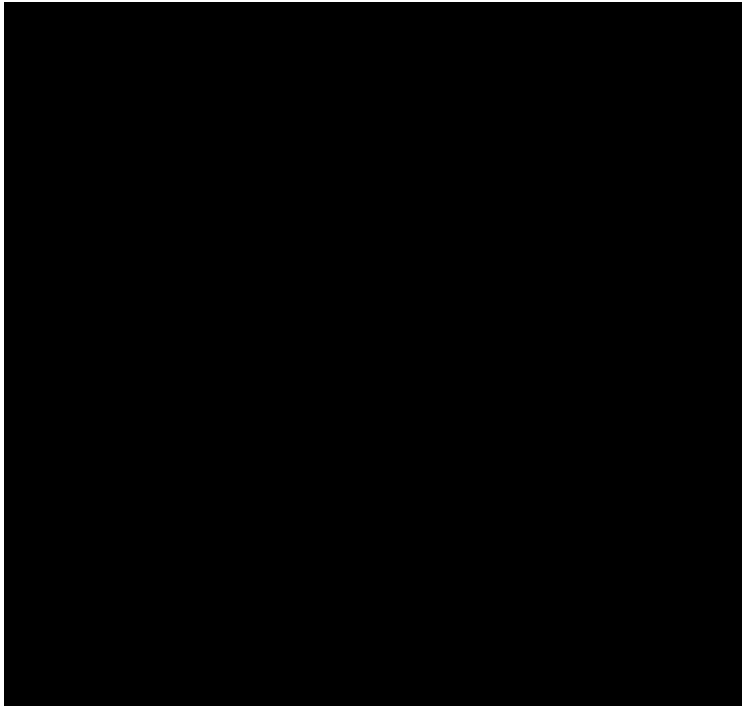


Final result



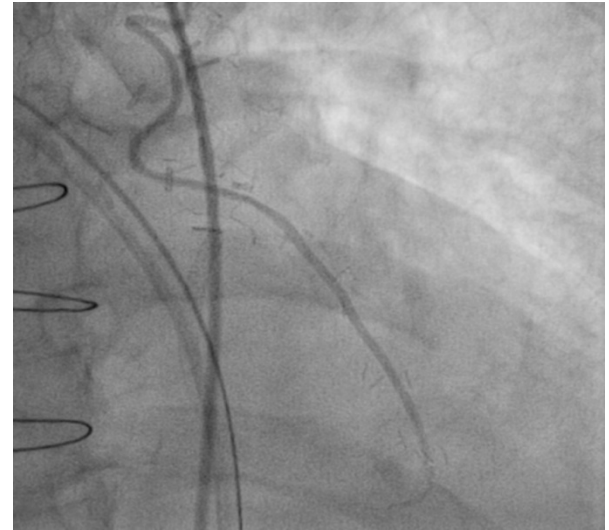
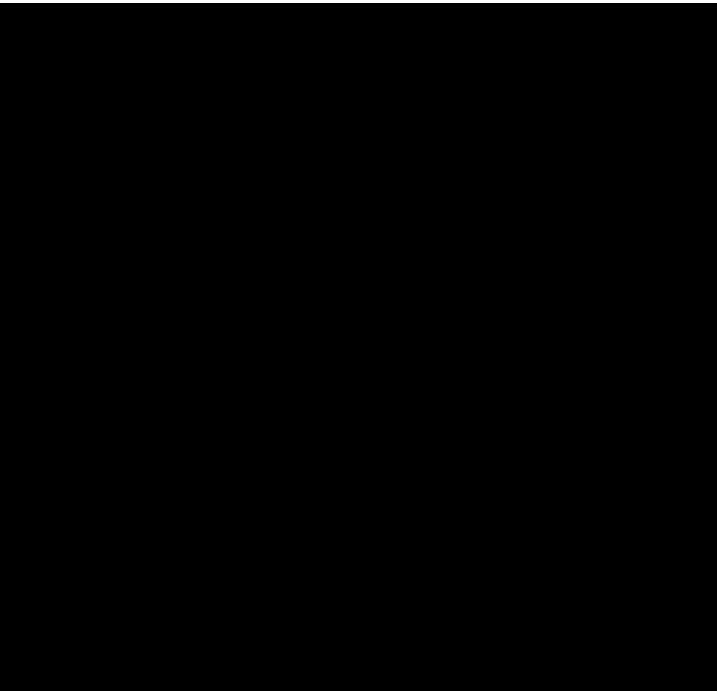
Discharged
Jan 5th 2017

January 7th 2017...



