Takotsubo Cardiomyopathy

계명의대 심장내과

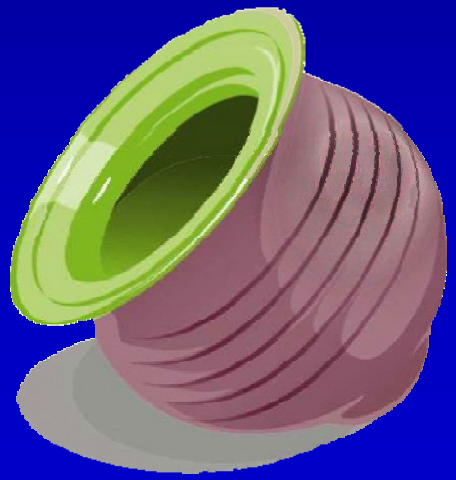
김 형 섭

Takotsubo Cardiomyopathy

Nomenclature

- **Takotsubo Cardiomyopathy**
- **Transient LV Apical Ballooning Syndrome**
- **Broken Heart Syndrome**
- **Ampulla Cardiomyopathy**
- **Stress-induced Cardiomyopathy**

Overstimulation of sympathetic component in pathophysiologic significance of stress hormones



Takotsubo Cardiomyopathy

General Misunderstandings

- **As early as 1940's**
  - **Intracranial lesion with ECG abnormalities**
  - **Cardiac syndrome X**
- **Not uncommon**
  - **Many different races (Caucasian, Asian, Mediterranean)**
- **Variant forms of Takotsubo cardiomyopathy**
  - **Inverted Takotsubo, Midventricular ballooning syndrome**

Takotsubo Cardiomyopathy

Guidelines for Diagnosis

Definition

- ✓ Acute LV apical ballooning of unknown cause
- ✓ Nearly complete resolution of apical akinesia *within a month*
- ✓ Abnormal contraction

  mainly LV with dynamic obstruction of LVOT
  or RV in some cases

Circ J 2007;71:990-992.

Takotsubo Cardiomyopathy

Guidelines for Diagnosis

Exclusion

A. Significant organic or spasm of coronary artery
   Desirable for CAG in acute stage
   Necessary for CAG in chronic stage

B. Cerebrovascular disease

C. Pheochromocytoma

D. Viral or idiopathic myocarditis

Note: Cerebrovascular disease or Pheochromocytoma with Takotsubo-like myocardial dysfunction

Circ J 2007;71:990-992.

Takotsubo Cardiomyopathy

Guidelines for Diagnosis

Reference for diagnosis

A. Symptoms
   Chest pain & Dyspnea such as ACS or No Symptoms

B. Triggers
   Emotional or physical stress or No apparent trigger

C. Age & Gender : Elderly, particularly female

D. Ventricular morphology
   Apical ballooning and rapid improvement in LVgram or Echo

E. ECG
   Variable changes of ST segment, T wave, Q wave and QT interval

F. Cardiac biomarker : modest elevations of cardiac enzyme and Troponin

G. Myocardial radionuclide study : Abnormal findings in some cases

H. Prognosis : rapidly repair, pulmonary edema, other sequelae or death

Circ J 2007;71:990-992.

Takotsubo Cardiomyopathy

Epidemiology

Prevalence of 2-2.5 % of ACS patients in US

Not confined to Asia and Japan, but all over the world

Mean age: 58~77 years (range:10~89 years)

Elderly Women; over 90 % of cases

Postmenopausal women: ~ 85 % of cases, regardless of origins

General cardiovascular risk factors

Hypertension; 40-50 %

Dyslipidemia; 25-30 %

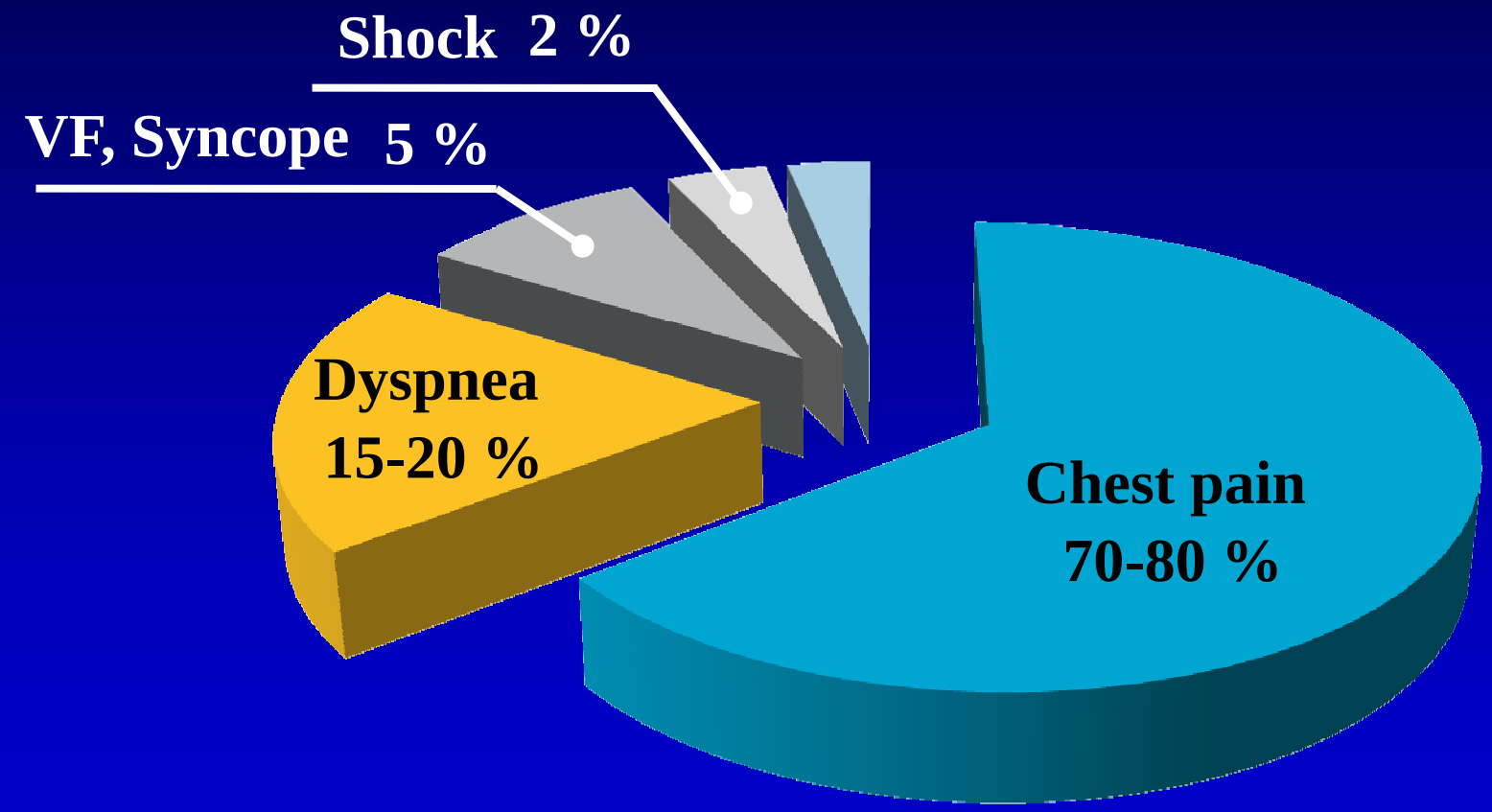
Smoking; 20-25 %

Diabetes; 10%

Family history of cardiac disease; 10%

Takotsubo Cardiomyopathy

Clinical Profile



Int J Cardiol 2008;124:283-292.
Eur Heart J 2006;27:1523-1529.

Takotsubo Cardiomyopathy

Stressful Events

Emotional stressor

Unexpected death of a relative or friend, Domestic abuse, Confrontational arguments, Catastrophic medical diagnosis, Devastating business, Gambling losses

Physical stressor

Exhausting work, Asthma attack, Gastric endoscopy, Exacerbated systemic disorders

However, in 35% of all patients, there was no preceding emotional or physical stressful events identified.

