권역심뇌혈관질환센터
REGIONAL CARDIOCEREBROVASCULAR CENTER

Takotsubo Cardiomyopathy

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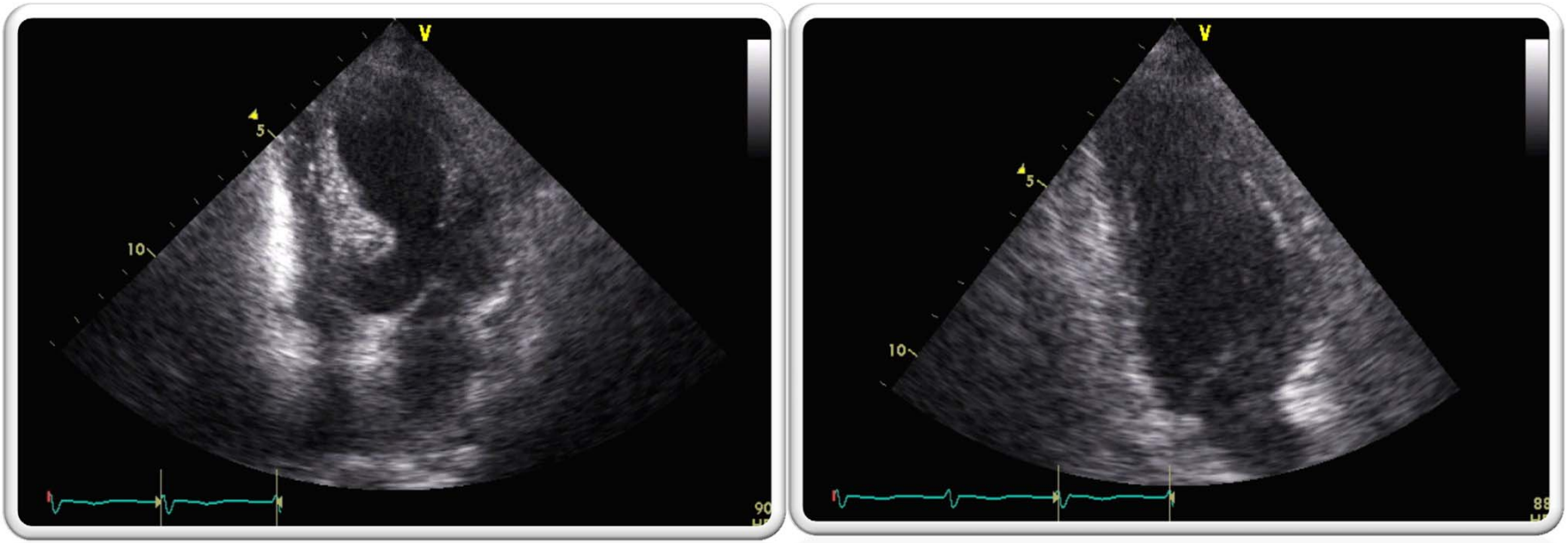
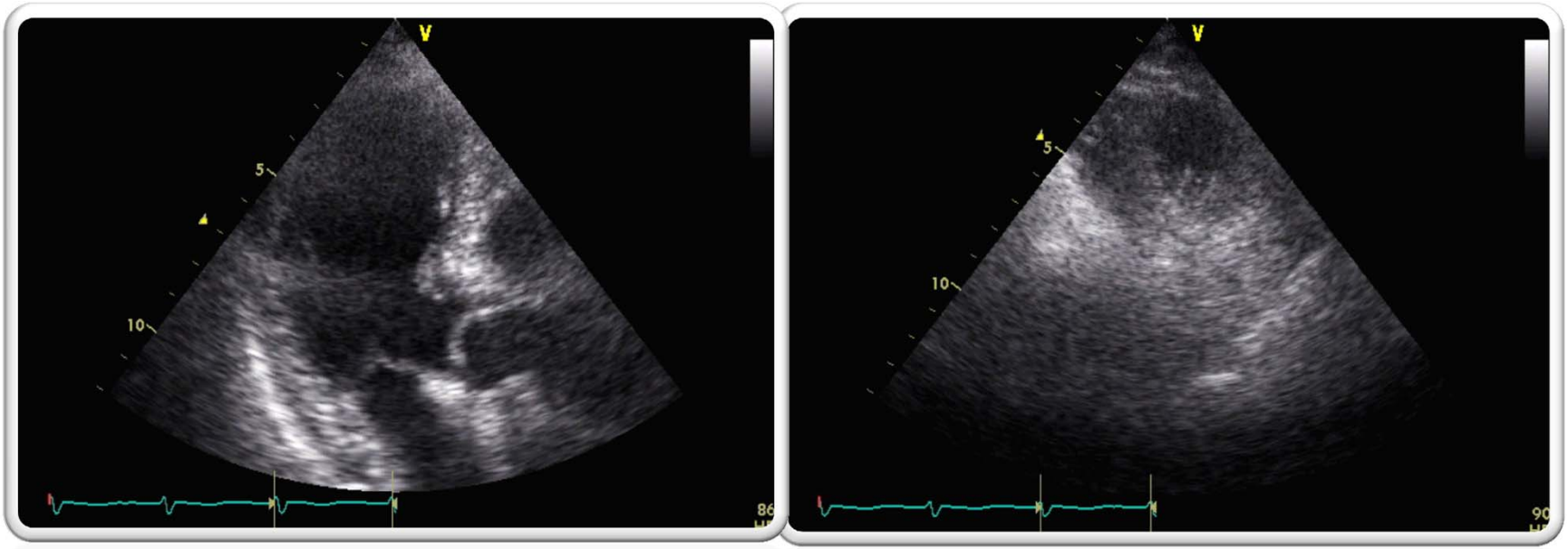
Case 1

81/F
C/C : G-weakness
Stressful event : none
ECG : deep T wave inversion, prolongation of QT interval (QTc 545msec)
Cardiac enzyme : CK 82 IU/L, CK-MB 6 IU/L, TnT 0.188ng/mL



