

# **Dolore Toracico Acuto associato a modifiche ECG & dismissione enzimatica ma con angiografia coronarica negativa**

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**VII Congresso di Ecocardiochirurgia  
Milano – 5-7 Maggio 2014**

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# ACS & Unobstructed Coronaries

## Definition ESC/ACCF/AHA/WHF

↑ cTn with at least one value above of 99<sup>o</sup> percentile with at least one of the following:  
a) Ischemic symptoms; b) ischemic ECG changes; c) loss of viable myocardium at Img

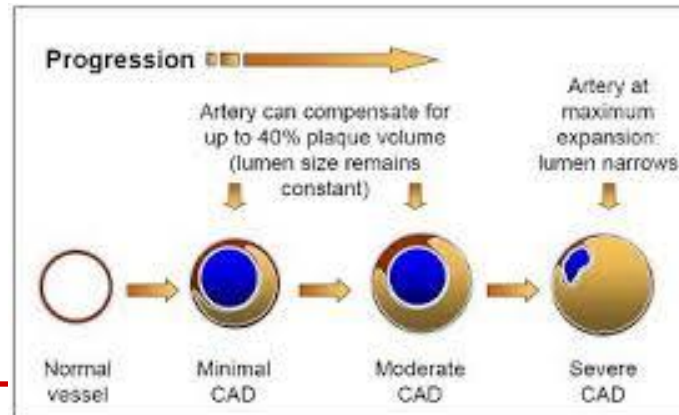
## Epidemiology

a) Prevalence between 1-12% of patients presenting with acute MI  
(depending on the definition of 'normal' coronary arteries)

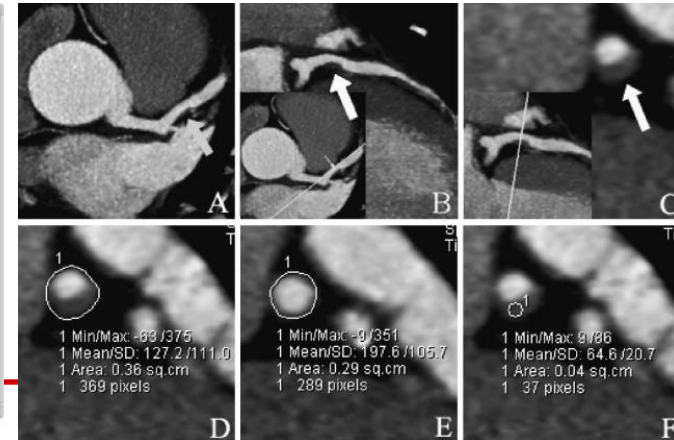
b) Bimodal distribution

- young men (mean age 36 yo, often strong smokers)
- women (mean age 56 yo, with few classical CV risk factors )

## Unobstructed Coronaries



Glagov S et al, *N Engl J Med*, 1987.



# ACS & Unobstructed Coronaries

## Pathogenetic Mechanisms

### Non-Ischemic Causes

Peri(myo)carditis

Tako-Tsubo (stress) CM

Cardiomyopathy/Heart Failure

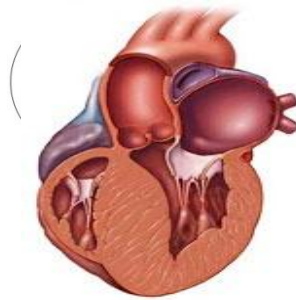
### Ischemic Causes

'Concealed' Plaque Destabilization

- > plaque ulceration/rupture
- > hypercoagulability and thrombosis

Coronary Vasospasm

Embolization



**NIHD**

Dying muscle



Other causes:

- Pulmonary Embolism
- Sepsis
- Cardiac Contusion
- pheochromocitoma

# ACS & Unobstructed Coronaries

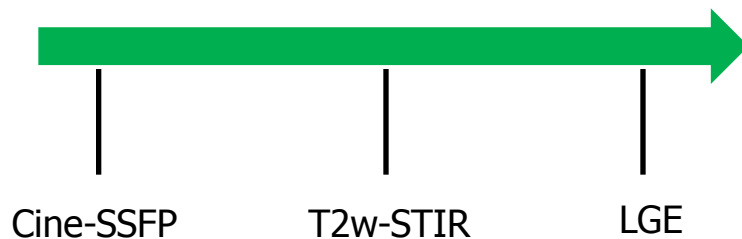
## Differential Diagnosis

The role of cardiovascular magnetic resonance in patients presenting with chest pain, raised troponin, and unobstructed coronary arteries

Ravi G. Assomull<sup>1,2</sup>, Jonathan C. Lyne<sup>1</sup>, Niall Keenan<sup>1</sup>, Ankur Gulati<sup>1</sup>, Nicholas H. Bunce<sup>3</sup>, Simon W. Davies<sup>1</sup>, Dudley J. Pennell<sup>1,2</sup>, and Sanjay K. Prasad\*

60 consecutive pts with:

- typical CP
- increased cTn
- non-obstructive CAD at X-ray  
(stenosis <50%)
- CMR within 1 – 90 days



Characteristics	Pts (n=60)
Mean age (years)	44 ± 17
Male sex n, (%)	43 (72)
<u>CV Risk Factors n, (%)</u>	
FH for CAD	9 (15)
Diabetes	3 (5)
Smoking	6 (10)
Alcohol abuse	3 (5)
Dyslipidaemia	19 (32)
<u>ECG abnormalities</u>	
Ischemic type	46 (77)
ST-segment elevation	24 (40)

# ACS & Unobstructed Coronaries

## Differential Diagnosis

CMR findings	n (%)
Myocarditis	30 (50.0)
Acute	19 (31.7)
Non-acute	11 (18.3)
Myocardial infarction	7 (11.6)
Takotsubo cardiomyopathy	1 (1.7)
Dilated cardiomyopathy	1 (1.7)
Normal CMR findings	21 (35)

Variables	Diagnostic CMR (n=39)	Non-diagnostic CMR (N=21)	P-Value
False positive cTnI	8%	57%	<0.001
cTnI <5ULN	13%	52%	<0.001
SVT / VT	5%	24%	0.045
LV-EF	56.1±14.7	65.5±5.6	0.007

'false positive' cTn: a single elevated cTn followed by a second normal troponin level within 24 h.