Takotsubo Cardiomyopathy

Laboratory Data

NT-ProBNP or BNP

Elevated in 85 %

Initially elevated and quickly decreased

Not correlated with severity of LV function or recovery

Troponin-I or T, CK-MB

Positive in 70-85 %

Usually only slightly elevated, despite the large extension of WMA

Serum catecholamine

Elevated in 75-80 %

Markedly two or three times higher, compared with AMI with Killip class III

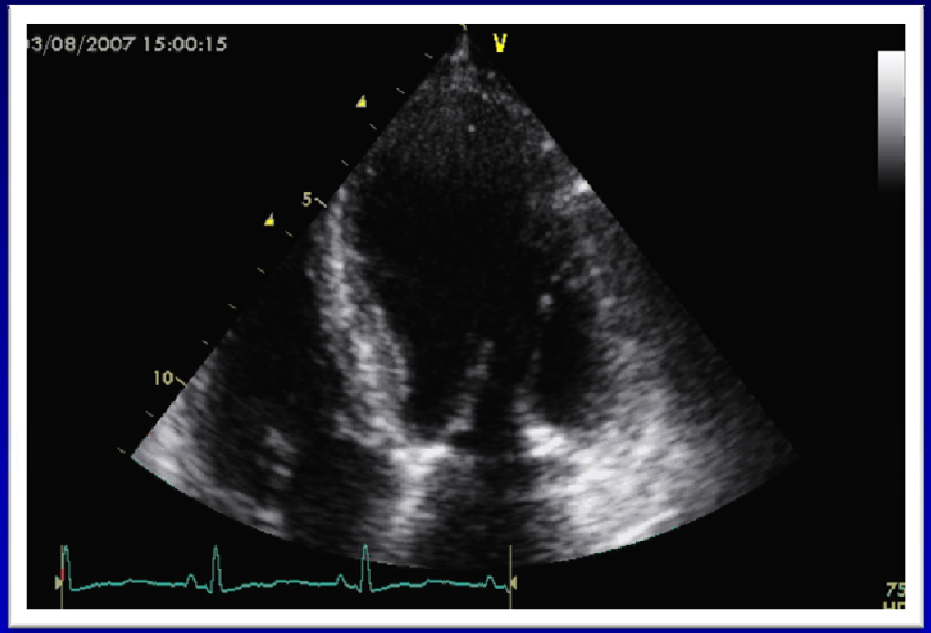
Takotsubo Cardiomyopathy

Echocardiography

Apical akinesis or dyskinesis

Moderate to severe midventricular dysfunction

Preserved or hyperkinetic basal function



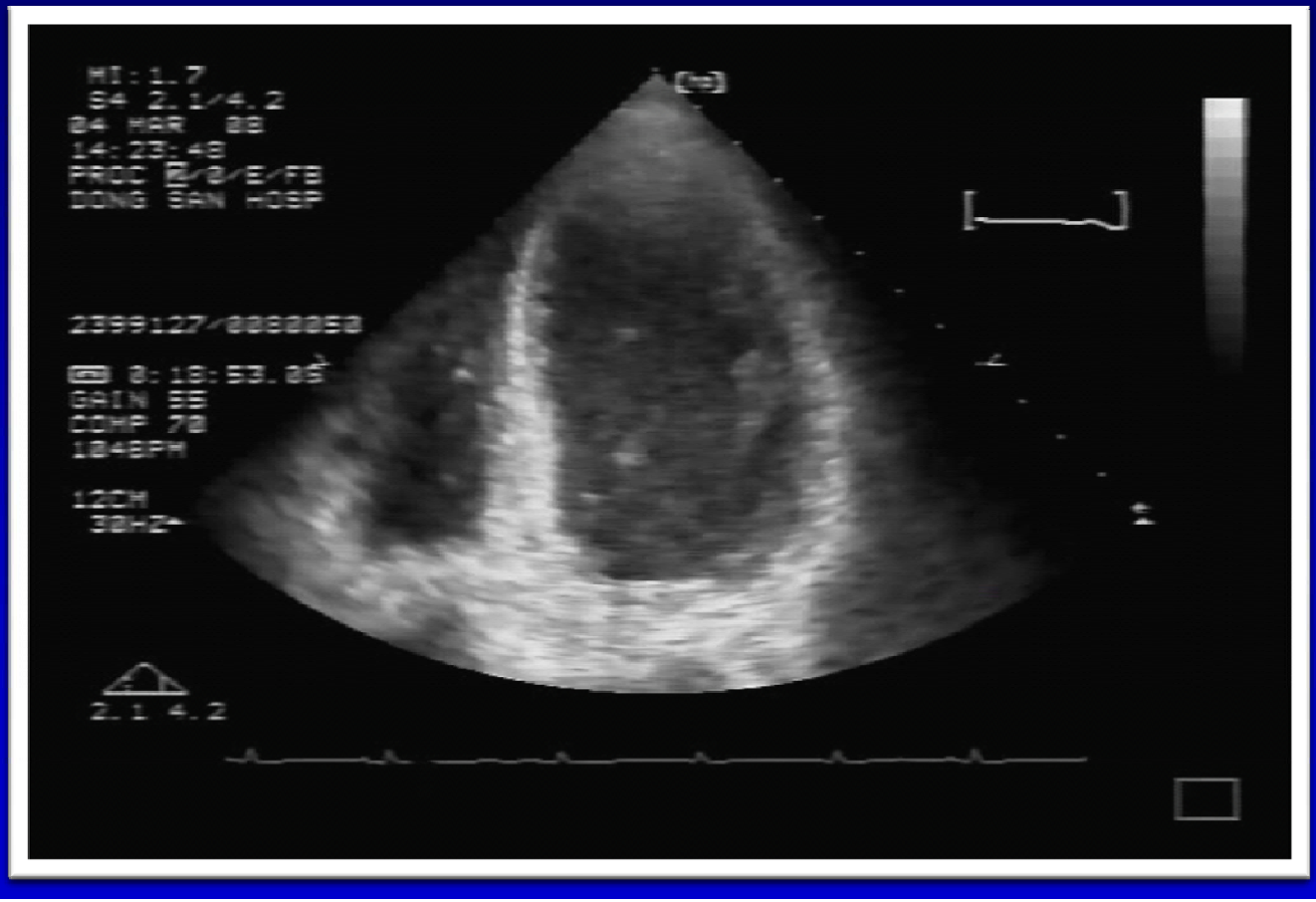
✓*Transient, dynamic intraventricular pressure gradients*

✓*Dramatic improvements* ***within 1 months or up to 6 – 12 months***

Takotsubo Cardiomyopathy

Echocardiography

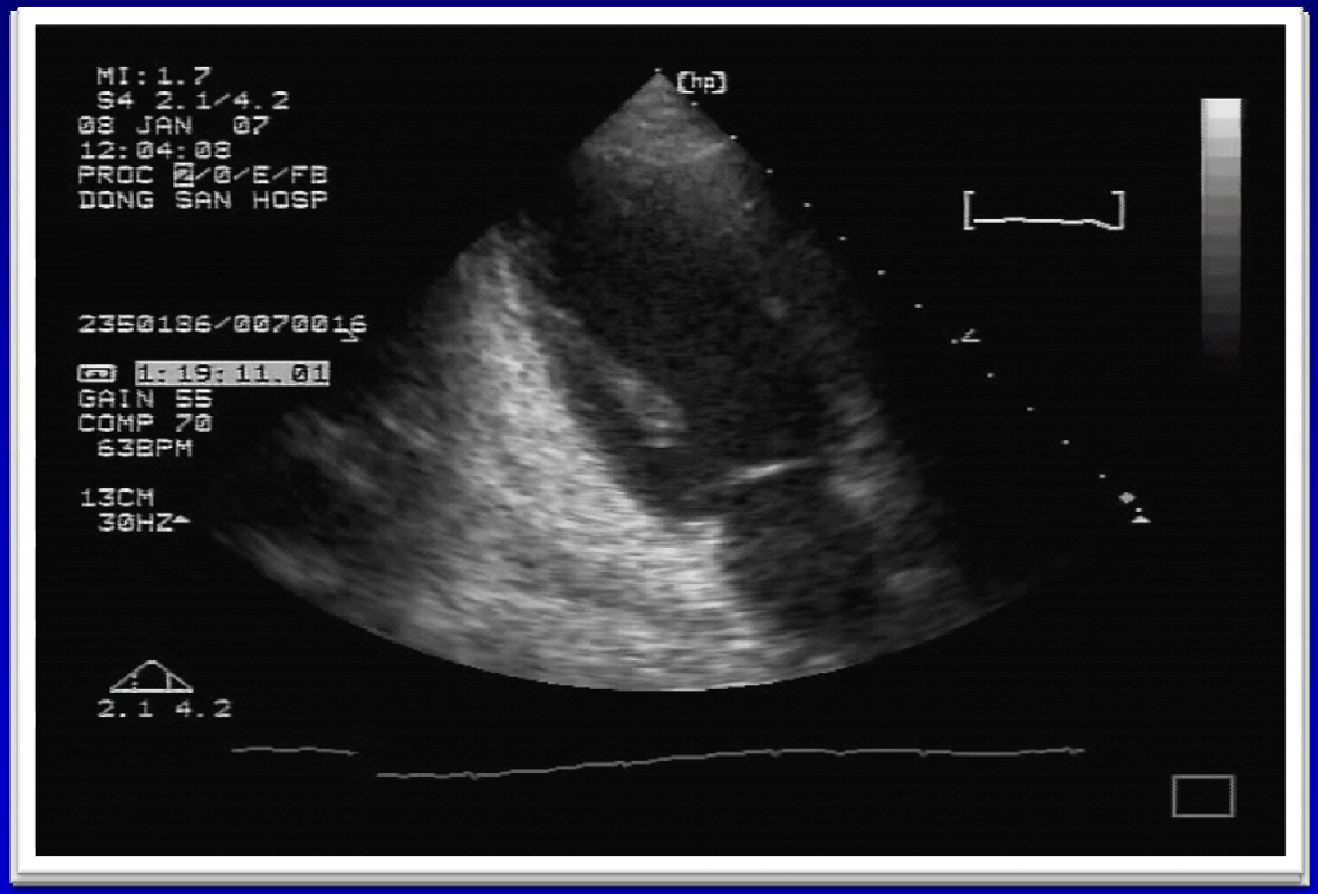
Variant form-Midventricular hypo/akinesis ; up to 30 %



Takotsubo Cardiomyopathy

Echocardiography

Inverted Takotsubo-like Myocarditis



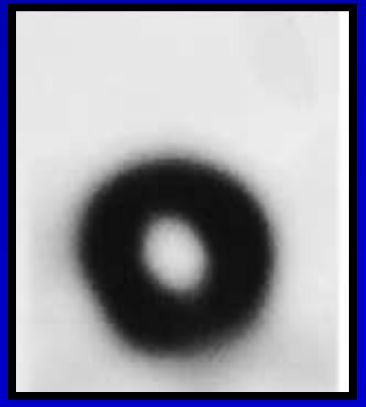
Takotsubo Cardiomyopathy

Radionuclide Study

Perfusion imaging of ^{99m}Tc-Tetrofosmin SPECT

Acute phase

Chronic phase

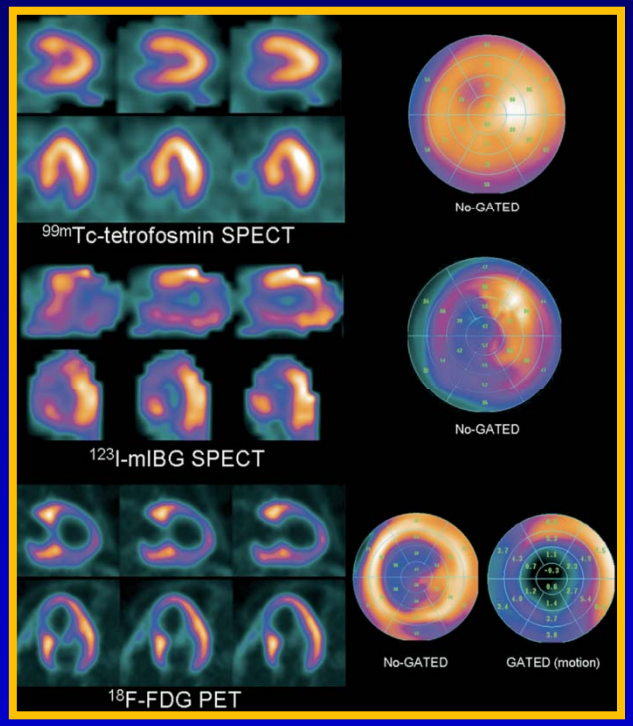


J Am Coll Cardiol 2003;41:737-742..