Case 1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10
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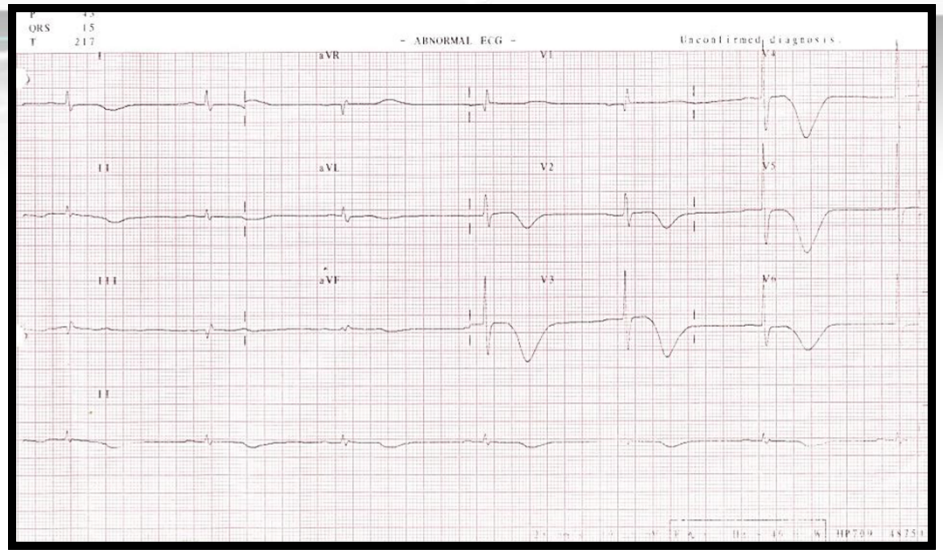
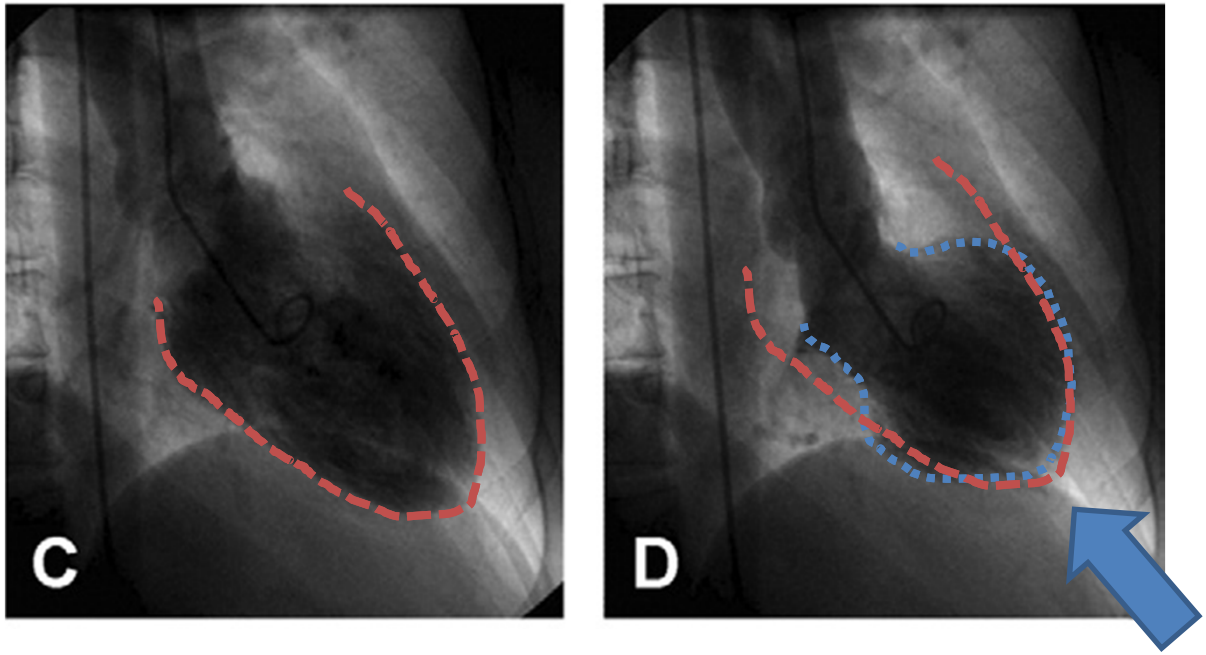
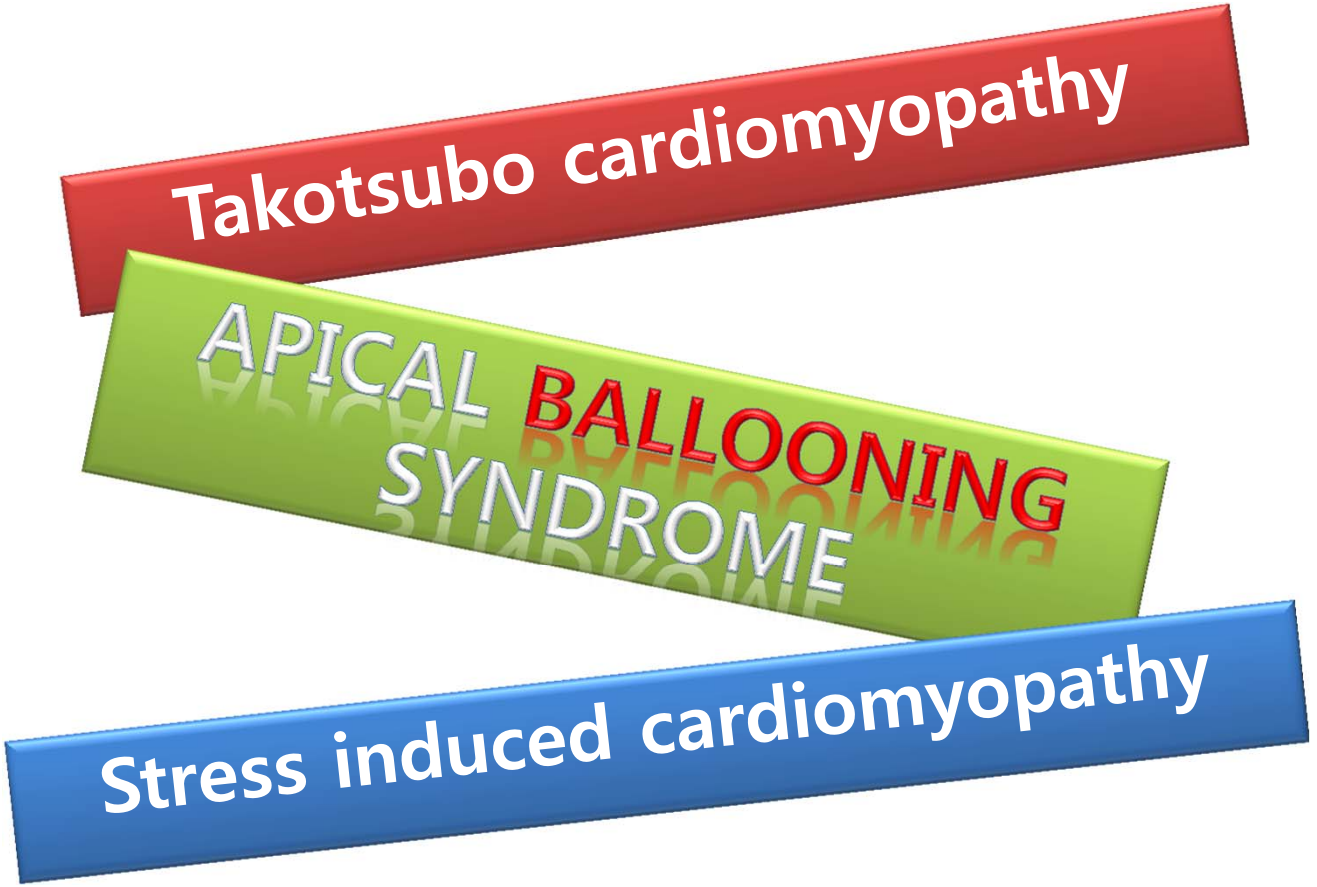

- ABNORMAL ECG -
Unconfirmed diagnosis.
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Japanese octopus fishing pot : Takotsubo



Apical Ballooning


Takotsubo cardiomyopathy
APICAL BALLOONING SYNDROME
Stress induced cardiomyopathy

History

- Iga et al
  reported a case of reversible left ventricular dysfunction
  associated with pheochromocytoma
  takotsubo appearance was first described,
  although they did not use the term **takotsubo**.

  ***Jpn Circ J.* 1989;53:813– 818**

- Sato et al
  first described this reversible cardiomyopathy
  as *tako-tsubo-like left ventricular dysfunction*
  Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure. Tokyo, Japan: Kagakuhyouronsha; **1990:56–64**.

- Outside Japan, this phenomenon was called **apical ballooning** or **stress cardiomyopathy**

Diagnosis

Proposed Mayo Clinic Criteria for Takotsubo Cardiomyopathy
1. **Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments, with or without apical involvement.** Regional wall motion abnormalities extent beyond a single coronary vascular bed. **A preceding physical or emotional stressor is often present.**
2. **No obstructive coronary disease or acute plaque rupture** (determined **angiographically**)
3. **New electrocardiographic abnormalities** **(ST-segment elevation, T-wave inversion, or both) or modest elevation in cardiac troponin level.**
4. **No pheochromocytoma or myocarditis,** For such patients, the diagnosis of takotsubo cardiomyopathy should be made cautiously, and a clear, stressful, precipitating event must be sought.