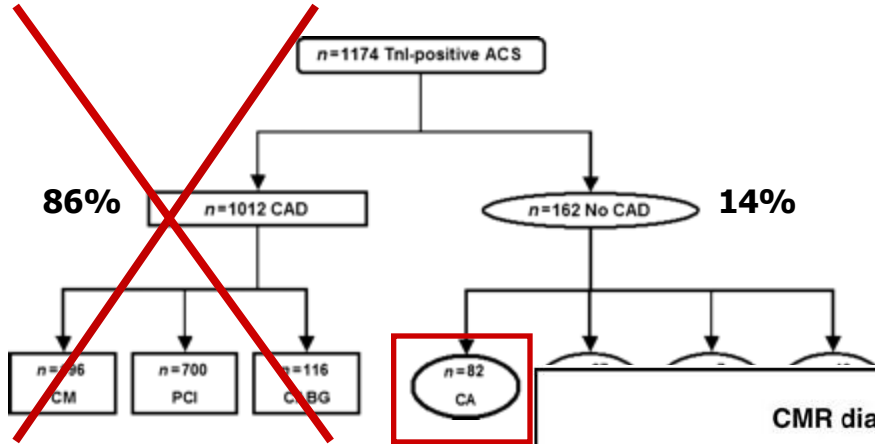
# ACS & Unobstructed Coronaries

## Differential Diagnosis



European Heart Journal (2009) 30, 2869–2879  
doi:10.1093/eurheartj/ehp328

**CLINICAL RESEARCH**  
Coronary heart disease



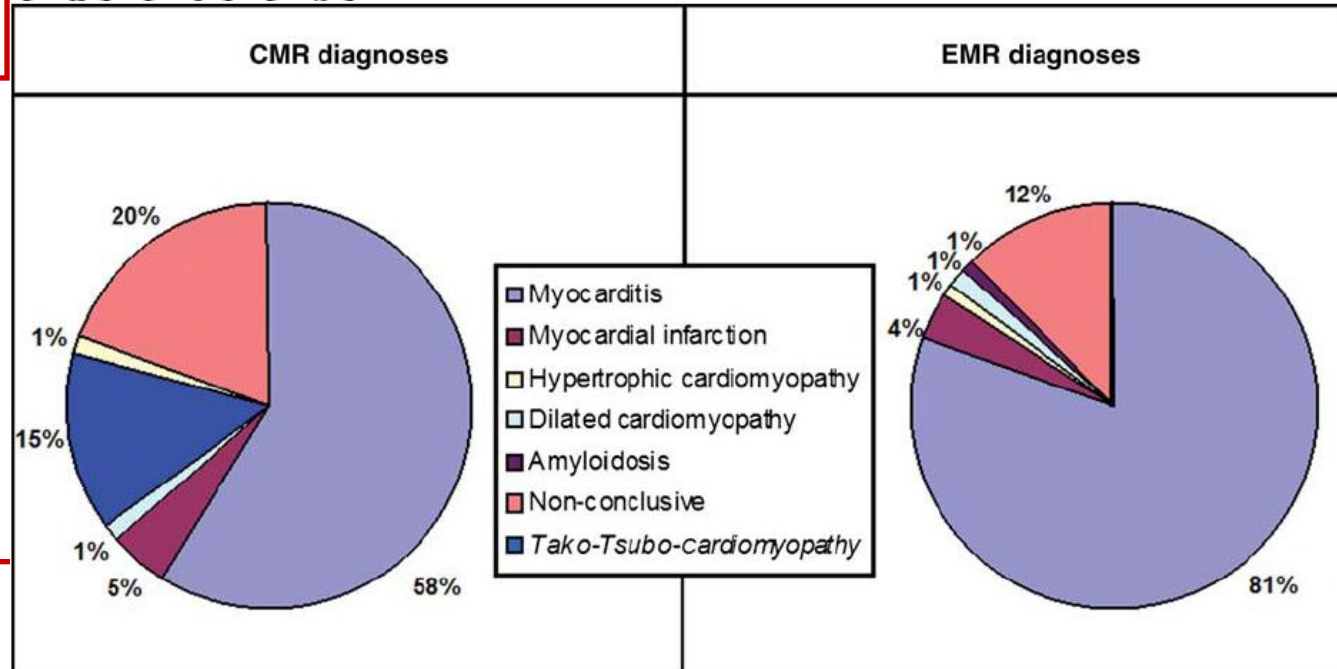
**Diagnostic synergy of non-invasive cardiovascular magnetic resonance and invasive endomyocardial biopsy in troponin-positive patients without coronary artery disease**

1174 pts with CP + cTn-positive at E&A undergoing invasive coronary angiography

**CMR** -> 1-4 days  
**EMB** -> 2-6 days



*Baccouche et EHJ 2009*



# ACS & Unobstructed Coronaries

## Differential Diagnosis

CMR failure (n = 16)		EMB failure (n = 10)		Combined-approach failure (n = 4)	
EMB diagnoses	Non-diagnostic CMR	CMR diagnoses	Non-diagnostic EMB	CMR diagnoses	EMB diagnoses
Active myocarditis	1	Myocarditis	5	Myocarditis	Focal amyloidosis
Borderline myocarditis	10	Myocardial infarction	1	Dilated CMP	Borderline myocarditis
Virus genome presence	3	Tako-Tsubo-CMP	3	Myocardial infarction	Borderline myocarditis
Dilated CMP	1	Normal CMR-scan	1	Normal CMR-scan	Normal histology
Normal histology	1				