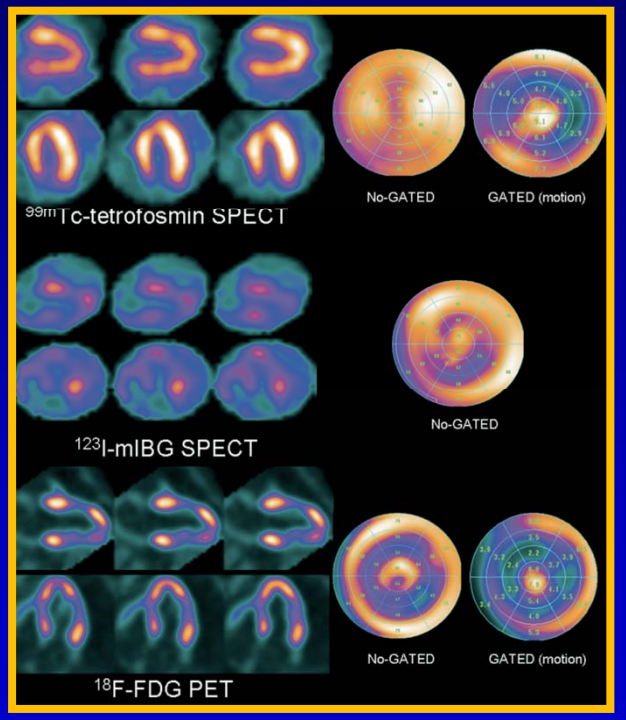
Takotsubo Cardiomyopathy

Radionuclide Study

Myocardial Stunning



Apical type in subacute phase



Midventricular type in subacute phase

J Nucl Cardiol 2008;15:137-141.

Takotsubo Cardiomyopathy

Radionuclide Study

Myocardial Perfusion

- ✓ **Acute phase**

  In the cases of 85 %, decreased radioisotope perfusion at apex
  impaired coronary microcirculation

- ✓ **Subacute phase**

  Improvement of perfusion after 3-5 days

- ✓ **In 3% of follow-up cases,**

  No-flow phenomenon compatible with *scar*

Myocardial Stunning

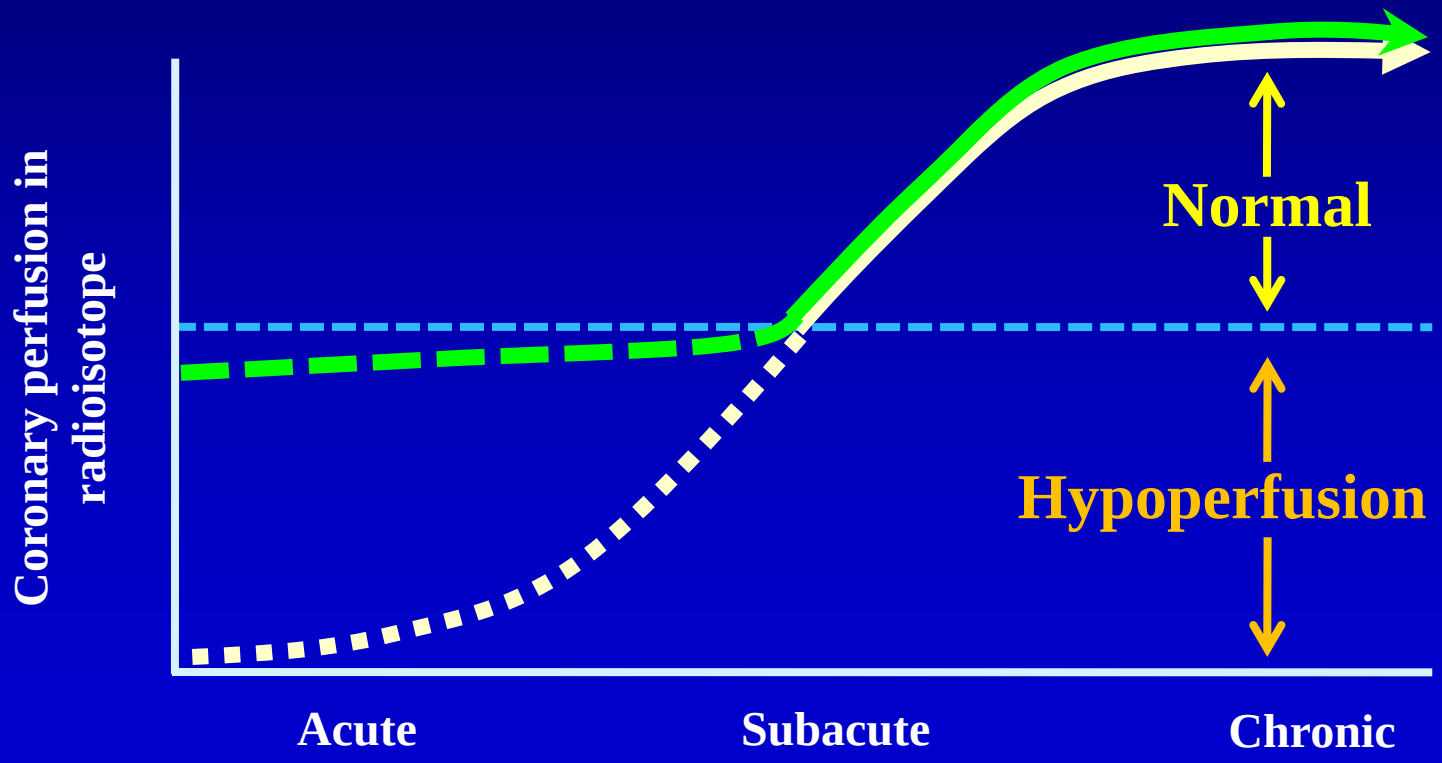
Decreased uptake of Fluorine-^{18}FDG
with relatively normal perfusion

Ann Nucl Med 2003;17:115-122.
J Am Coll Cardiol 2003;41:737-742.

Takotsubo Cardiomyopathy

Radionuclide Study

Radioisotope uptake according to time phase



Takotsubo Cardiomyopathy

ECG Changes

ST-T changes in Takotsubo cardiomyopathy and in coronary disease

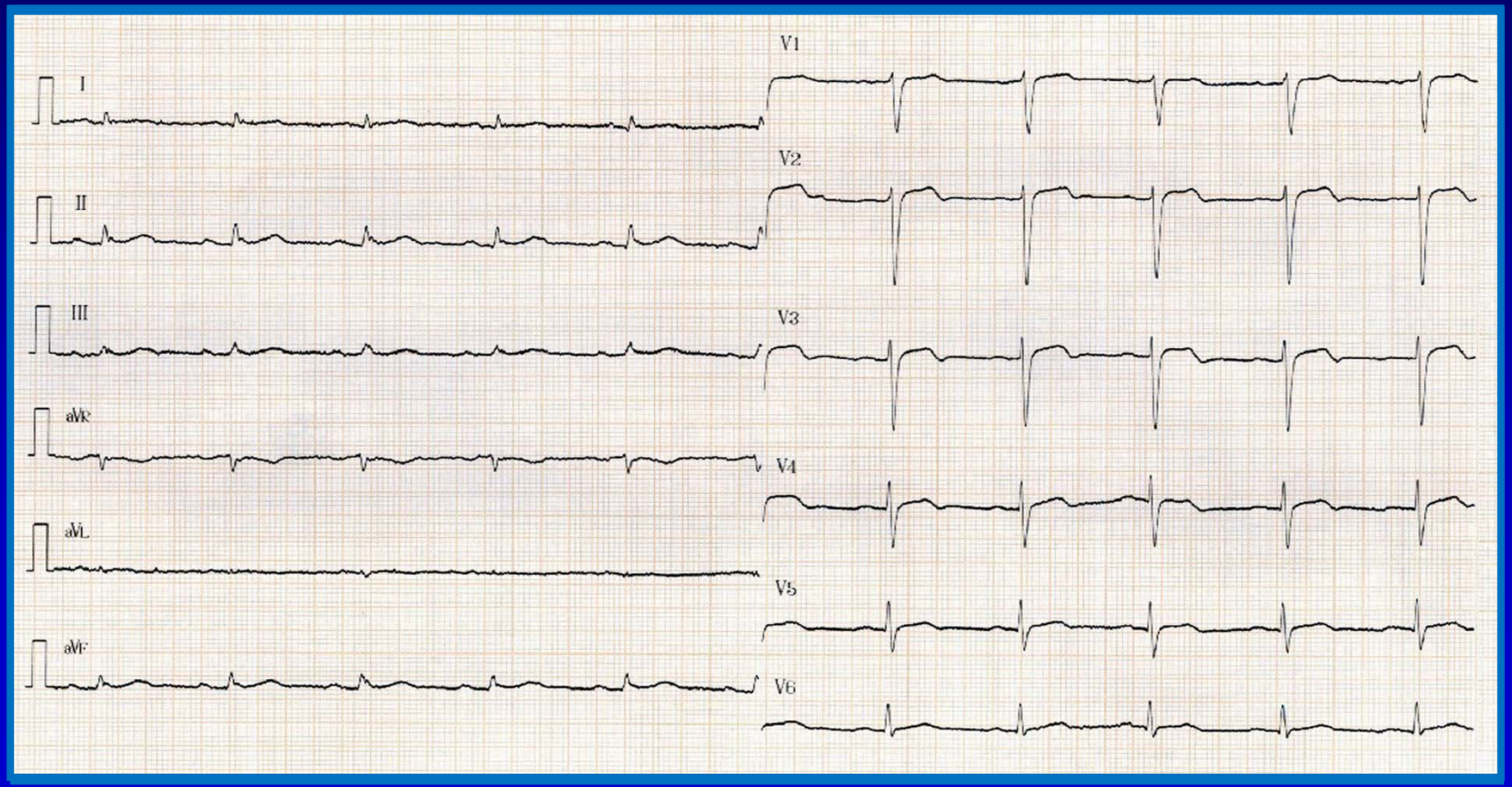
Takotsubo cardiomyopathy	Coronary diseases
The direction of the ST segment deviation, Not accurately localize an involved region.	ST elevation, directed toward ischemic region. ST depression, directed away from ischemic region
ST changes, mostly in lateral or inferior leads, and rarely in V_1-V_3.	ST changes, mostly in V_1-V_3, rather than in III and aVF.
T changes, not parallel to the ST deviation	T changes, accompany the ST changes in the involved lesion.
Giant negative T wave in 86%, especially on the 3rd day and fluctuated changes.	Giant negative T wave in < 20%, and rare fluctuated.
Prolonged QT interval in 26%	Prolonged QT interval, Not typical of coronary artery diseases

Eur J Intern Med 2007;71:990-992.