Referred to urgent CABG

After few days



Patent LIMA to LAD



Patent VGS to OM

Spontaneous coronary dissection

Prevalence 0.3%

But women less than 50

Table 1 Etiology of non-atherosclerotic SCAD

Predisposing arteriopathy

Fibromuscular dysplasia

Pregnancy: history of multiple pregnancy, peri-partum

Connective tissue disorder: Marfan's syndrome, Ehler Danlos syndrome, cystic medial necrosis, fibromuscular dysplasia

Systemic inflammation: systemic lupus erythematosus, Crohn's disease, polyarteritis nodosa, sarcoidosis

Hormonal therapy

Coronary artery spasm

Idiopathic

Precipitating stress events

Intense exercise (aerobic or isometric)

Intense emotional stress

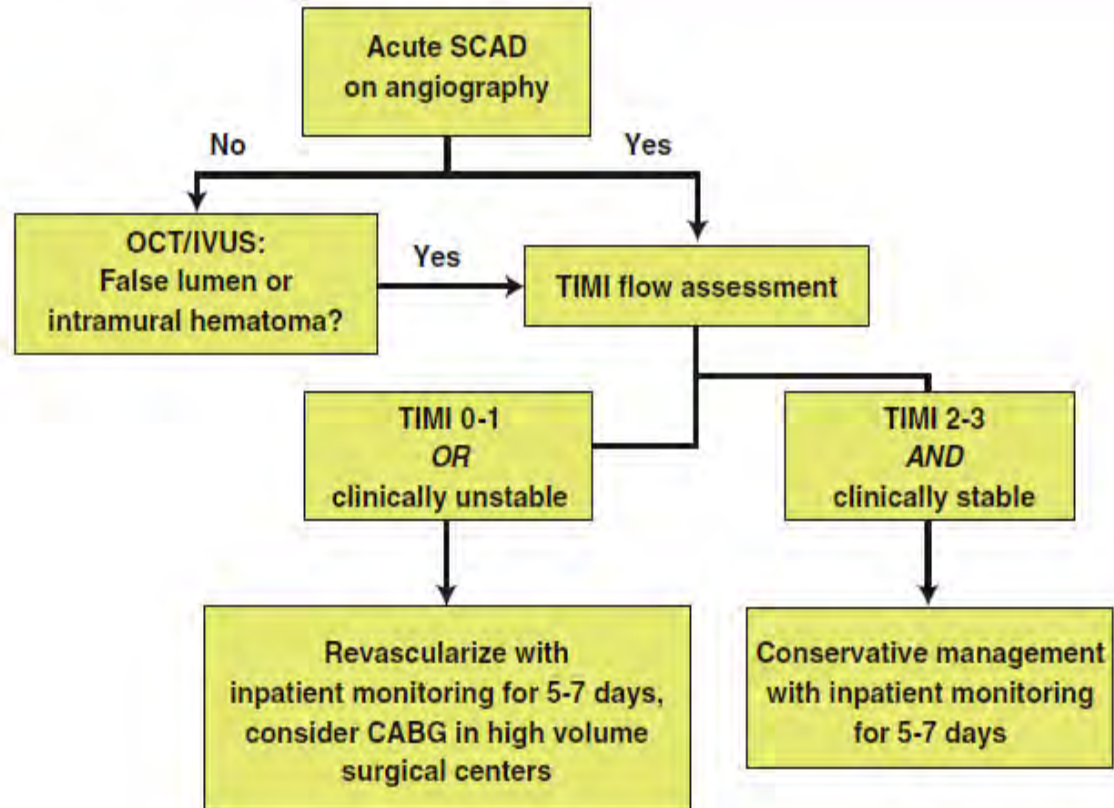
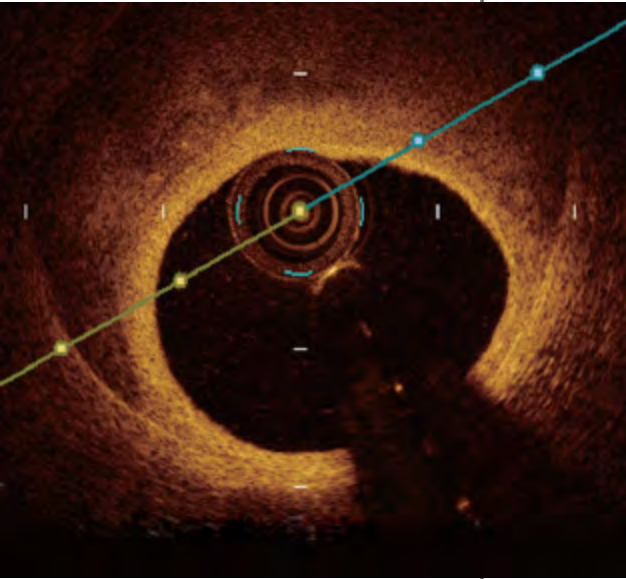
Labor & delivery