This table is adapted and modified from ***Ann Intern Med.*** **2004;141:858-865**.

Diagnosis

1. **Criteria**
   Transient hypokinesis, akinesis, or dyskinesis in the left ventricular mid segments
   with or without apical involvement;
   Regional wall motion abnormalities that extend beyond a single epicardial vascular distribution;
   A stressful trigger is often but not always present
   Mayo clinic propose, 2004
   modified recently 2008. **(Prasad A, el al, Am Heart J)**
- **Necessary to establish worldwide consensus on diagnostic criteria for Takotsubo cardiomyopathy.**
2. **Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.**
3. **New ECG abnormalities**
   (ST-segment elevation and/or T-wave inversion)
   or
   Modest elevation in cardiac troponin.
4. **Absence of pheochromocytoma and myocarditis.**

Epidermiology

- Until 2000, a few case reports were published, but the presentation of Takotsubo cardiomyopathy has **increased gradually since 2001**.
- The true prevalence of the apical ballooning syndrome **remains uncertain**.

- probably accounts for **1% to 2%** of all cases of suspected acute myocardial infarction. ***Chest*. 2007;132:809–816**

- Bybee et al. reported that the apical ballooning syndrome accounted for **2.2%** of the ST-segment elevation ACS presenting **J Nucl Med 2004;45:1121–1127**
- Matsuoka et al.: **2.2%** of suspected ACS **Am J Cardiol 2003;92:230–233**

- Akashi et al.: **2.0%** of patients with sudden onset of heart failure and abnormal Q waves of ST-T changes (suggestive of acute MI on admission) **Am J Cardiol 2004;94:343–346**

Clinical manifestation

- Clear gender discrepancy, much **more common in women** than men
- preceded by exposure to **emotional or physical stressors**
  such as an unexpected death in the family, abuse, a quarrel, or exhausting work
- in some cases, precipitant stressors have **not been identified**
- In small study, with conservative treatment, the apical ballooning resolves spontaneously within an average of **18 days**
  (range 9 to 53 days)
- most frequent clinical symptoms
  : **chest pain & dyspnea**, resembling acute myocardial infarction

Clinical manifestation

- ECG change : frequently found
  ST elevation in precordial leads.(proximately 1/3)
  Subsequent **deep T-wave inversion**
  & nonspecific ST-T wave change
  Q-wave formation
  during serial f/u ECG,
  prolongation of QT interval and
  deep, symmetric T-wave inversion
  (Torsades de pointes is rare)

- **Coronary angiography** is the best single tool to diagnose
  but Small Studies shows that incidence of incidental coronary artery disease((75% stenosis of a major epicardial coronary artery) is **10%**

Clinical manifestation

- High levels of **serum catecholamines** & of plasma **brain natriuretic peptide (BNP)**
- Cardiac enzyme levels (eg, creatinine kinase, troponin T) are **slightly increased or modest increased.**
- cMR : to assess subendocardial necrosis with delayed contrast enhancement techniques
  → findings are still a matter of debate,
  lack of delayed enhancement may predict wall motion recovery
- Histological changes have been identified by myocardial biopsy in some studies. Further evidence is required
- Both MRI and histopathological findings can differentiate patients with takotsubo cardiomyopathy from those with acute myocardial infarction resulting from coronary arterial occlusion.

Clinical manifestation

69.8	Tsuchihashi et al	Kurowski et al	Kurisu et al	Sharkey et al	Wittstein et al	Inoue et al	Sato et al	Bybee et al	Yoshida et al	Akashi et al
Subject, n	88	35	30	22	19	18	16	16	15	13
Country	Japan	Germany	Japan	US	US	Japan	Japan	US	Japan	Japan
Age, y			70	65	61	76	71	71	72	73
Women, %	86	94	93			)4	94	100	80	85
Preceding emotional stressor, %	20	42	17	86	100	11		38	40	31
Preceding physical stressor, %	43	42	17	14		39	100	44	40	69
Sum of stressor, %	**63**	**84**	**34**	**100**	**100**	**50**	**100**	**82**	**80**	**100**

Average 69.8

Average 91.2

Clinical manifestation

	Tsuchihashi et al	Kurowski et al	Kurisu et al	Sharkey et al	Wittstein et al	Inoue et al	Sato et al	Bybee et al	Yoshida et al	Akashi et al
Chest pain, %	67		67	91	95	72	100	69	87	54
ST elevation,%	90	69	100	59	11	100	56	81	87	92
ST elevation in precordial leads, %	85		97	59		100		81		92
Q waves, %	27			45	37	56		31	7	
Mean QTc, ms					542			501	508	
Elevation in cardiac enzyme, %	56						56	100		85
Initial EF, %	41	50	49	29	20		49	40	43	42
F/u EF, %	64	68	69	63	60		66	60	76	65

Clinical manifestation

	Tsuchihashi et al	Kurowski et al	Kurisu et al	Sharkey et al	Wittstein et al	Inoue et al	Sato et al	Bybee et al	Yoshida et al	Akashi et al
Time of recovery, d	Average 15.7		11.3	24	21		17.7	8	11	17
Pul. Edema, %	22		3	0	16	28	6	44		0
IABP, %	8		0	18	16	6	0	6	7	15
Coronary stenosis >50%	0	0	0	0	5	0	0	0		0
Spont. Multivessel spasm, %	0	0	10		0	0	0	0	0	0
Provocable multivessel spasm, n/n(%)	5/48(10)		6/14(43)				0/6(0)		1/6(17)	0/11(0)
Transient intraventricular pressure gredient, %	18			23				13	14	
In-hospital mortality, %	1	3(9)	0	0	0	6	0	0	0	8
Documented recurrence, n/n(%)	2/72(3)	2(6)	0	2/22(9)				1/16(6)		0

Less than 10%

Less than 10%

This table is adapted and modified from ***Circulation*. 2008;118:2754-2762**

Atypical variant

- Ferrer et al. described patients with similar appearances to Takotsubo CMP but having ECG changes and transient inferior akinesia suggestive of an **inferior wall MI**