**94% Interprocedural agreement**

# ACS & Unobstructed Coronaries

## Differential Diagnosis

Active myocarditis



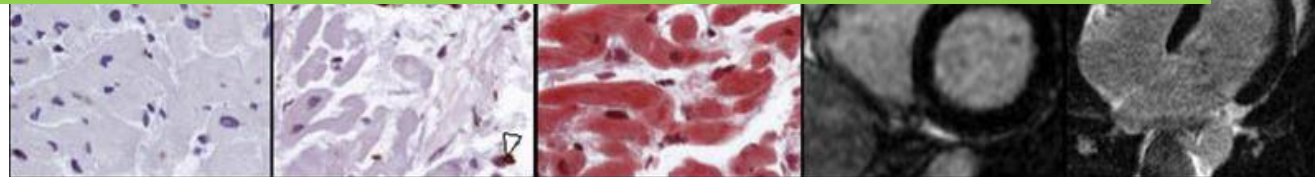
**Active myocarditis**  
LGE (+) 86-95%

CD3<sup>+</sup>

Variables	Diagnostic-CMR (n=54)	Non-diagnostic CMR (n=16)	P-Value
Max CK release	278 (144-605)	108 (75-203)	0.004
Max CK-MB release	30 (17-67)	15 (14-27)	0.030
LVEDV (ml)	154 (130-194)	130 (96-156)	0.015
LV-EF	53 (43-57)	56 (47-66)	NS