Takotsubo Cardiomyopathy

ECG Changes

On admission Monday



Suggested Mechanism of Takotsubo Cardiomyopathy

Suggested Pathophysiology

Hypoplastic Coronary

Hypoplastic Coronary System With *Smaller and Shorter Branch* to Apex

Mediterranean or *Asian* origin
Particularly, *Postmenopausal women*

40 % of these women ;
Hypoplastic branching vessels from PDA

⇩

Apical/Mid hypokinesia of LV or RV

Suggested Pathophysiology

Endothelial dysfunction

Postmenopausal women with estrogen deficiency
Increased platelet aggregation
Mitochondrial dysfunction

- ***Microcirculatory or platelet impairment***
- ***Induce Cardiomyopathy***

Suggested Pathophysiology

Epicardial Coronary Spasm

? Less than 3 % of apical ventricular dyskinesia

Incidence of provocable multivessel spasm; 0 – 43%

? Not always have a long, distal LAD supplying the diaphragmatic region

? Distribution of all three coronary territory and transient RV systolic dysfunction

Suggested Pathophysiology

Coronary Microcirculation

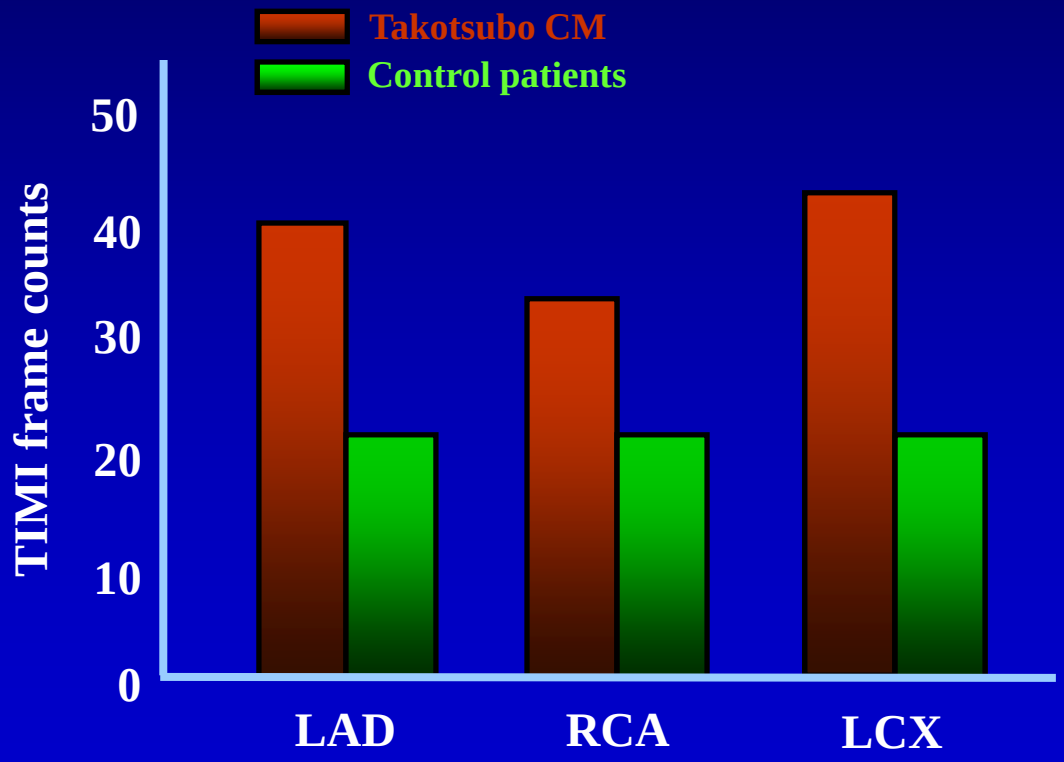
1) Flow heterogeneity between subendocardial and subepicardial perfusion

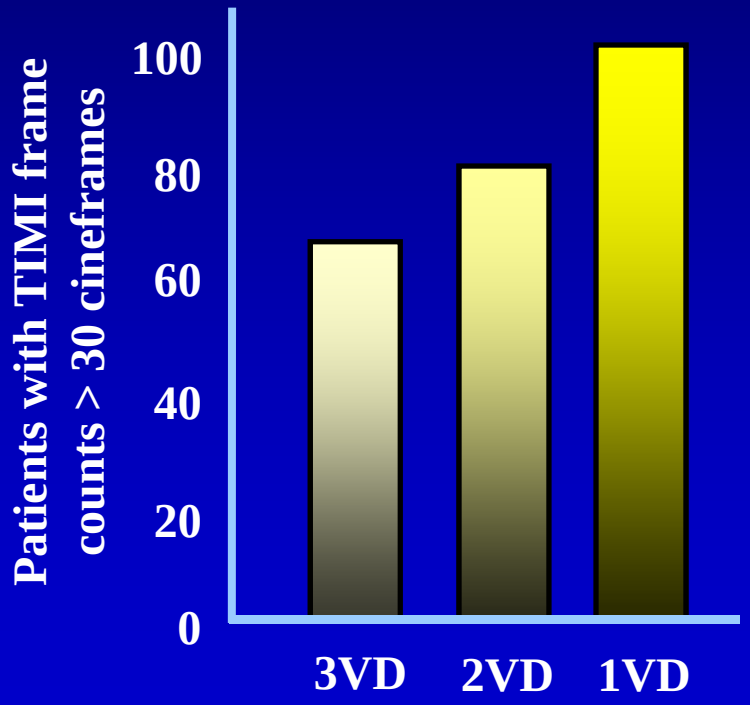
2) Mismatch between oxygen demand and supply

- ***CAG***
  identify epicardial lumen vessel anatomy
- ***ECG with Echocardiography***
  reflect the physiology of myocardium during a disease

Suggested Pathophysiology

Coronary Microcirculation





Am J Cardiol 2004;94:343-346.

Suggested Pathophysiology

Coronary Microcirculation

Indicative of diffuse coronary microvascular dysfunction

However,

- ✓ **Not always consistent findings or**
- ✓ **Not demonstrated by Doppler guidewire or Contrast echocardiograpahy**
- ✓ **Unclear whether primary cause or secondary phenomenon**

Suggested Pathophysiology

Catecholamiergic hyperdynamics

- ✓ *Increments of Heart rate, Contractility, O_2 Consumption, Platelet aggregation*
- ✓ *Create a sudden hemodynamic burden*
- ✓ *Activate a cascade of microhormonal coronary change*
  Nitric oxide, Prostacyclin, Thrombomodulin, Neuropeptide Y
- ✓ *Worsening of endothelial function & microcirculation*

Suggested Pathophysiology

Catecholamiergic overloads

Direct myocyte injury

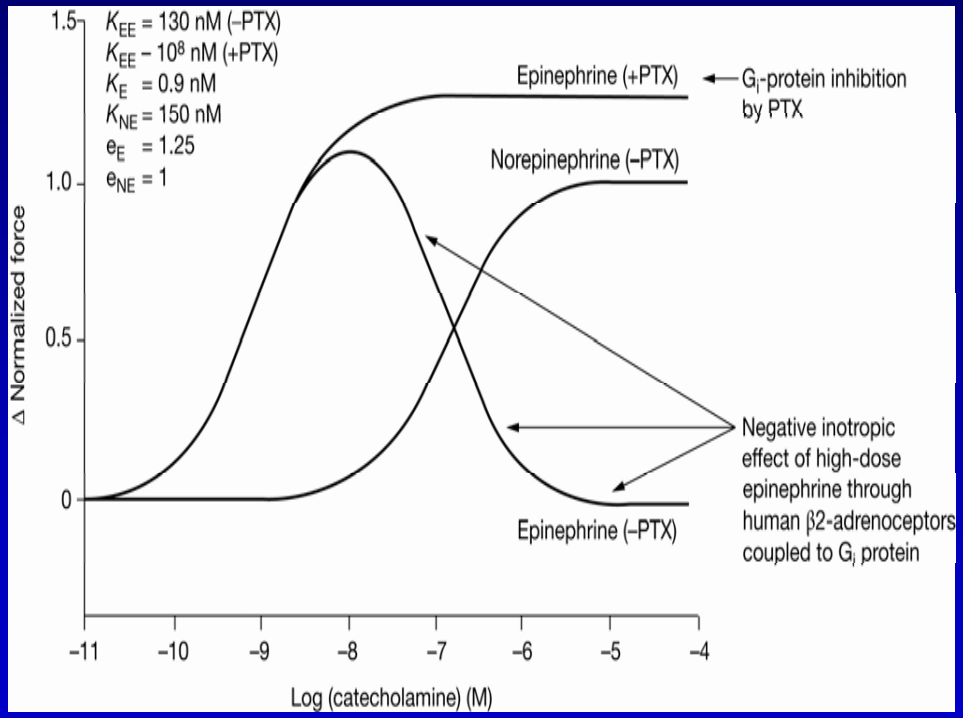
- ✓ *cAMP mediated Ca^{++} overloads with resultant Ca^{++} leakage*
- ✓ *Decrements of synthetic activity and viability*

- *? Near normal level of catecholamine in other studies*
- *? Epiphenomenon or hemodynamic results*