  : not have coronary artery stenosis on emergency angiography

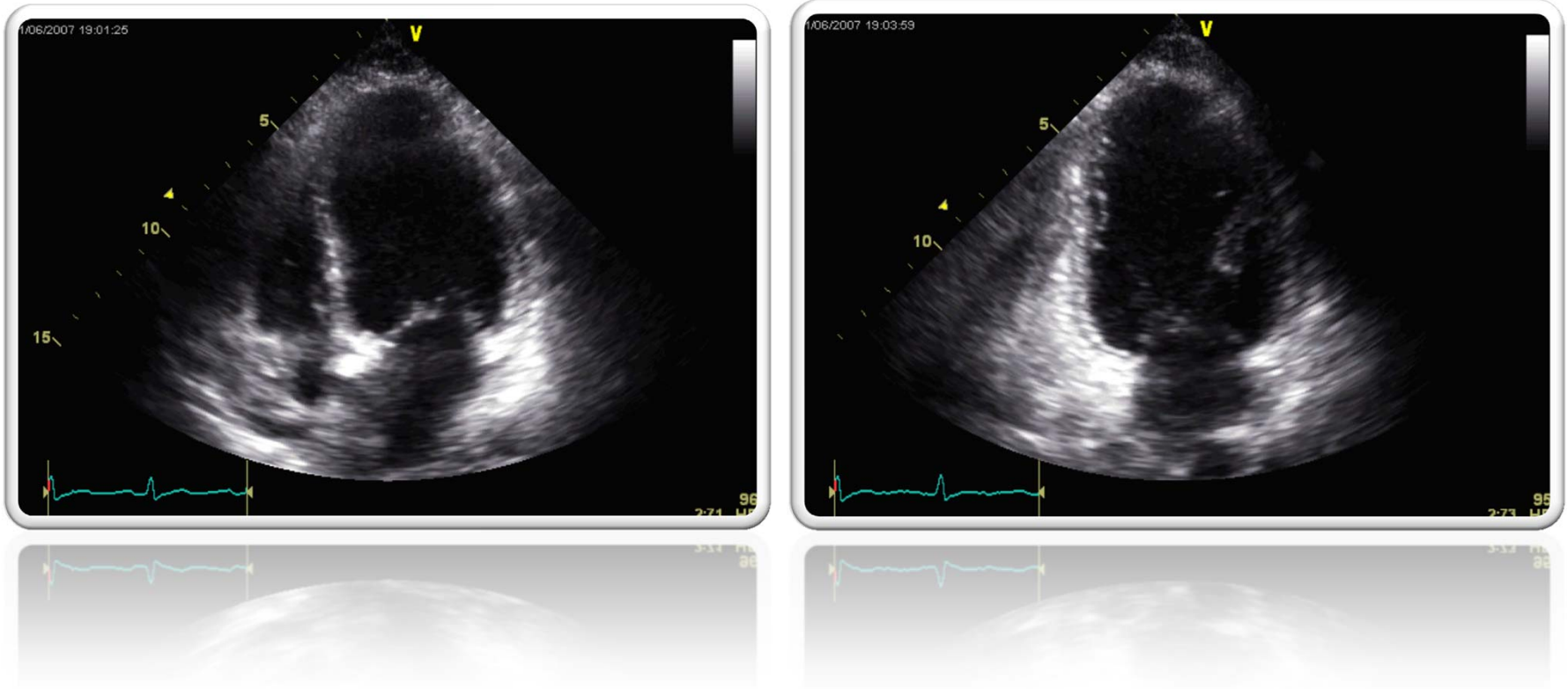
- Suggested that the Takotsubo phenomenon could also be observed in **areas of the heart other than the apex**

- A variant of Takotsubo CMP has now been recognized involving the **base or midcavity of the LV** which spares the cardiac apex

- **Right ventricular apical involvement** can also occur

Case 2

Atypical SCM (basal type)
54/M
Stressful event : Acute pancreatitis



Courtesy by SH Lee

Case 2

Atypical SCM (basal type)
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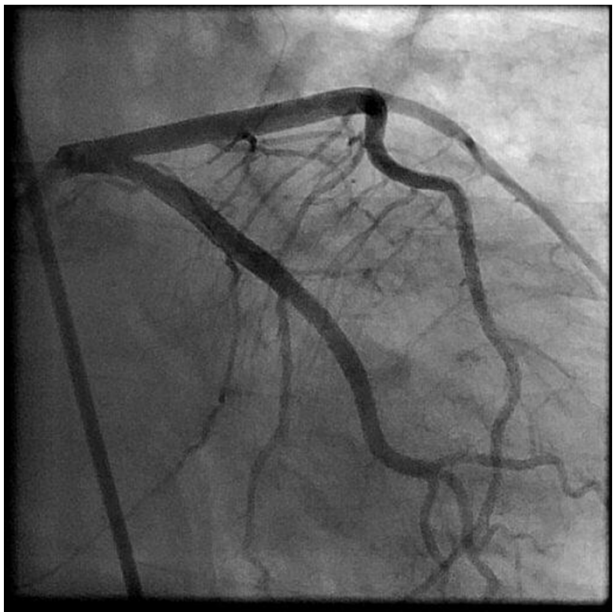
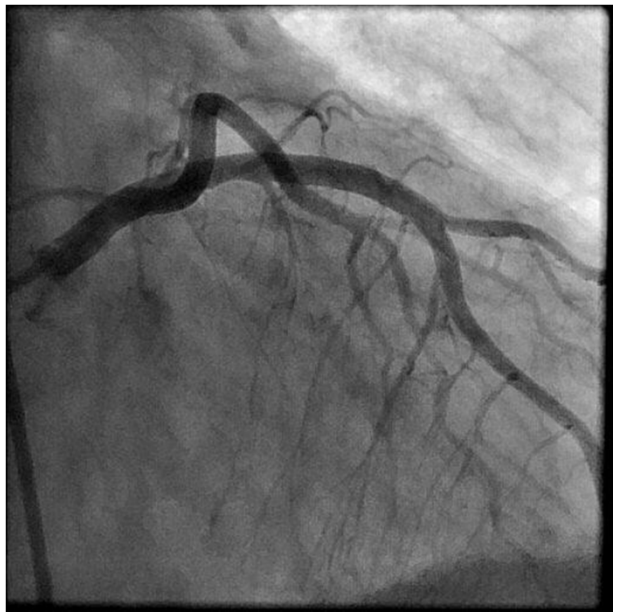
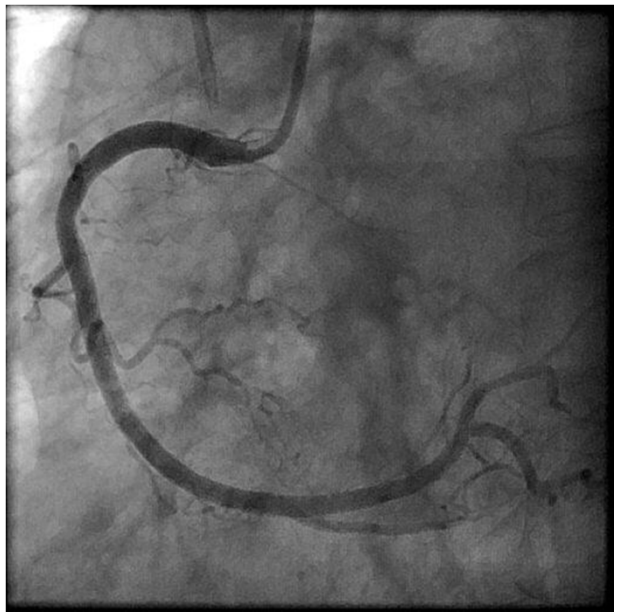
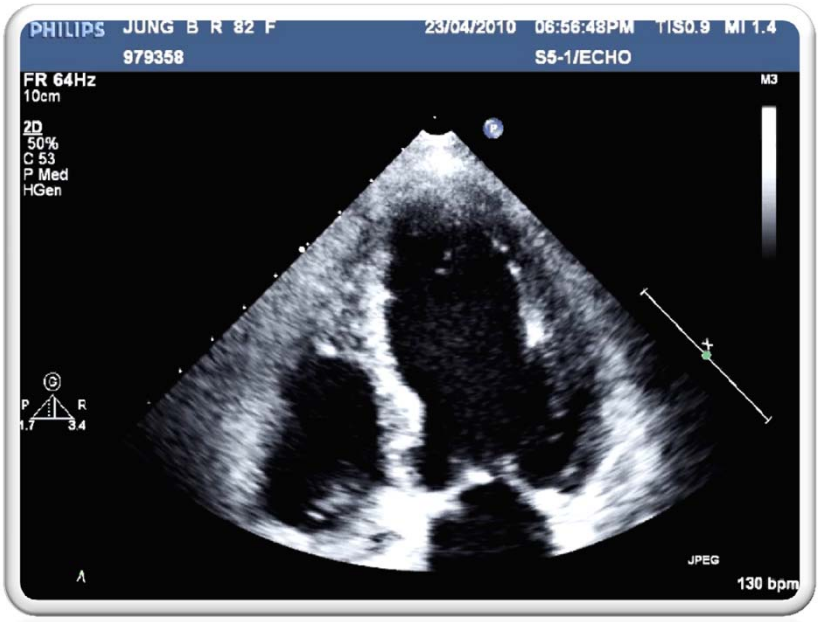
Stressful event : Acute pancreatitis