### Borderline myocarditis

LGE (+) 40-44%



Borderline myocarditis

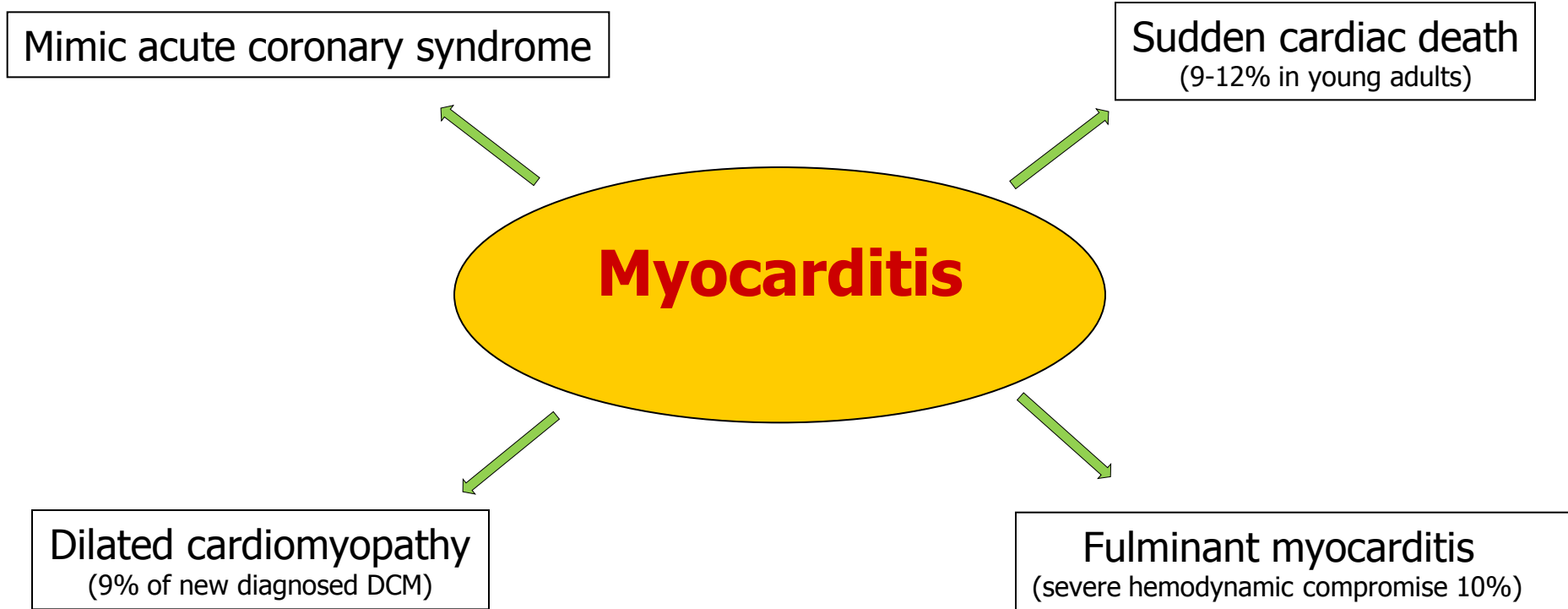


# ACS & Unobstructed Coronaries

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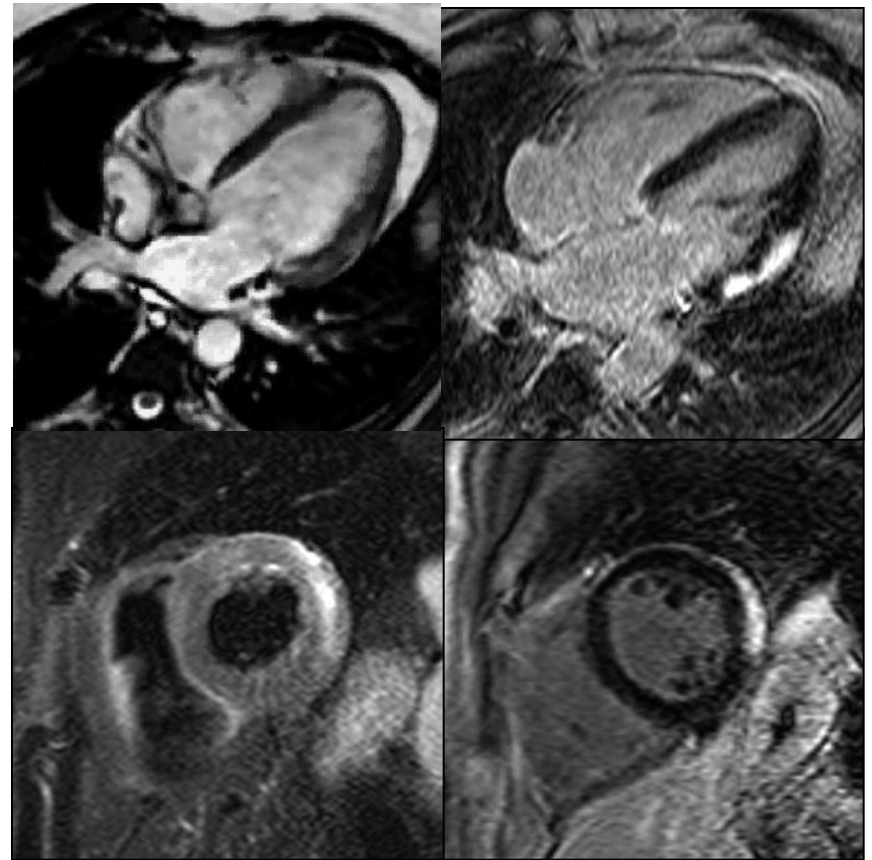
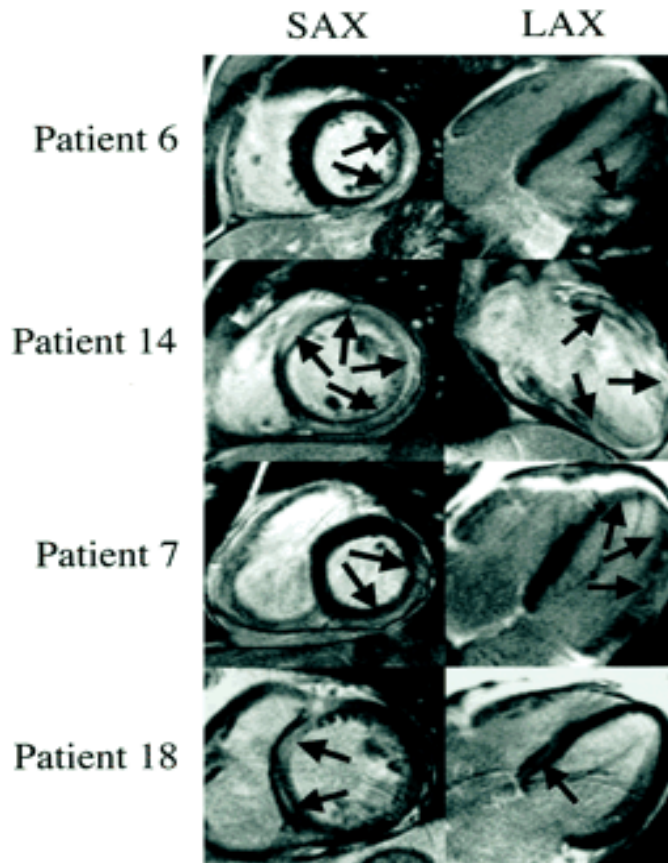
## Differential Diagnosis

### Multifacets Clinical Presentation



# ACS & Unobstructed Coronaries

## Acute Myocarditis



# ACS & Unobstructed Coronaries

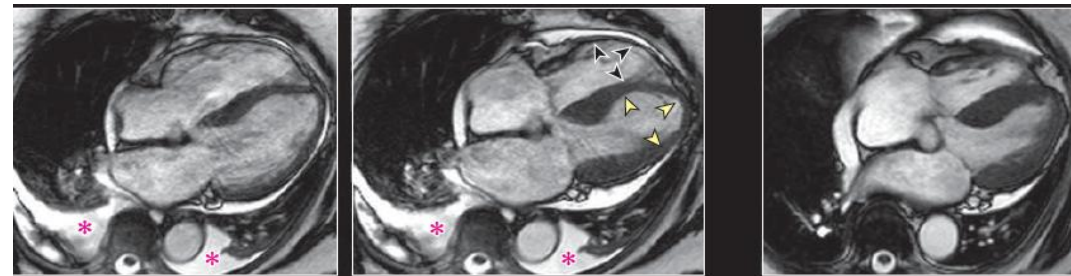
## - Differential Diagnosis- -Stress (Tako-Tsubo) CM-



256 pts with SCM based on clinical consensus (Mayo criteria)

- > 89% were women (mostly at post-menopausal age)
- > 88% ACS-like presentation
- > 71% with a stressful event <48-h