Intense Valsalva-type activities (e.g., severe repetitive coughing, retching/vomiting, bowel movement)

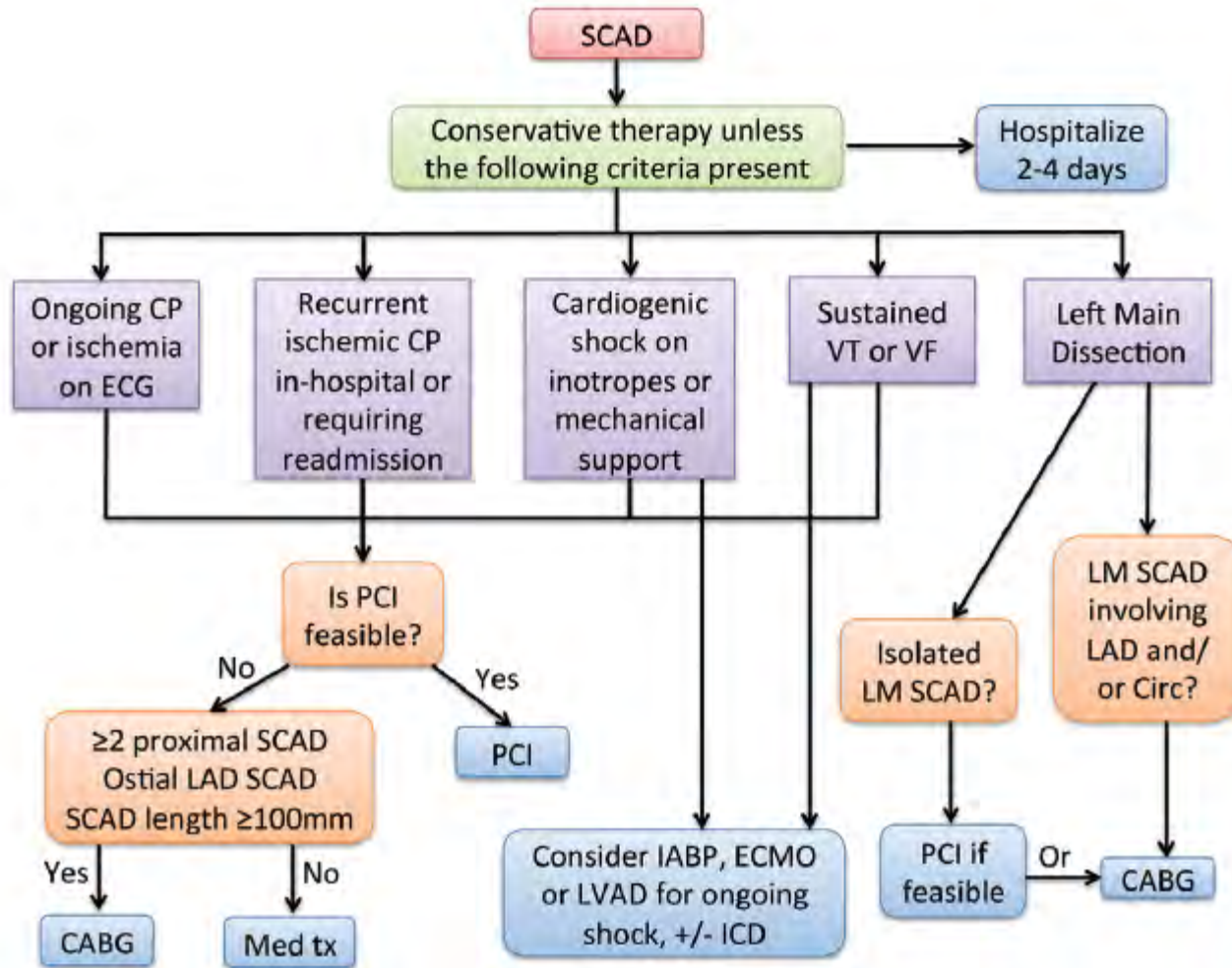
Cocaine, amphetamines, met-amphetamines, beta-HCG