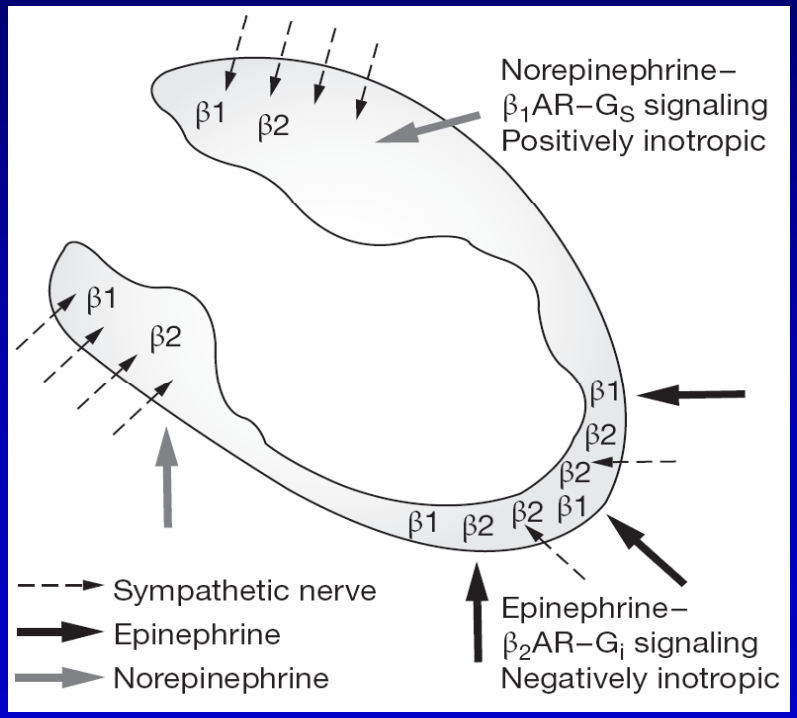
Suggested Pathophysiology

Different Adrenoreceptor

Beta 1-AR and Beta 2-AR vs. Gs protein and Gi protein



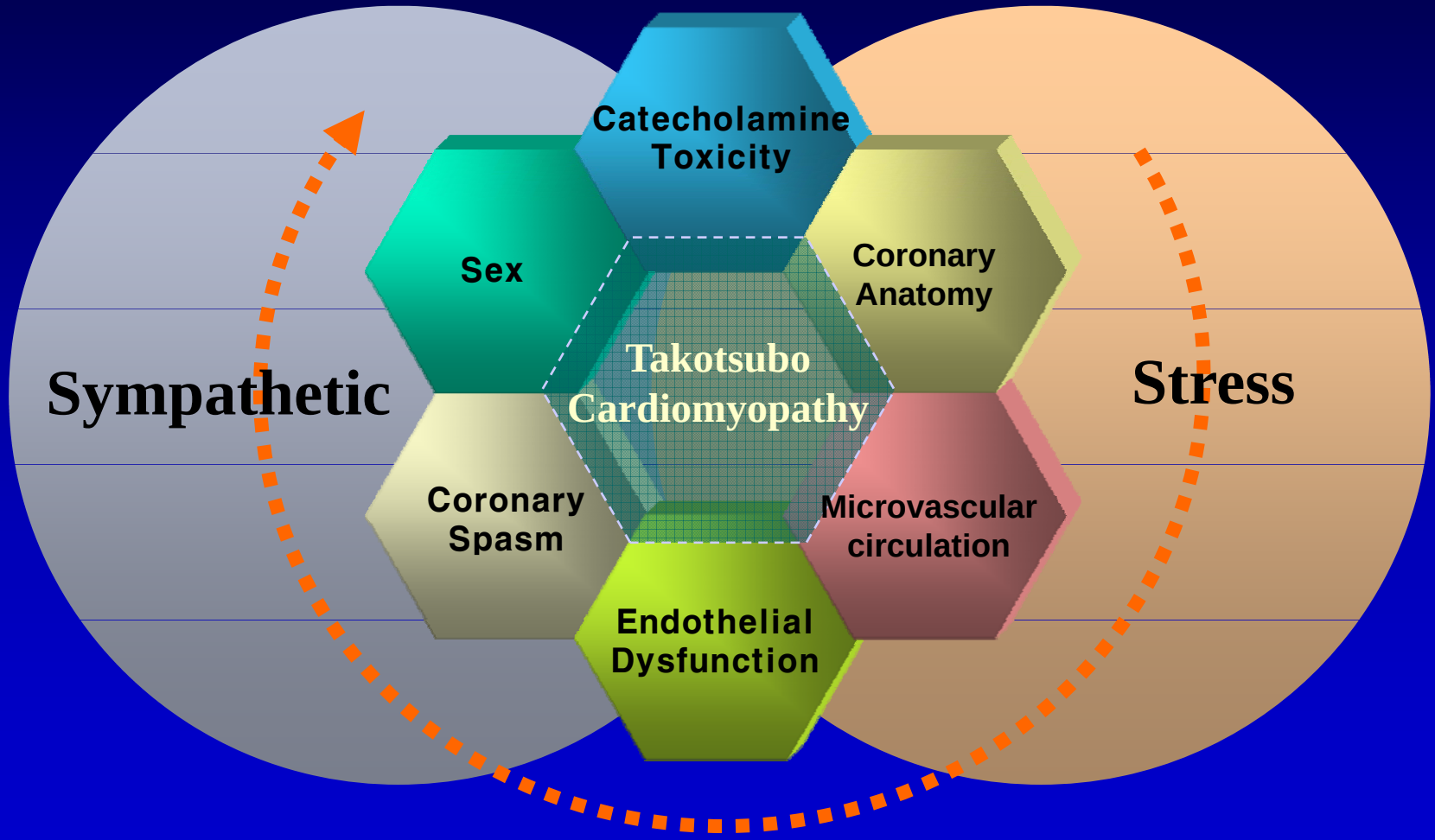
Stimulus Trafficking



Regional Differences of Beta-Subreceptor

Nat Clin Pract Cariovasc Med 2008;5:22-29.

Suggested Pathophysiology



RV Involvement in Takotsubo Cardiomyopathy

Journal of the American College of Cardiology

Published by Elsevier Inc.

CORRESPONDENCE

Research Correspondence

Transient Cardiac Apical Ballooning Syndrome:
Prevalence and Clinical Implications of Right Ventricular Involvement

Elesber et al. J Am Coll Cardiol 2006;47:1082-1083.

25 Patients Takotsubo CM With RV Involvement

- ✓ RV Dysfunction
- ✓ Lower LVEF
- ✓ Longer Hospitalization

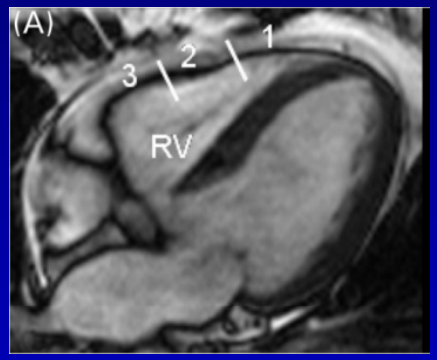
More complications

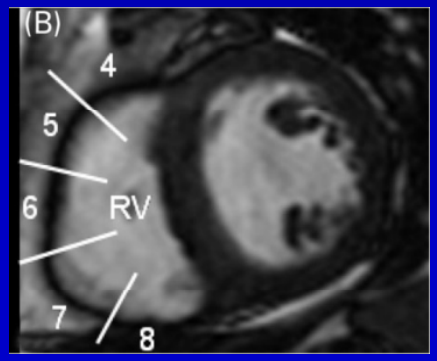
- Severe CHF
- IABP
- CPR

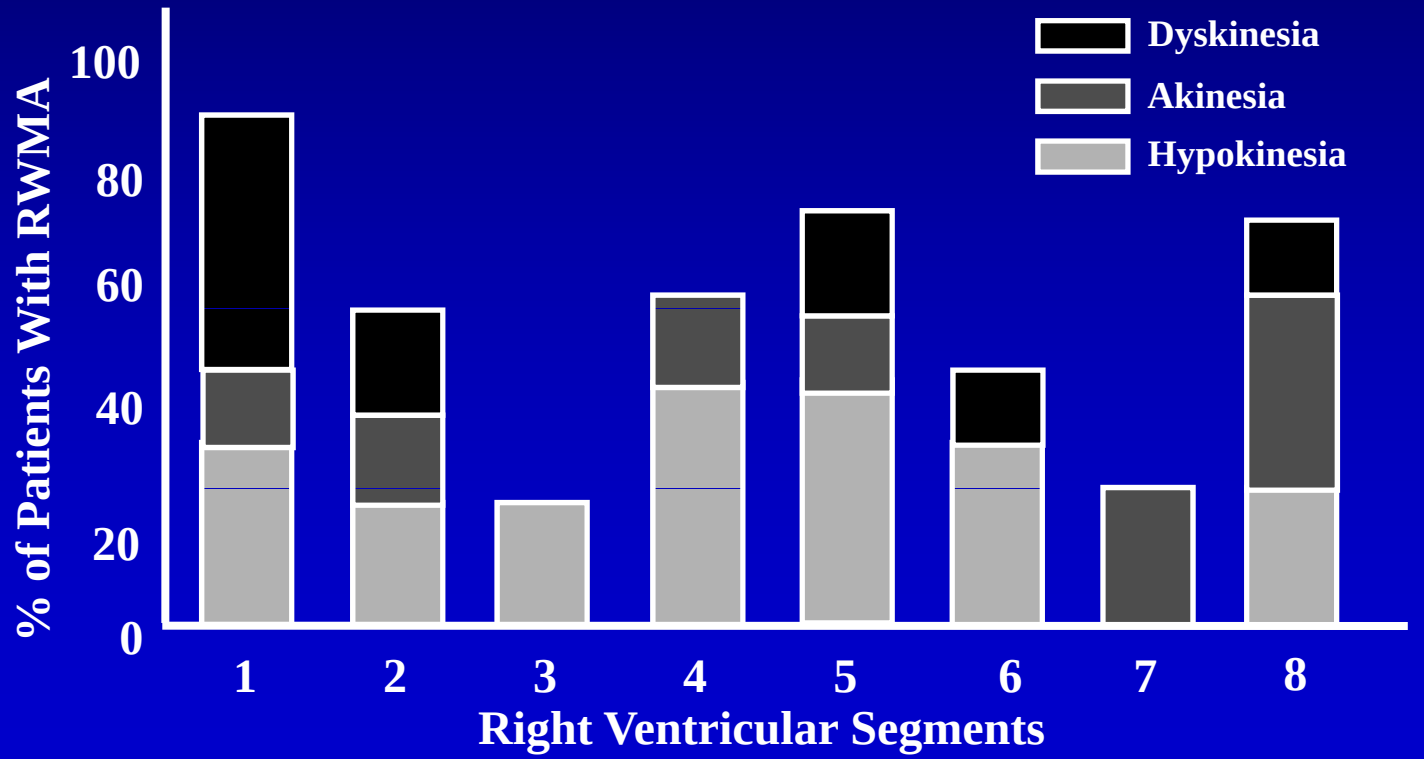
RV Involvement in Takotsubo Cardiomyopathy