**Cine Imaging**  
(Biv ballooning in 34%)

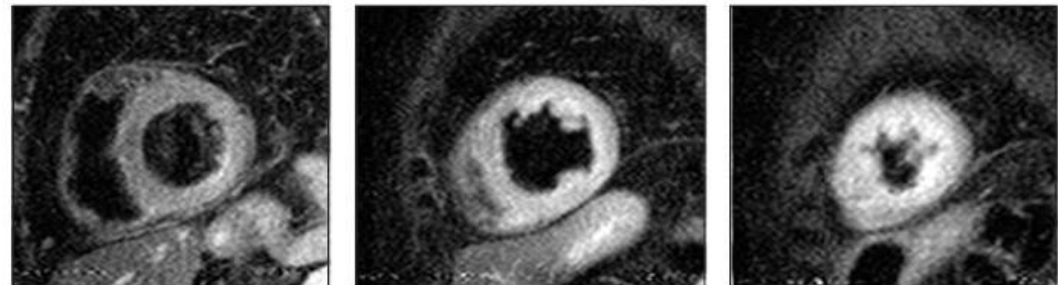


Basal myocardium

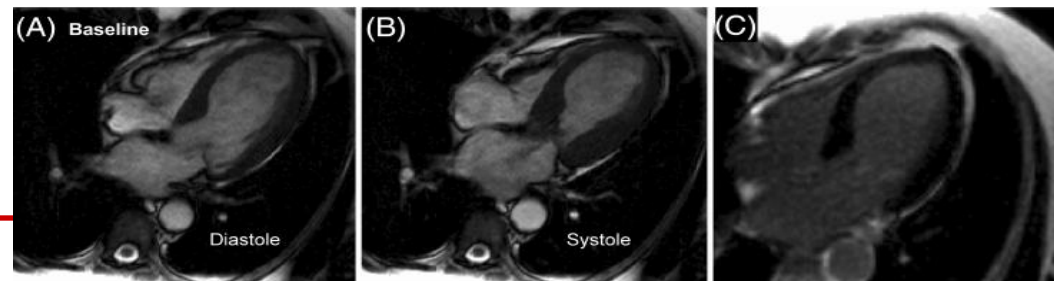
Middle myocardium

Apical myocardium

**T2-weighted imaging**  
(81% of patients myo/SM $\geq$ 1.9)



**Late Gd Imaging**  
(9% of pts with threshold of 3SD)



# ACS & Unobstructed Coronaries

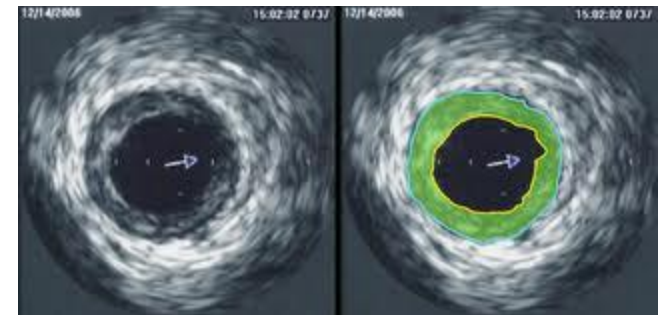
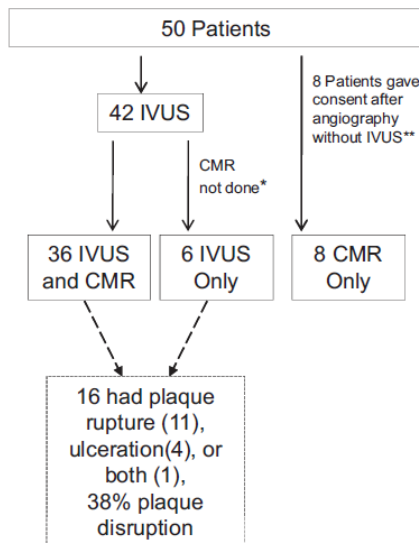


## Differential Diagnosis - Does gender matter?-



### Mechanisms of Myocardial Infarction in Women Without Angiographically Obstructive Coronary Artery Disease

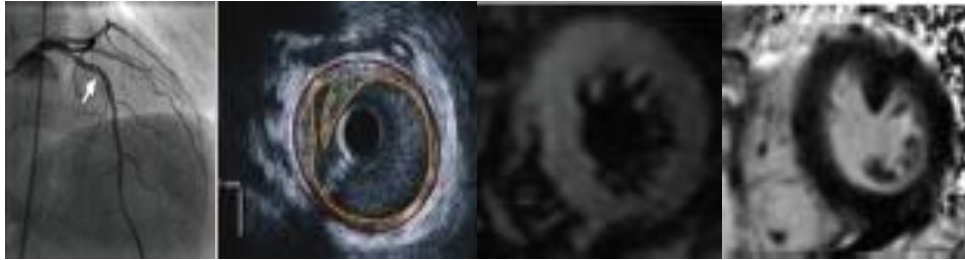
- 50 women (57 ± 17 yrs), with CP and cTn(+) with CA stenosis < 50% at ICA
- 11 with ST-segment elevation
- Median cTnI = 1.60 ng/mL
- Median CA stenosis (worst lesion) was 20% (30% with completely normal angio)