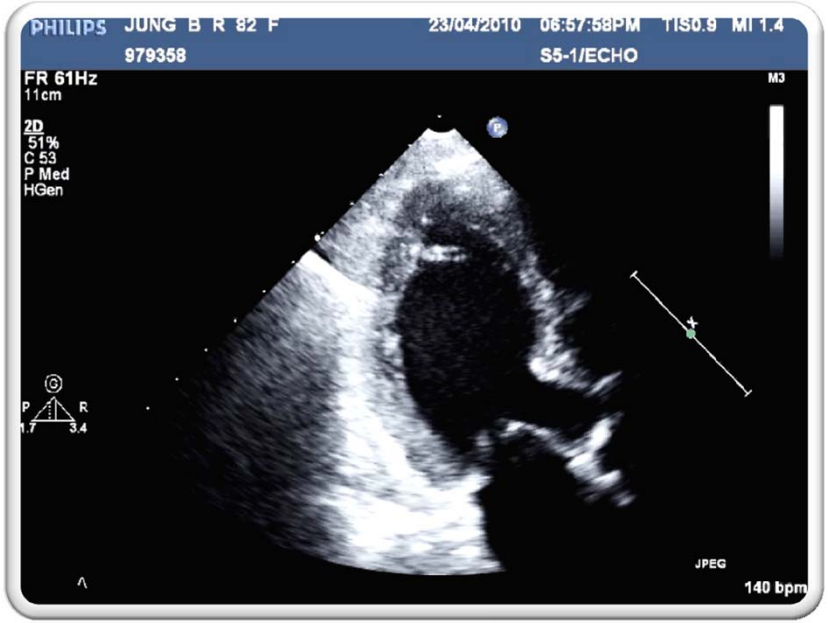




Courtesy by SH Lee

Case 3

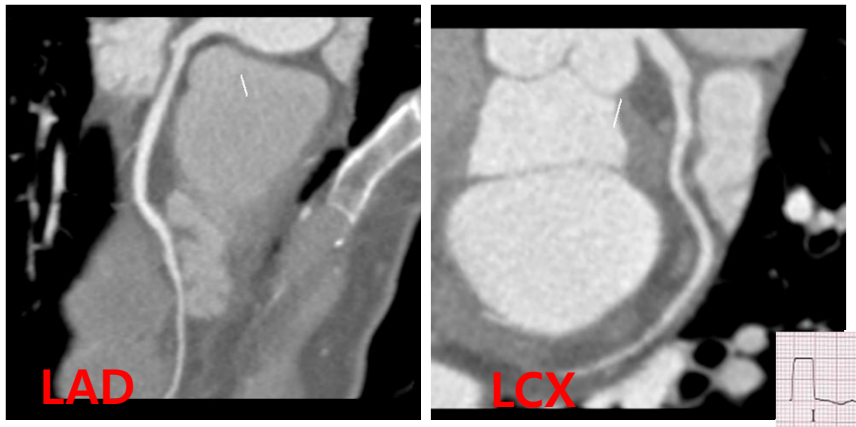
Atypical SCM (mid-ventricular type)
82/F
Stressful event : OP of femur neck Fx