Right ventricular involvement in Takotsubo cardiomyopathy

Dariusch Haghi[1], Anastasios Athanasiadis[2], Theano Papavassiliu[1*], Tim Suselbeck[1], Stephan Fluechter[1], Heiko Mahrholdt[2], Martin Borggrefe[1], and Udo Sechtem[2]



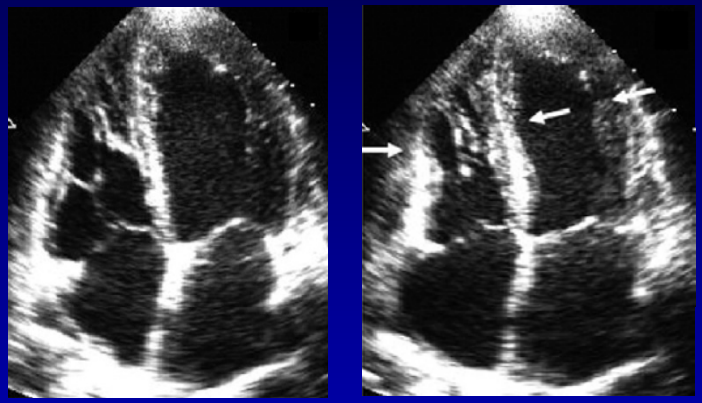




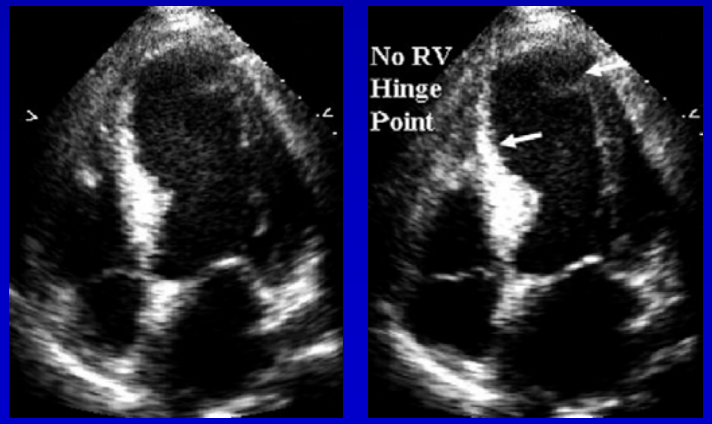
Eur Heart J 2006;27:2433-2439.

RV Involvement in Takotsubo Cardiomyopathy

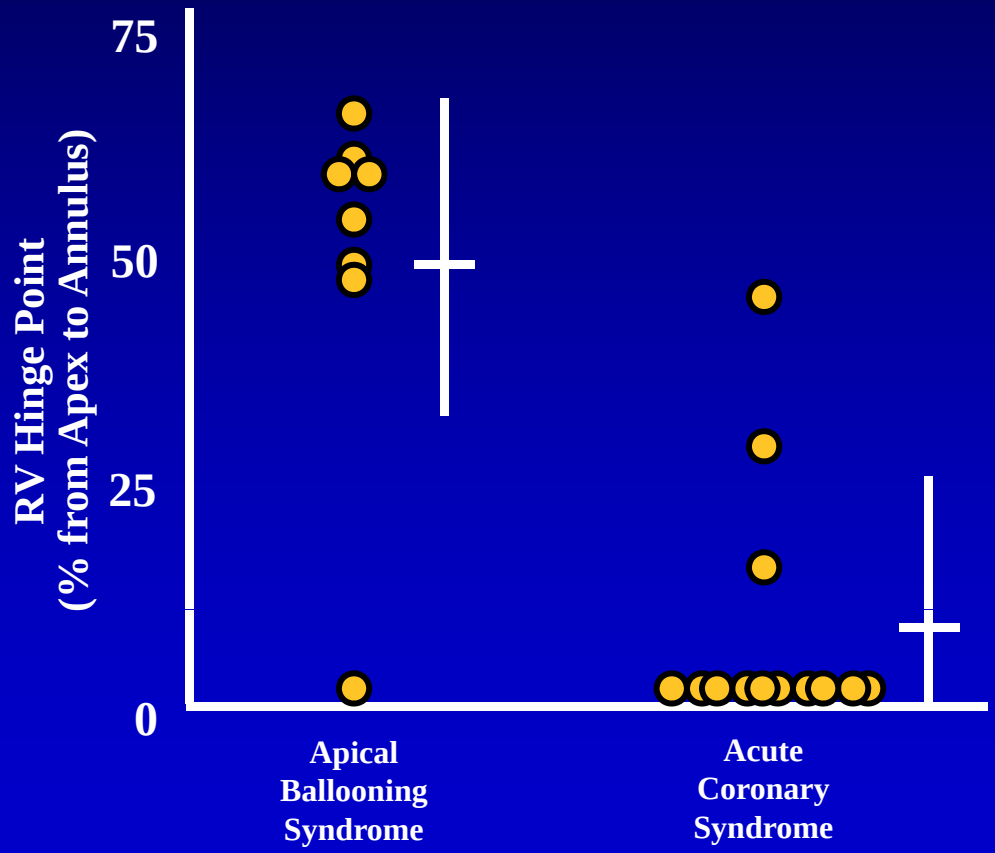
RV Hinge Point of Takotsubo Cardiomyopathy



Takotsubo Cardiomyopathy



Acute Coronary Syndrome



J Am Soc Echocardiogr 2007;20:144-150.

RV Involvement in Takotsubo Cardiomyopathy

Implications of RV Involvement

- ✓ More Severe LV Systolic Dysfunction
- ✓ More Severe Congestive Heart Failure
- ✓ Longer Hospital Stay

1) More Common than Reported Previously

2) Possible Systemic Etiology

3) Careful Assessment of RV Wall Motion

4) Useful in The Early Differentiation from ACS

RV Involvement in Takotsubo Cardiomyopathy

Case

Female 87 Yr

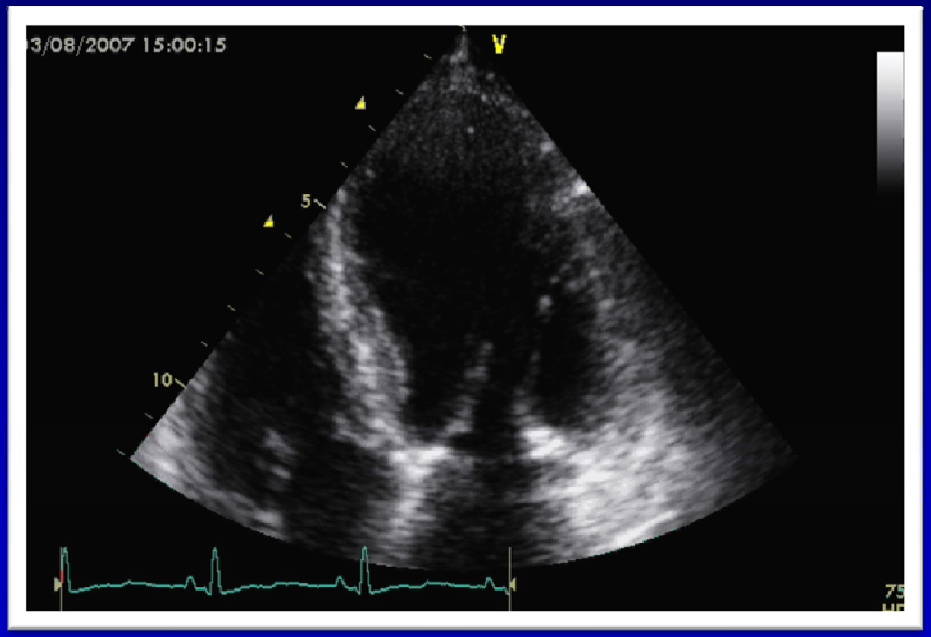
Sudden onset of dyspena

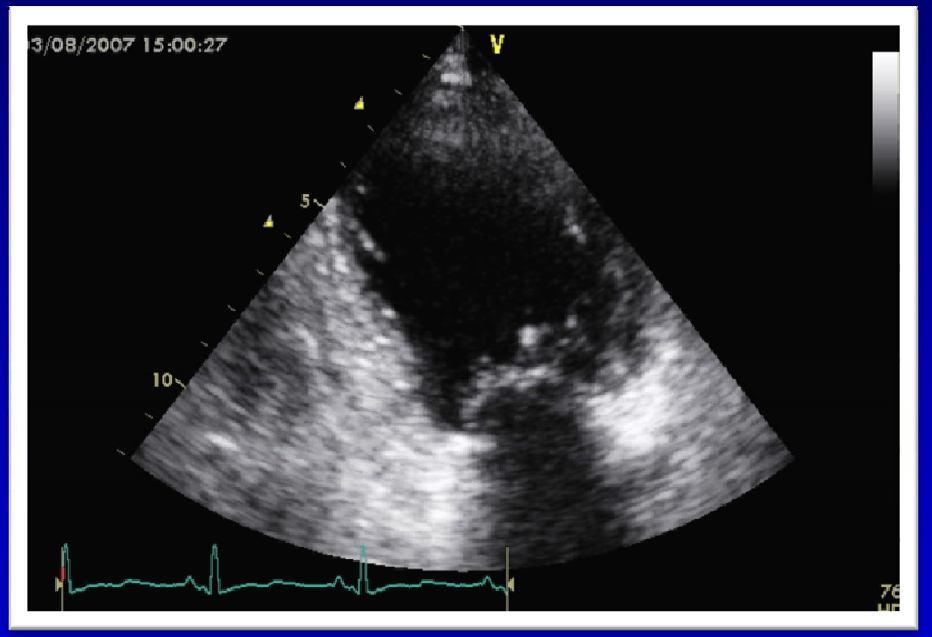
Stressful event: a bitter quarrel

Hospital courses

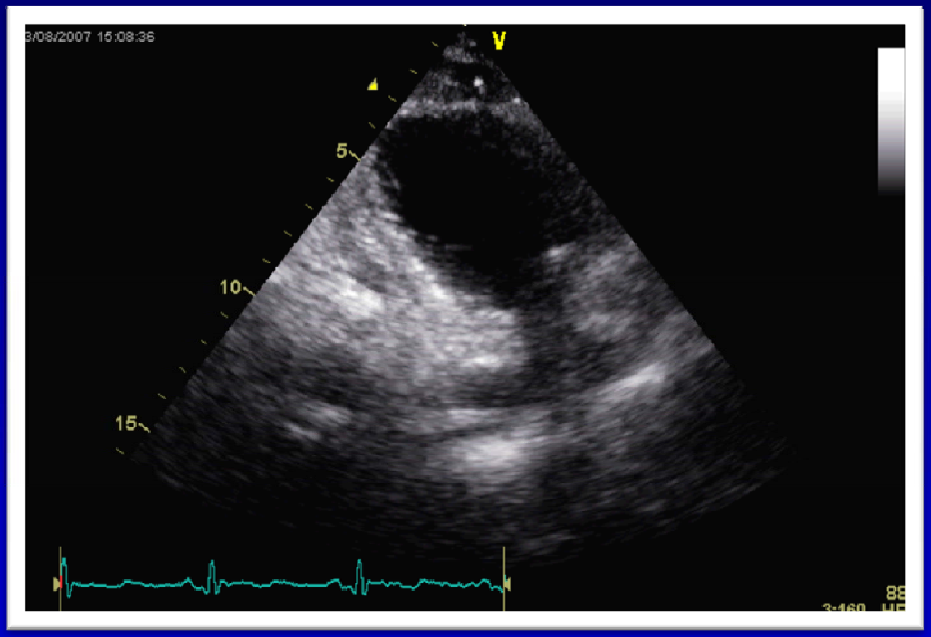
Hypotension ; 80/40mmHg
Conduction disorder ; 2:1 AV block