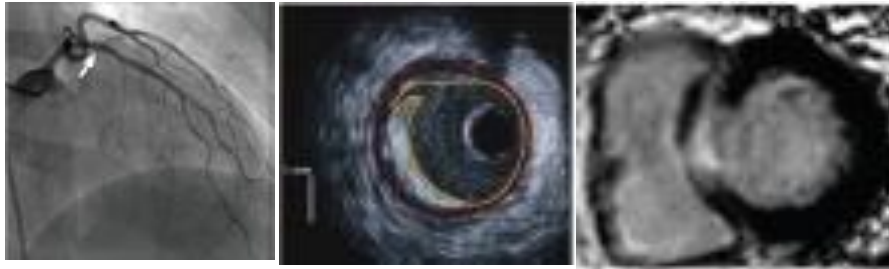
# ACS & Unobstructed Coronaries

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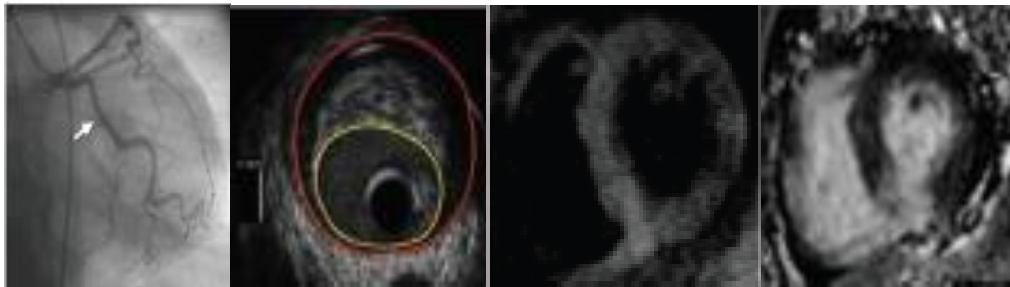
- **IVUS:** plaque disruption (ulceration/rupture) in 38% of cases
- **CMR:** abnormal in 59% of cases, mostly ischemic type  
(non ischemic-pattern in only 4 pts; none with plaque disruption)



**Plaque disruption** was accompanied by **myocardial edema** in 75% of cases



**Plaque disruption** with myocardial **LGE** in 1 case

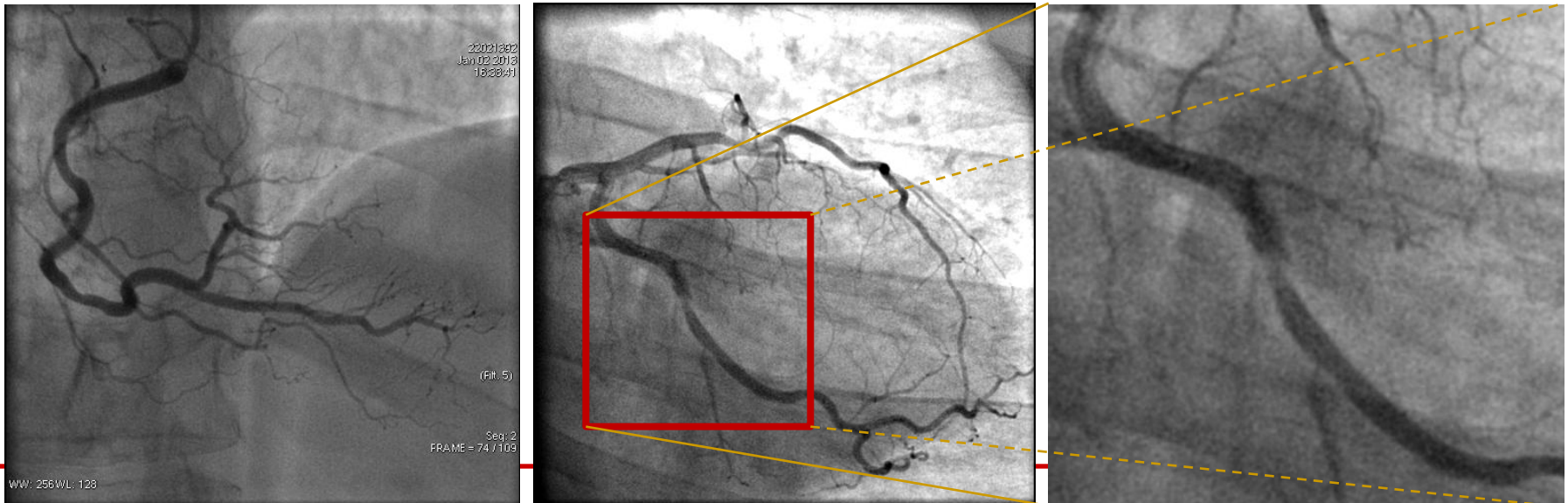


**Atherosclerosis & LGE**

# ACS & Unobstructed Coronaries

## Differential Diagnosis - Clinical Case #1-

43 y.o man smoker, typical long-lasting CP,  
cTnI 3.41 ng/ml, no WM abnormalities at echo