SCAD management (1)

FIGURE 1 SCAD Management



SCAD management (2)



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- **Sindrome di Tako-Tsubo**



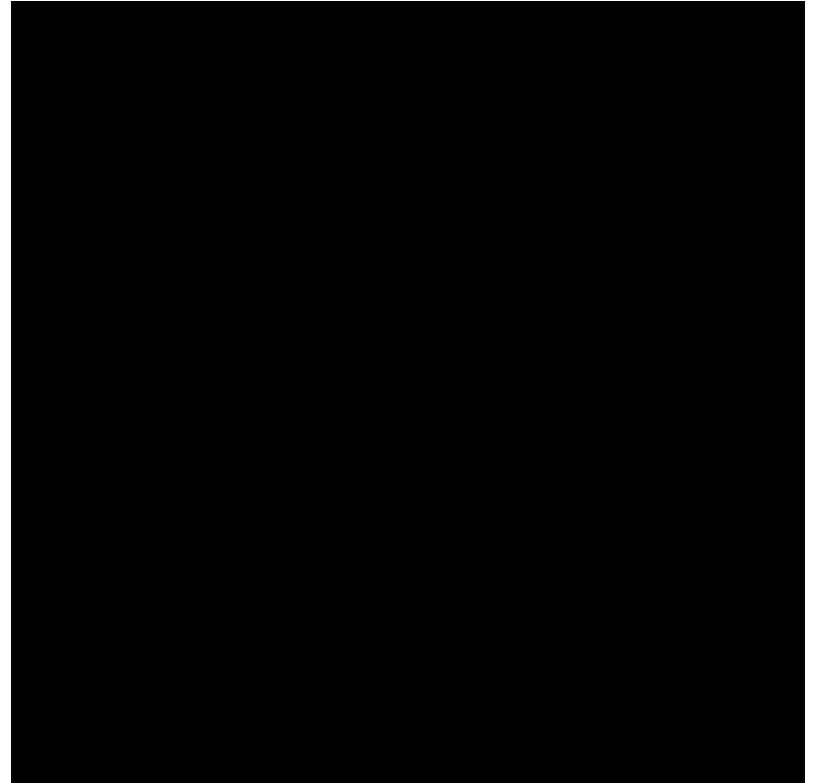
Clinical case

Woman, 64 yrs

Same day husband's death

No previous CV history

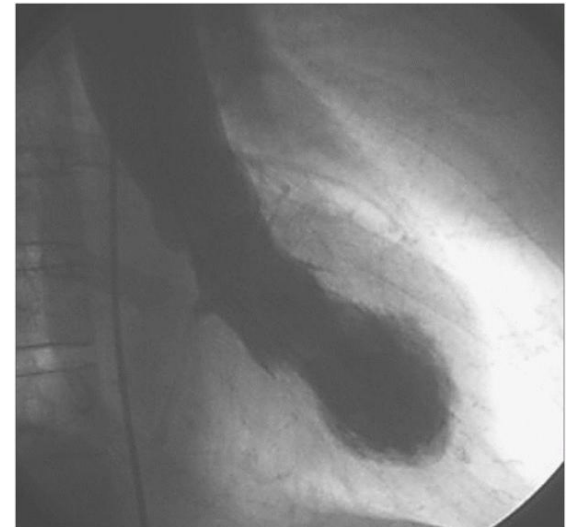
STE-ACS



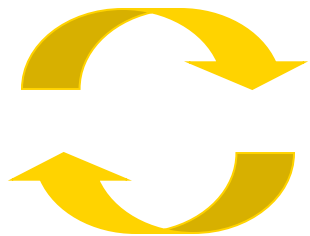
Tako-Tsubo Syndrome

Clinical presentation

- Emotional or physical stress