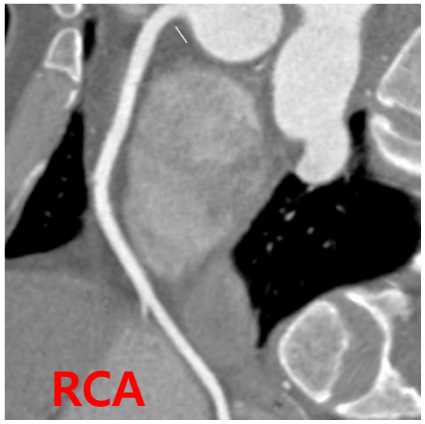




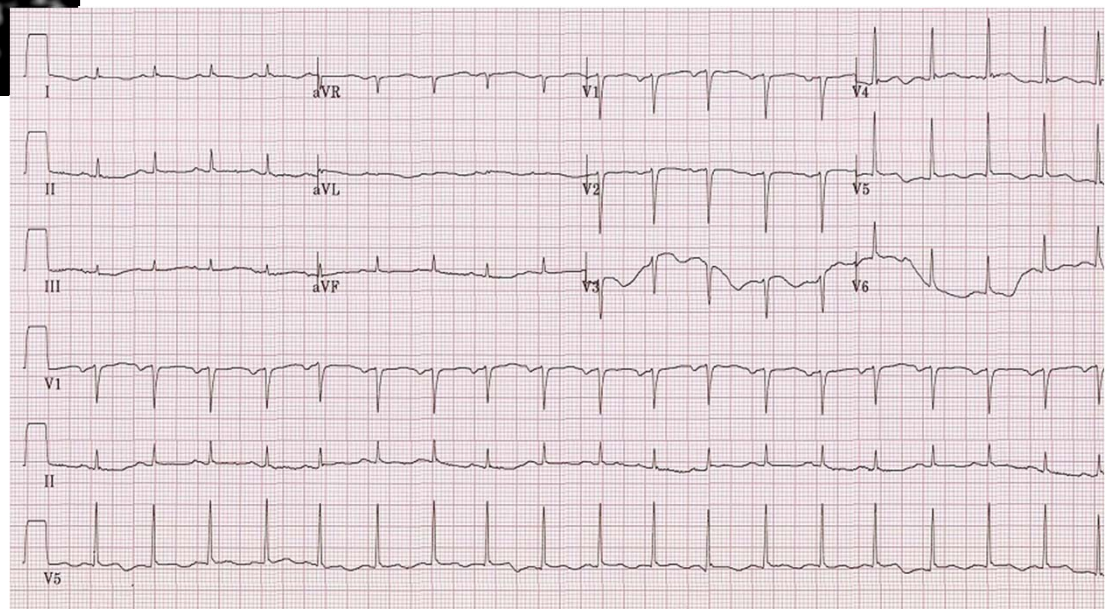
Case 3

Atypical SCM (mid-ventricular type)
82/F
Stressful event : OP of femur neck Fx



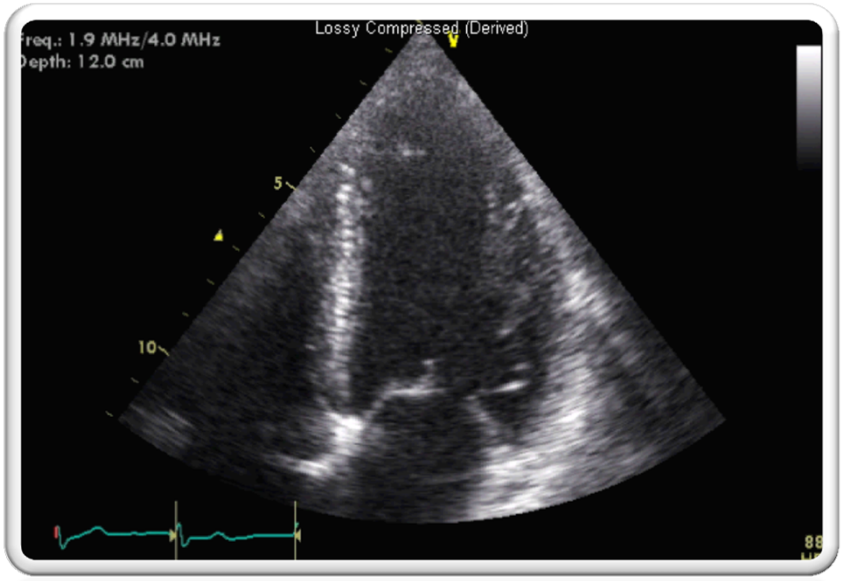


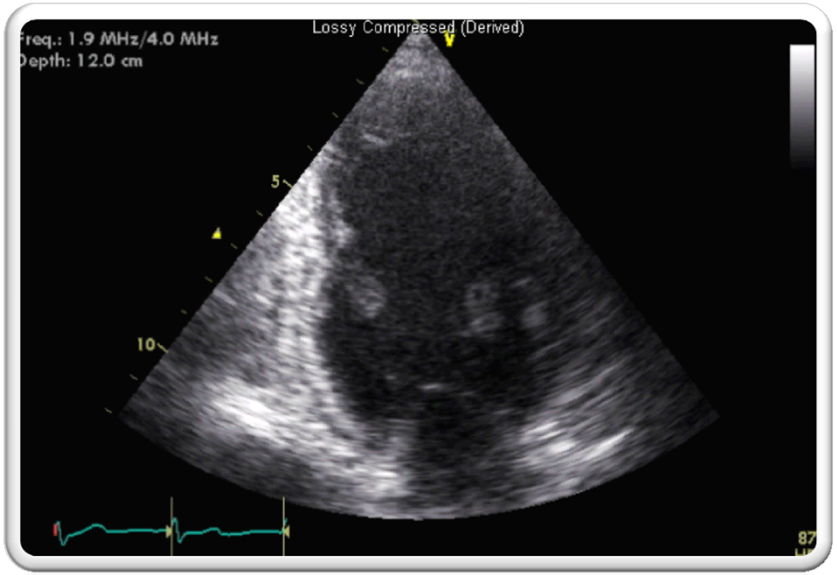
Peak TnI 1.17 ng/mL
NT-proBNP 8,396 pg/mL

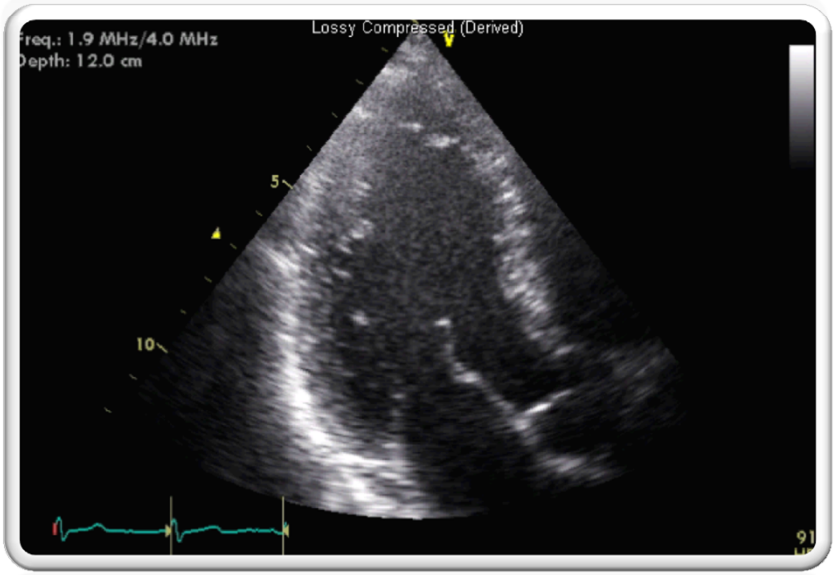


Case 4

Atypical SCM (Focal RWMA type)
69/M
Stressful event : Dental surgery

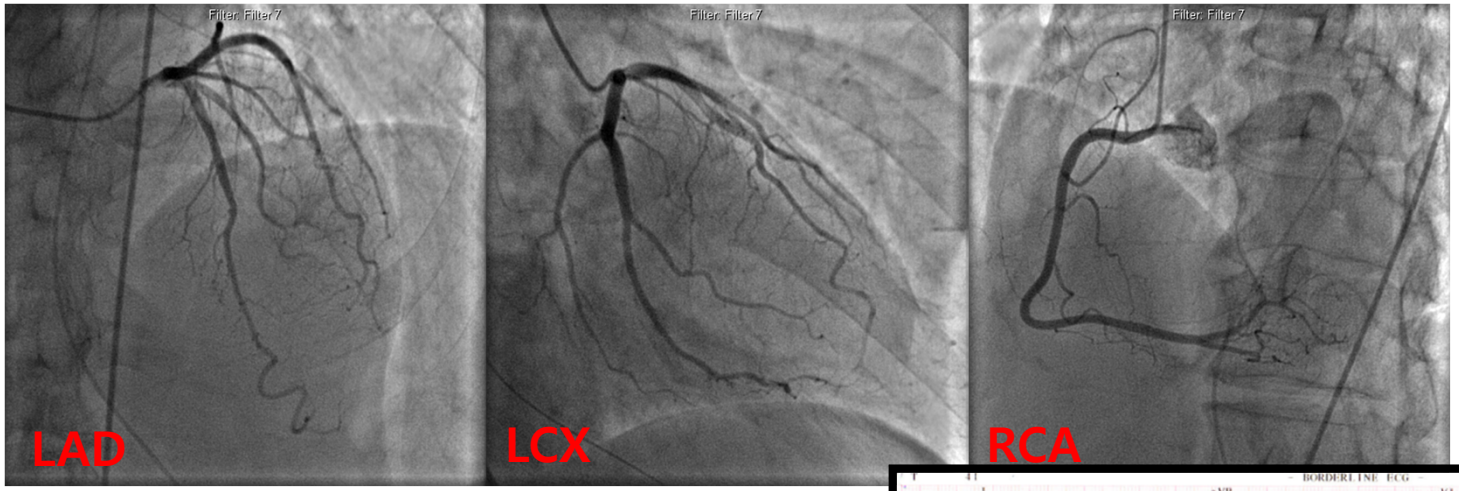




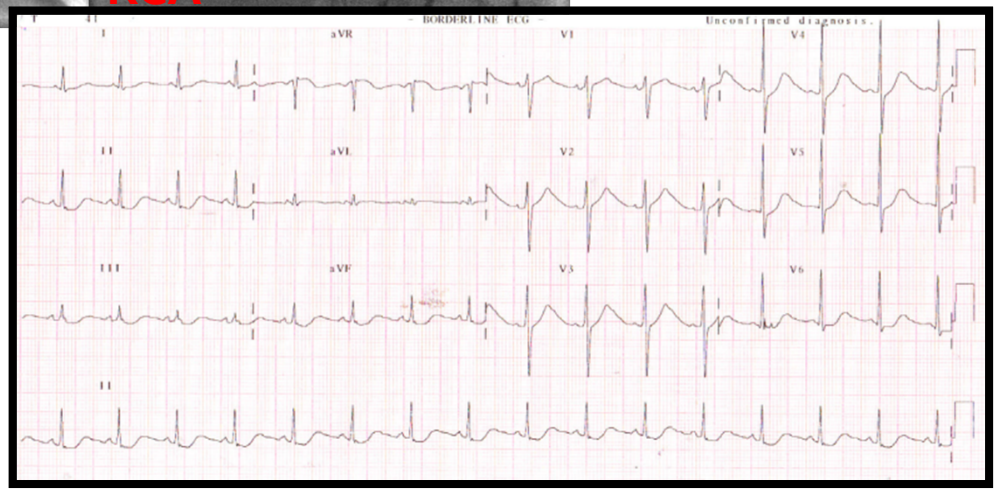


Case 4

Atypical SCM (Focal RWMA type)
69/M
Stressful event : Dental surgery



Peak CK-MB 117 IU/L, TnT 0.22ng/mL
ECG : prolongation of QT interval



Pathophysiology

- Myocardial biopsy :

  Interstitial infiltrates

  : mainly mononuclear lymphocytes, leukocytes, and macrophages;

  myocardial fibrosis;

  Contraction bands with or without overt myocyte necrosis

- The inflammatory changes and contraction bands **distinguish takotsubo cardiomyopathy** from **coagulation necrosis**, as seen in myocardial infarction resulting from coronary artery occlusion

- **Exact pathophysiological basis** of the distinctive contractile pattern in takotsubo cardiomyopathy **remains to be elucidated**

Concepts

- Multivessel Epicardial Coronary Artery Spasm
- Coronary Microvascular Impairment
- **Catecholamine Cardiotoxicity (major contribution)**
- Neurogenic Stunned Myocardium
- Focal myocarditis
- Structural changes and oxidative stress theory

Multivessel Epicardial Coronary Artery Spasm

- Reversible ventricular dysfunction might result from epicardial coronary artery spasm and consequently regionally stunned myocardium

Accordingly, myocardial stunning resulting from epicardial coronary artery spasm **does not seem** to cause takotsubo cardiomyopathy.