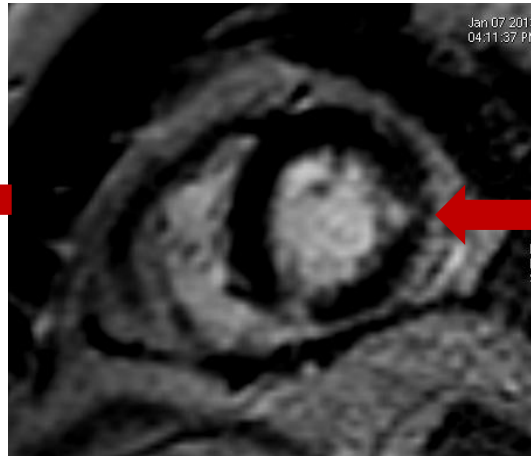


# ACS & Unobstructed Coronaries

## Differential Diagnosis - Ischemic Causes -

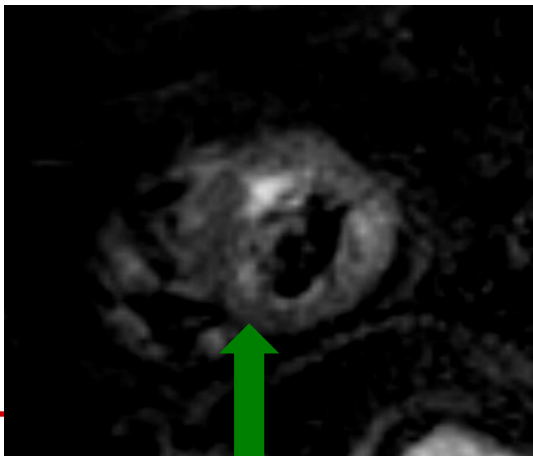


T2w-STIR



Late GE

**Plaque disruption and  
distal embolization**



**Previous irreversible  
Ischemic damage**

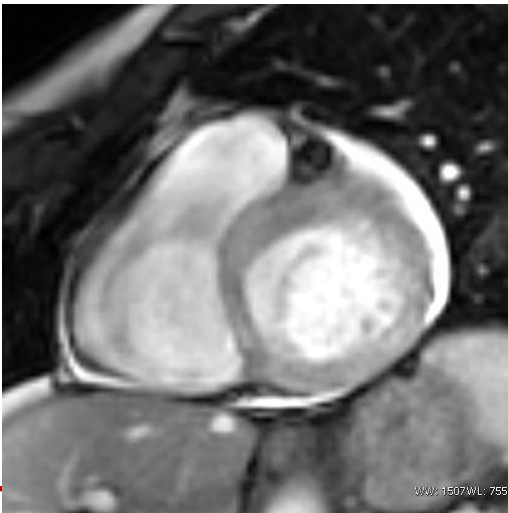
# ACS & Unobstructed Coronaries

## Differential Diagnosis

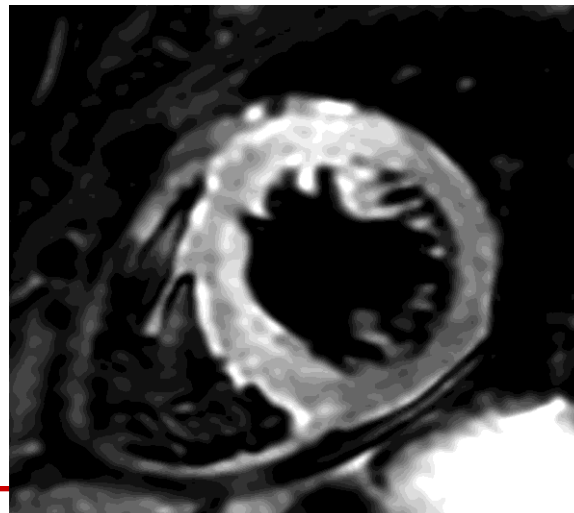
### - Clinical Case #2-

63-year old woman with typical chest pain, late presentation at E&A, minimal increment of cTnI (=0.06 ng/ml), ECG: negative T wave in DI and V2-V5, normal coronary angiograms

## Coronary Vasospasm



Cine Imaging



T2-w imaging



Late Gd Enhancement



# ACS & Unobstructed Coronaries

## Myocarditis / Clinical Case

2007

2008

2009

2011

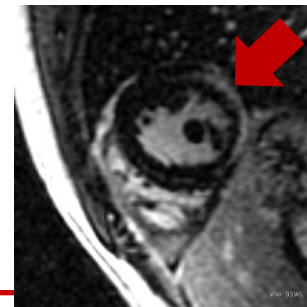
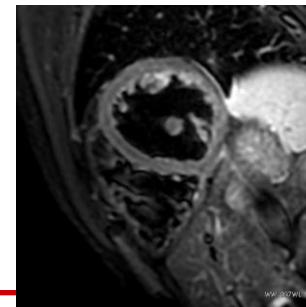
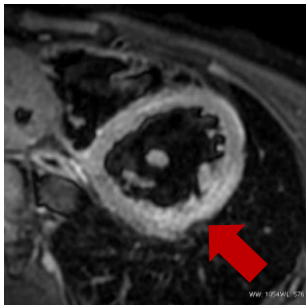
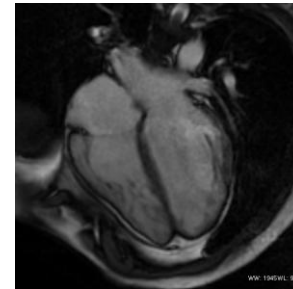
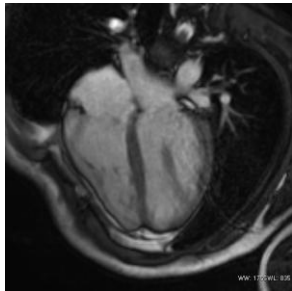
LVEDVi/ESVi=98/47 ml/mq  
LVEF=52%; LGE=23% of LV

LVEDVi/ESVi=108/51 ml/mq  
LVEF=52%; LGE=18% of LV

**24h-Holter:**  
mean 58 bpm  
SD-RR: 196ms  
1 VEB  
**CP test**  
175W, 80% FCTM  
Peak O2: 30ml/kg/min  
**Medication:**  
Candesartan 8 mg/die

**24h-Holter:**  
mean 63 bpm  
SD-RR: 262ms  
504 VEB

**24h-Holter:**  
mean 53 bpm  
SD-RR: 272ms  
1061 VEB(2-pattern)  
**CP test:**  
240 W  
Peak O2: 47ml/kg/min  
**Medications**  
Candesartan 8 mg/die



T2-w

LGE

T2-w

LGE

# Magnetic Resonance and Risk of Arrhythmic Death

## Long-Term Follow-Up of Biopsy-Proven Viral Myocarditis

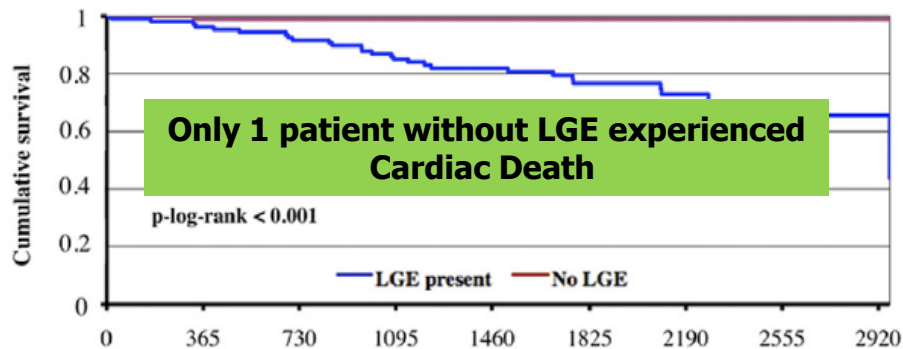
Predictors of Mortality and Incomplete Recovery