- Acute chest pain +/- ST-T abnormalities
- Increased serum cardiac enzyme levels
- Normal coronary arteries
- Regional (apical) transient myocardial dysfunction extended over a single vessel territory



Acute coronary
syndrome



Acquired
Cardiomyopathy

ORIGINAL ARTICLE

Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy

1750 TTS

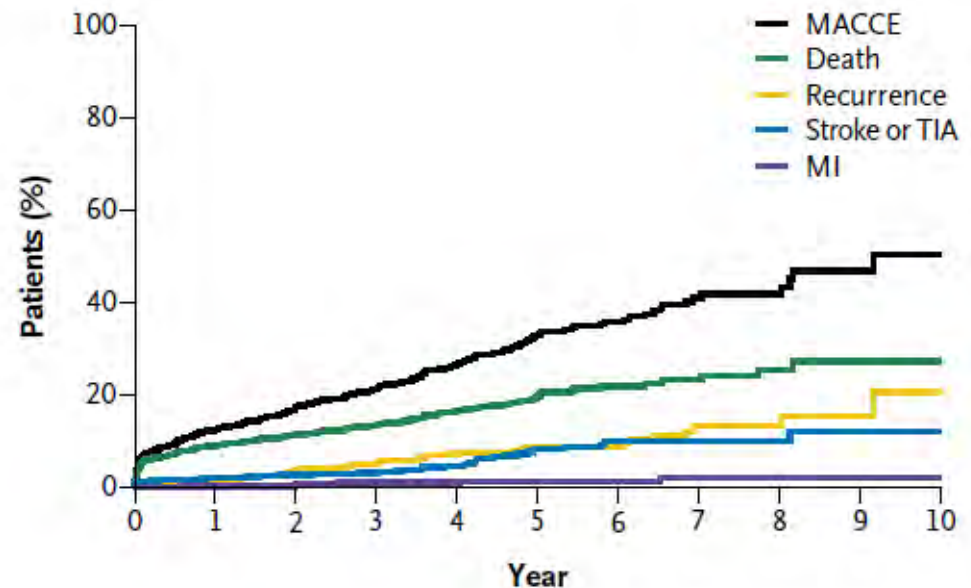
89.8% women

Characteristic

In-hospital outcomes — no./total no. (%)