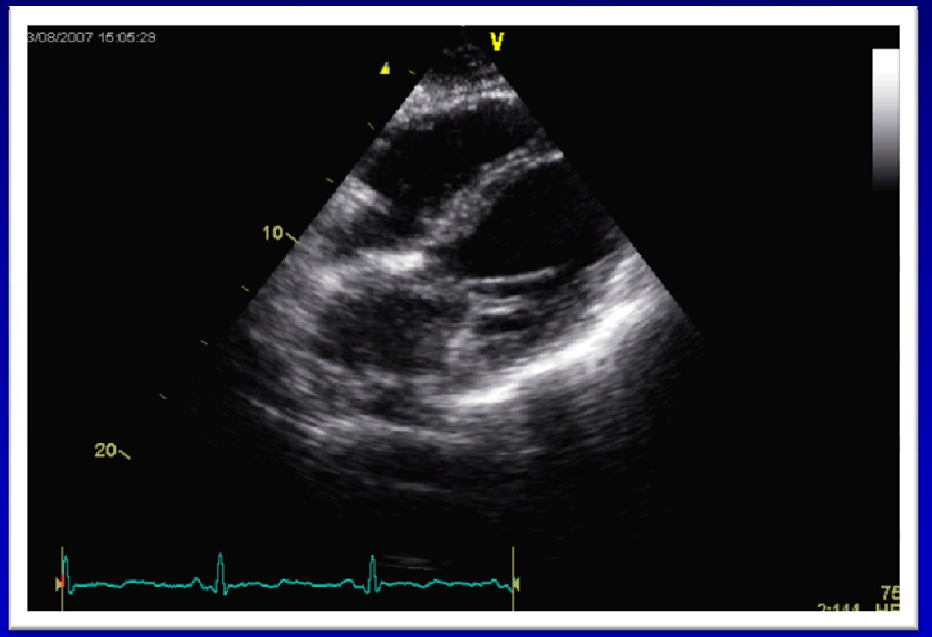
RV Involvement in Takotsubo Cardiomyopathy





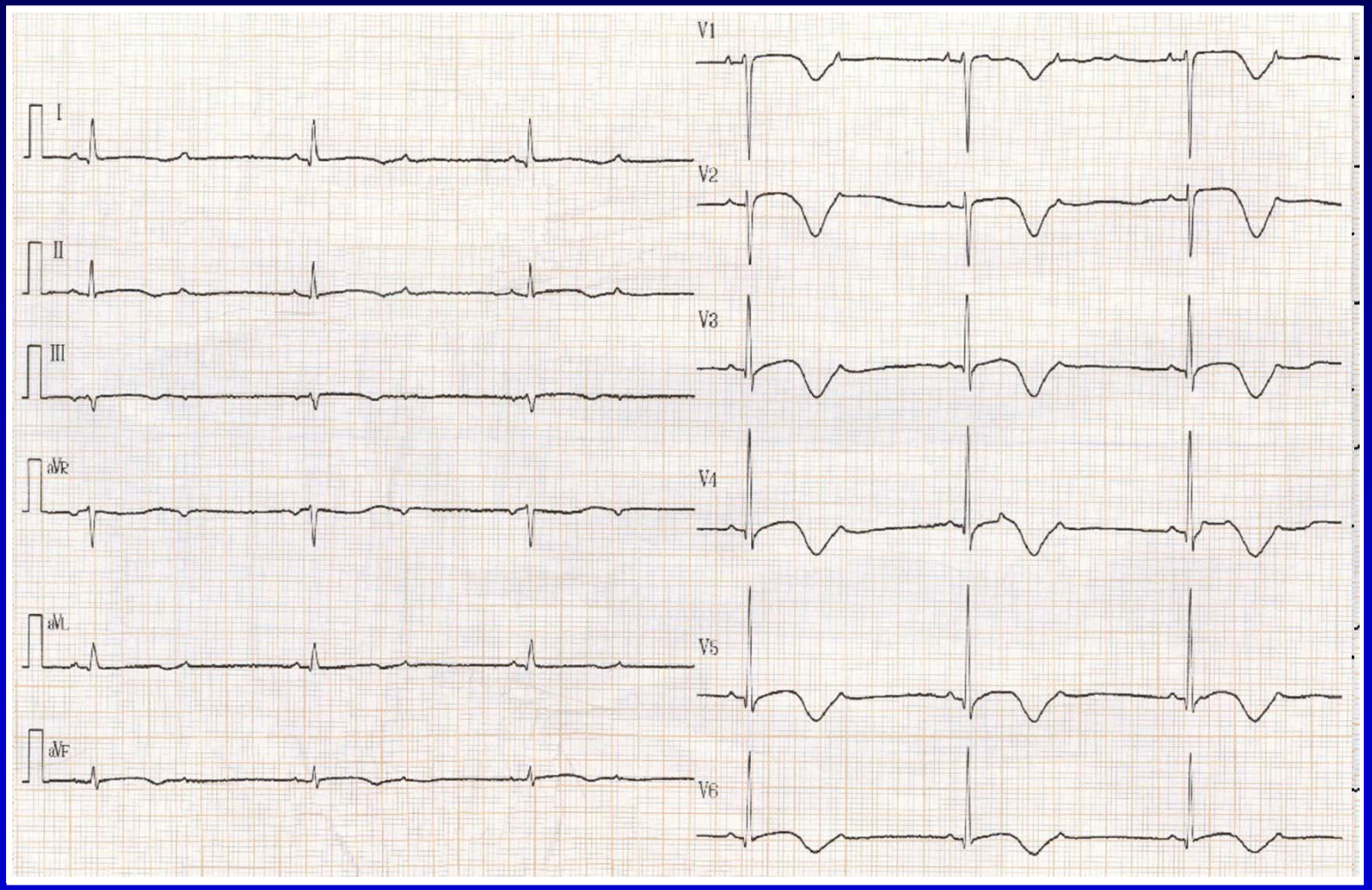
RV Involvement in Takotsubo Cardiomyopathy