222 pts with biopsy-proven myocarditis  
(inflammation+viral genome) & CMR

LGE(+)/(-) = 108/95 pts; median FU: 4.3 years

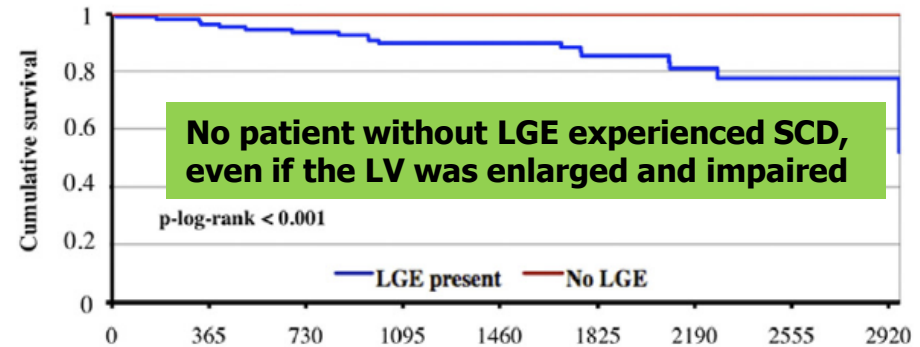
15% CV mortality; 9.9% SCD

Characteristics	LGE(+) (n=108)	LGE(-) (n=95)	P-Value
Mean age (years)	55 (41-67)	50 (38-59)	0.08
Female n, (%)	26 (24)	37 (29)	<0.05
Primary CP n, (%)			
ACS	37 (34)	37 (39)	0.49
New-onset HF	37 (34)	25 (26)	0.22
Recurring HF	11 (10)	7 (7)	0.48
Aspecific aborted SCD	23 (21) 0 (0)	26 (27) 0 (0)	0.31
NYHA class III-IV	51 (54)	40 (42)	<0.05
BNP, pg/ml	336 (82-983)	67 (27-457)	<0.001
CMR			
LV-EDV	188 (140-263)	155 (120-193)	<0.001
LV-ESV	199 (57-179)	73 (43-113)	<0.001
LV-EF	38 (25-57)	53 (39-64)	<0.001



### Cardiac Mortality

(Adjusted HR: 12.8, P<0.01)



### Sudden Cardiac Death

Marholdt H J Am Coll Cardiol 2012

# ACS & Unobstructed Coronaries

## Differential Diagnosis - How to improve it -

Variables	Diagnostic CMR (n=39)	Non-diagnostic CMR (N=21)	P-Value
False positive cTnI	8%	57%	<0.001
cTnI <5ULN	13%	52%	<0.001
SVT / VT	5%	24%	0.045
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*Assomoull et al  
EHJ 2007*

*Boccuccheet al  
EHJ 2009*

Variables	Diagnostic-CMR (n=54)	Non-diagnostic CMR (n=16)	P-Value
Max CK release	278 (144-605)	108 (75-203)	0.004
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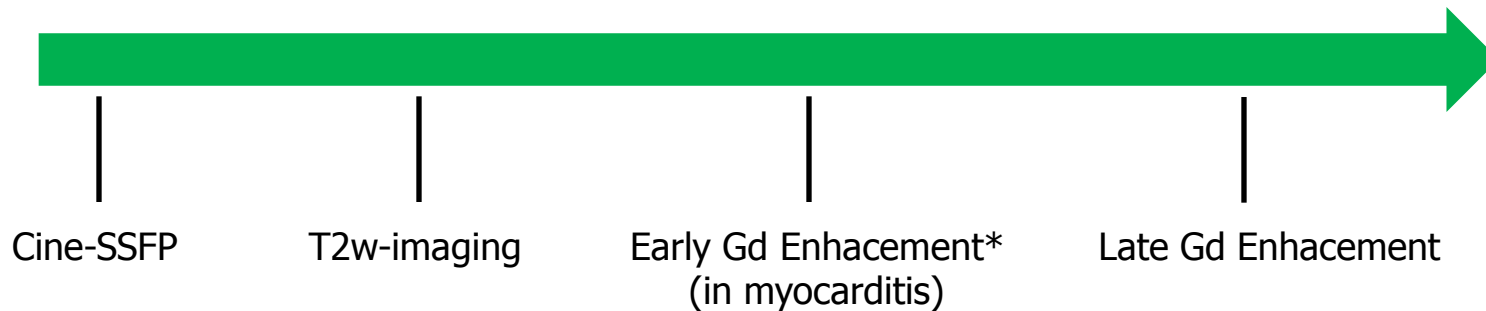
# ACS & Unobstructed Coronaries

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## Differential Diagnosis - How to improve it -



1. Use a comprehensive CMR protocol



2. Novel techniques (T1 and T2 mapping & inflammation-based <sup>19</sup>F MRI)

3. Pathophysiological reasoning

4. Multimodality diagnostic approach

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Leuven (Belgium)**

# ACS & Unobstructed Coronaries

## Differential Diagnosis - How to improve it -

### Improved Detection of Myocardial Involvement in Acute Inflammatory Cardiomyopathies Using T2 Mapping