- Area of abnormal left ventricular wall motion would **not be expected to extend beyond the perfusion territory** normally supplied by the artery
- ECG findings seem to differ
  : **not evince reciprocal changes**
- Ischemic myocardial stunning does **not produce the histological changes** usually observed in takotsubo cardiomyopathy.
- Spontaneous or inducible coronary arterial spasm has not been found in most cases of takotsubo cardiomyopathy

Coronary Microvascular Impairment

- abnormal left ventricular wall motion occurs in a relatively large area of the apical myocardium
  - because the abnormalities are dynamic rather than fixed disturbances in the coronary microcirculation might occur

- **The possibility remains that the microcirculatory abnormalities result from increased mechanical wall stress as a consequence of apical ballooning**

  : not explained

emission tomography.

- Elesber et al
  : presence of microvascular dysfunction in a significant proportion, correlation between microvascular dysfunction and the severity of myonecrosis and ECG abnormalities

Catecholamine Cardiotoxicity
(major contribution)

- Plasma levels of both **epinephrine** and **norepinephrine** were remarkably increased in the stress cardiopathy patients than acute MI

- Wittstein et al.
  : elevated catecholamine levels are not uniformly found in patients with this syndrome, *N Engl J Med*. 2005;352:539 –548

- Myocardial histological changes :
  strikingly resemble in **catecholamine cardiotoxicity** in both animals and humans.
  Int J Cardiol. 1994;45:23–33,; *Chest*. 1991; 99:382–385

  differ from in ischemic cardiac necrosis

Catecholamine Cardiotoxicity
(major contribution)

- High intracellular concentrations of Ca^{2+} in myocardial cell
  → ventricular dysfunction

- **Circulating epinephrine exerts far more potent hormonal effects** on the heart than norepinephrine
  → **epinephrine-induced toxicity**

- Emotional stress:
  Concurrent cardiac **neuronal** and **adrenomedullary** hormonal stimulation

- Lyon et al,
  : hypothesized that the high circulating epinephrine levels might trigger a **switch in cardiomyocyte intracellular signaling** after occupation of β_2-adrenoceptors from Gs protein to Gi protein coupling.

***Nat Clin Pract Cardiovasc Med*. 2008;5:22–29**

Neurogenic Stunned Myocardium

- Activation of central neurogenic mechanisms analogous to those evoked by subarachnoid hemorrhage
- Intracranial pathology can produce the same myocardial histopathological findings seen in takotsubo cardiomyopathy

- Basal myocardium has a somewhat **higher norepinephrine content** and greater density of sympathetic nerves than the apical myocardium
- Left ventricular apex contains a higher concentration of adrenoceptors.

  → myocardial responsiveness to adrenergic stimulation is pronounced **in the apex**

- High circulating catecholamine levels such as in pheochromocytoma **can interfere with the neuronal uptake process** and **augment occupation of adrenoceptors** on myocardial cells. ***Hypertension*. 2004;43: 1227–1232**
  - These findings help to explain why emotional distress would induce mainly cardiac toxicity as a result of high plasma catecholamine levels despite being delivered to all organs via the arterial blood.

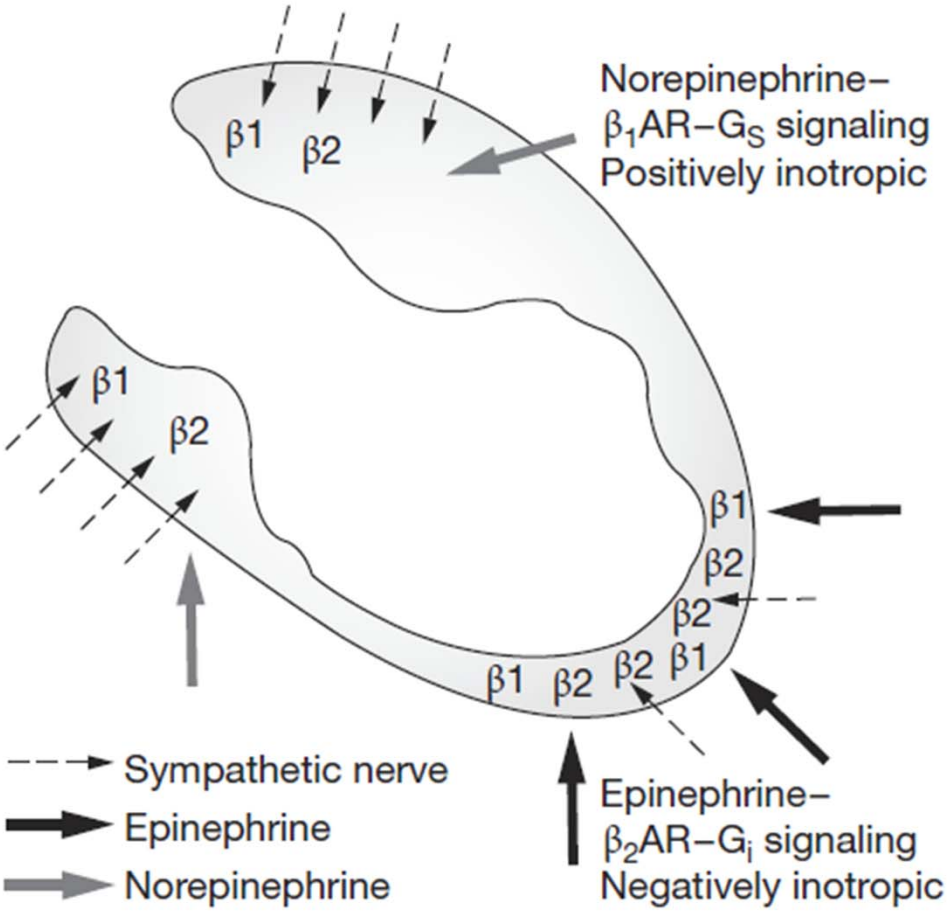


Figure 3 Schematic representation of the regional differences in response to high catecholamine levels, explaining stress cardiomyopathy.