Cardiogenic shock

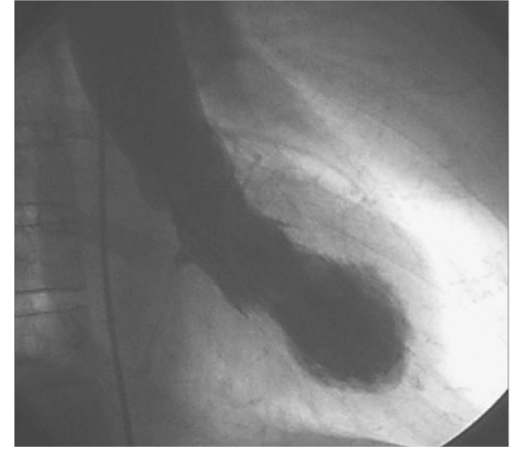
Death



No. of Patients 1750 786 570 431 300 191 126 71 38 17 9

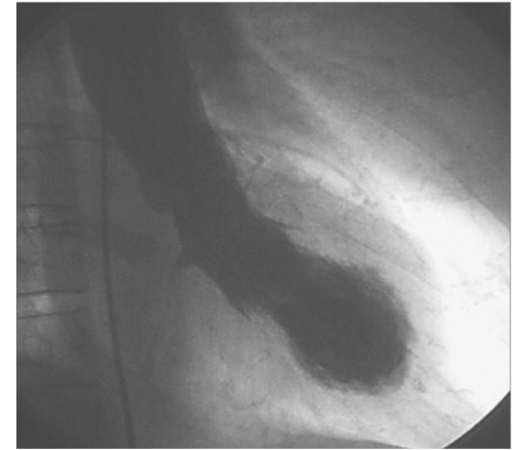
Templin et al, NEJM 2015

Etiopathogenesis



1. *The stress hypothesis*
2. *The coronary macrovascular spasm hypothesis*
3. *The spontaneously thrombolised coronary thrombus hypothesis*
4. *The infective hypothesis*
5. *The coronary microvascular hypothesis*

Etiopathogenesis

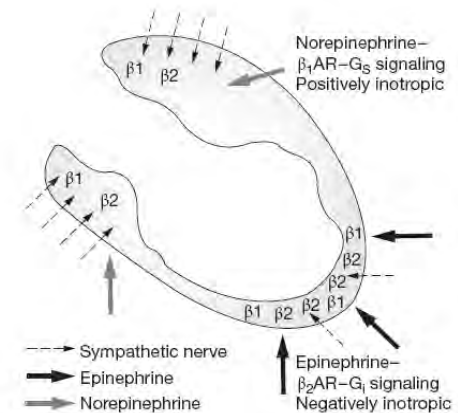


1. The stress hypothesis

Catecholamines toxicity

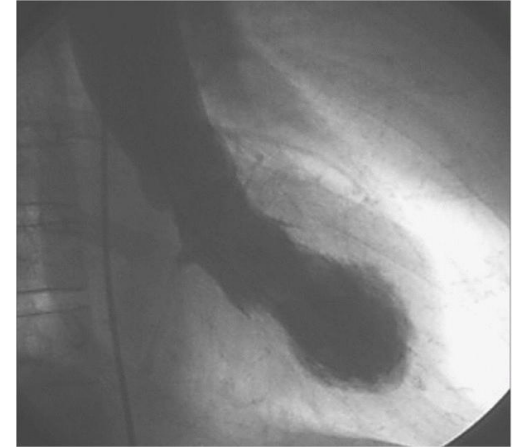
A) Epinephrine
Norepinephrine vs Killip III AMI Wittstein et al *NEJM* 2005
Dopamine

B) Increased density of beta adrenoceptors
in the apical myocardium



Lyon et al *Nat Clin Prac* 2008

Etiopathogenesis



2. *The coronary macrovascular spasm hypothesis*

The “Japanese” hypothesis

A) *Myocardial stunning due to simultaneous multivessel spasms: a review of five cases*