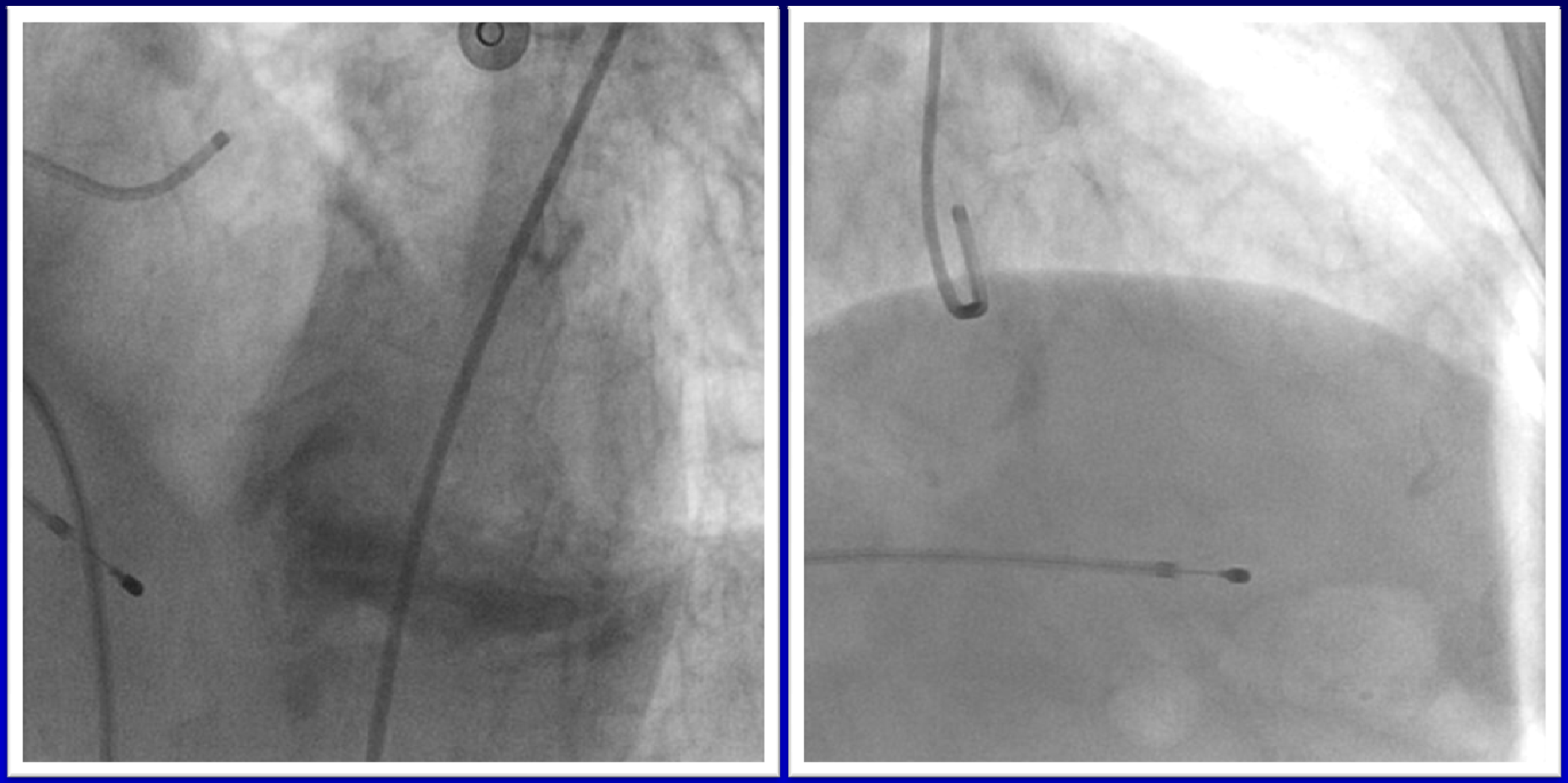


RV Involvement in Takotsubo Cardiomyopathy

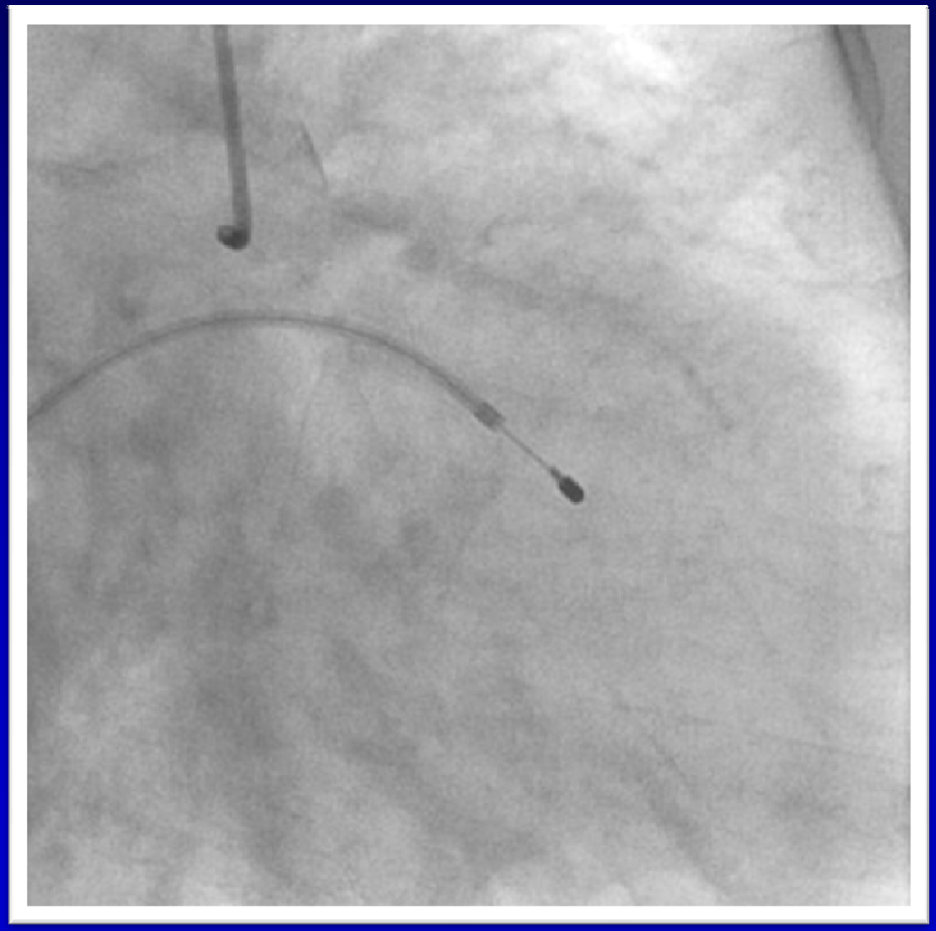
On admission **On 3 day, Temporary pacemaker**

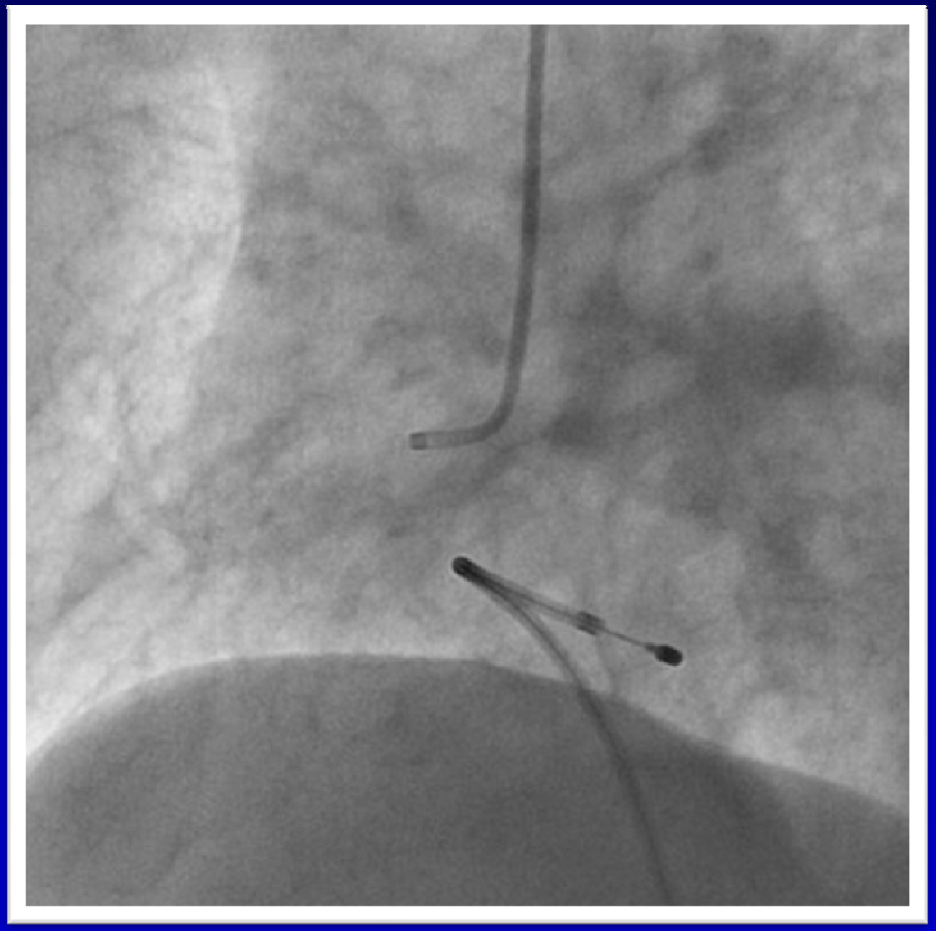


RV Involvement in Takotsubo Cardiomyopathy



RV Involvement in Takotsubo Cardiomyopathy





Treatment & Outcomes of Takotsubo Cardiomyopathy

Treatment of Takotsubo Cardiomyopathy

Empirical treatment

Supportive care

- ✓ **Fluid resuscitation**
- ✓ **Positive inotropes**
- ✓ **Vasopressor**

Controversy over the use of vasopressor; Excessive levels of catecholamine and resultant myocardial stunning

- ✓ **Intra-aortic balloon conterpulsation**
- ✓ **Left ventricular assist device**

Treatment of Takotsubo Cardiomyopathy

Empirical treatment

Conventional treatment for heart failure

- ✓ **Beta-blockers**
- ✓ **ACE inhibitors, ARBs**
- ✓ **Calcium channel blockers**
- ✓ **Diuretics**
- ✓ **Antiarrhythmic agents**

Consideration of prolonged QT-interval in Takotsubo cardiomyopathy itself

Treatment of Takotsubo Cardiomyopathy

Empirical treatment

Modulation of cardiac risk factors

Lifestyle changes;
smoking cessation, weight reduction, dietetic changes, increased physical activity

Platelet inhibitors, Statins, Antioxidants

Short-term anticoagulation

Especially, in severely decreased LV function

To prevent left ventricular mural thrombus formation

Continued until improvement of LV function

Outcomes of Takotsubo Cardiomyopathy

Outcomes

Overall prognosis

Mortality rate; 0-8%, Recurrence rate; ~ 3%

Relatively good, provided survival of the severe CHF

Hallmark of the syndrome

" the reversibility of left ventricular dysfunction "

Complications

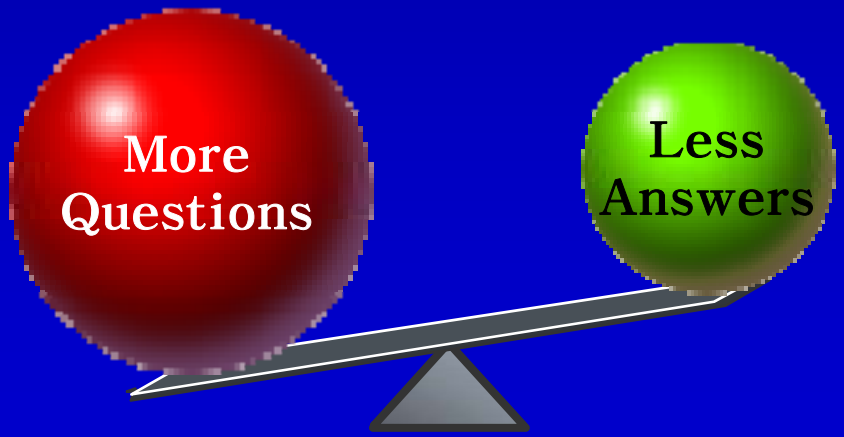
Most common; Left HF with pulmonary edema

Ventricular arrhythmia, LV mural thrombus, Mitral valve dysfunction, Pulmonary embolism, Cardiogenic shock, LV rupture

Takotsubo Cardiomyopathy

Unresolved Potential Issues

- ? Different Entities Under The “Umbrella” of Takotsubo Cardiomyopathy
- ? Different Pathophysiological Etiologies With The Same Ventriculographic Manifestation
- ? The genetic role or modifiable risk factors



Takotsubo Cardiomyopathy

Take Home Message

1. Should be aware of the existence and the typical clinical manifestations of this syndrome
2. Should consider this syndrome in differential diagnosis of ACS, especially in post-menopausal women with a recent history of acute emotional or physical stress
3. LV function would be recovered with appropriate supportive treatment all alone

Takotsubo Cardiomyopathy

감 사 합 니 다