Dote et al, *J Cardiol* 1991

3 multivessel
spontaneous

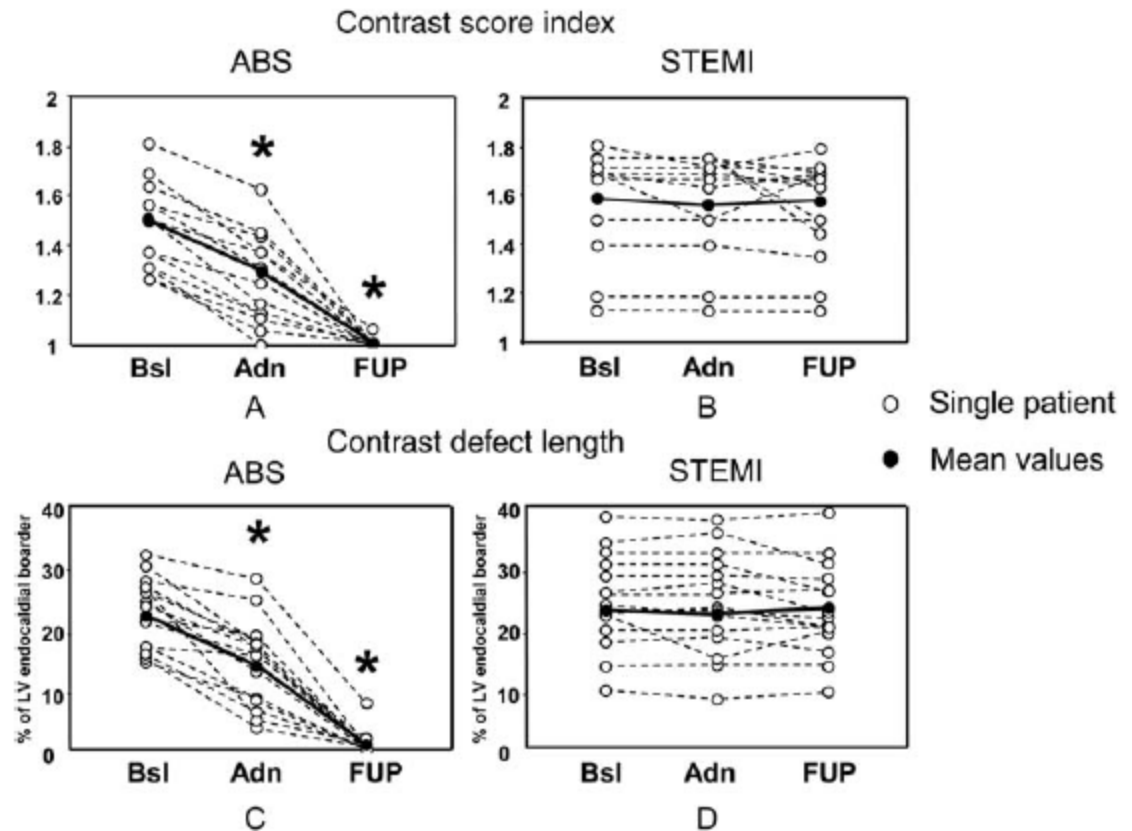
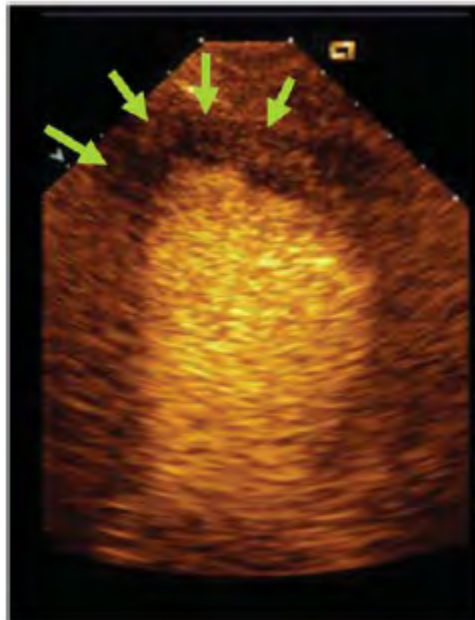
B) 30 cases
4 multivessel
pharmacologically-induced

Kurisu et al
Am Heart J 2002

6 single vessel
pharmacologically-induced

Reversible coronary microvascular dysfunction: a common pathogenetic mechanism in Apical Ballooning or Tako-Tsubo Syndrome

Leonarda Galiuto*, Alberto Ranieri De Caterina, Angelo Porfidia, Lazzaro Paraggio, Sabrina Barchetta, Gabriella Locorotondo, Antonio Giuseppe Rebuzzi, and Filippo Crea



Quello che le donne non dicono...

- **Coronaropatia ostruttiva**

*Mortalità più alta,
più fattori di rischio,
sintomi atipici*

- **Dissezione coronarica**

*Quasi il 10% delle ACS
sotto i 50 anni*

- **Sindrome di Tako-Tsubo**

*Modello fisiopatologico di ACS
su base microcircolatoria*



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