Nat Clin Pract Cardiovasc Med. **2008;5:22–29**

Focal myocarditis

- not well supported by the data
- Viral titers do not rise after the initial event
- Biopsy findings are not suggestive of myocarditis

Structural changes and oxidative stress theory

- Transient structural alteration, including **disorganization of the contractile and cytoskeletal proteins** with an increase of the extracellular matrix, has been demonstrated in the myocardium
- Important factor in the development of takotsubo CMP is the presence of **abnormal myocardial functional architecture such as localized midventricular septal thickening**.
- Wittstein et al. reported supraphysiological levels of plasma catecholamines and -related neuropeptides as potential sources of **reactive oxygen species (ROS)**
- ROS production is activated and results in OS when stimulated by catecholamines cardiac myocytes directly
- initiate erations amplification of the initial ROS-mediate toxicity
- Exposure myocardium to ROS generating systems alters myocardial function through persistent cellular loss of K^+, depletion of high-energy phosphates, elevated intracellular calcium concentration, loss of systolic force development, a progressive diastolic tension and depressed metabolic function
- In Biopsies : different functional gene sets such as Nrf2-induced genes, were triggered by oxidative stress

Just only hypothesis, Not enough support data until now

Summary

- Takotsubo cardiomyopathy reflects **toxic high local concentrations** of **catecholamines**, not coronary artery or microvascular disease
- **Pattern** of left ventricular dysfunction may result from both **myocardial cellular rupture** and **withdrawal of β-adrenoceptors**

- The "first cause" would be **neurogenic**, with the precipitant sudden, unexpected, severe emotional distress

- Individual differences in **the anatomy of cardiac sympathetic innervation or the distributions of adrenoceptors** might result in the involvement of a variety of left ventricular myocardial segments

- In typical apical ballooning, high local concentrations of norepinephrine might evoke basal hyperkinesis, increasing mechanical wall stress at the apex and thereby increasing end-diastolic pressure and BNP levels

Prognosis

- Generally **favorable**
- Some fatal complications : **very rare**

  Left ventricular free wall rupture *Mayo Clin Proc*. 2004;79:821– 824

  Ventricular septal defect

  Ventricular fibrillation,

  Stroke and apical thrombus formation
- **Heart failure**, with or without pulmonary edema

  : m/c clinical complication
- published in-hospital mortality data are underestimated

  : attention to the hemodynamics in the acute phase,

  which often correspond to NYHA III heart failure
- Recurrence :

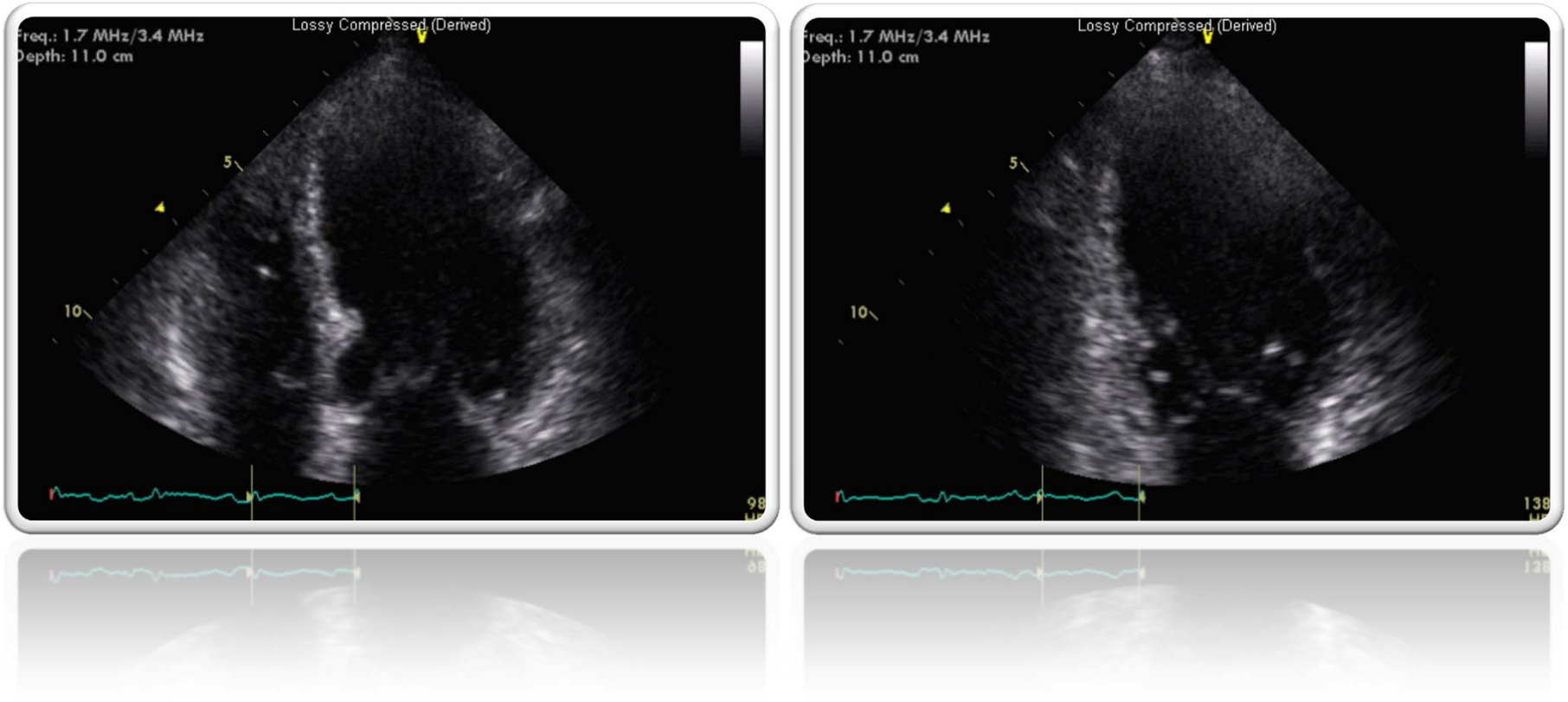
  recurrence rate is **10%** *J Am Coll Cardiol*. 2007;50:448–452

Reported complication associated with Takotsubo CMP
Left heart failure with and without pulmonary edema
Cardiogenic shock
Dynamic intraventricular obstruction with left ventricular intracavitary pressure gradient generation
Mitral regurgitation resulting from chordal tethering as well as systolic anterior motion of the mitral valve apparatus
Ventricular arrhythmias
Left ventricular mural thrombus formation with and without embolic event
Left ventricular free-wall rupture or ventricular septal defect
Death

This table is adapted and modified from ***Ann Intern Med.*** **2004;141:858-865**.

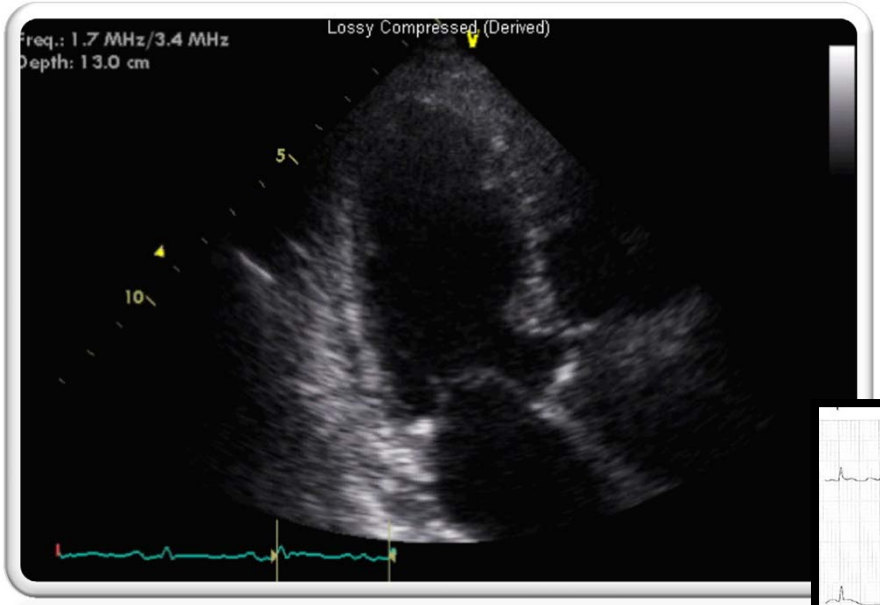
Case 5

Complication Case
77/F
Stressful event : Biliary sepsis and ERCP procedure

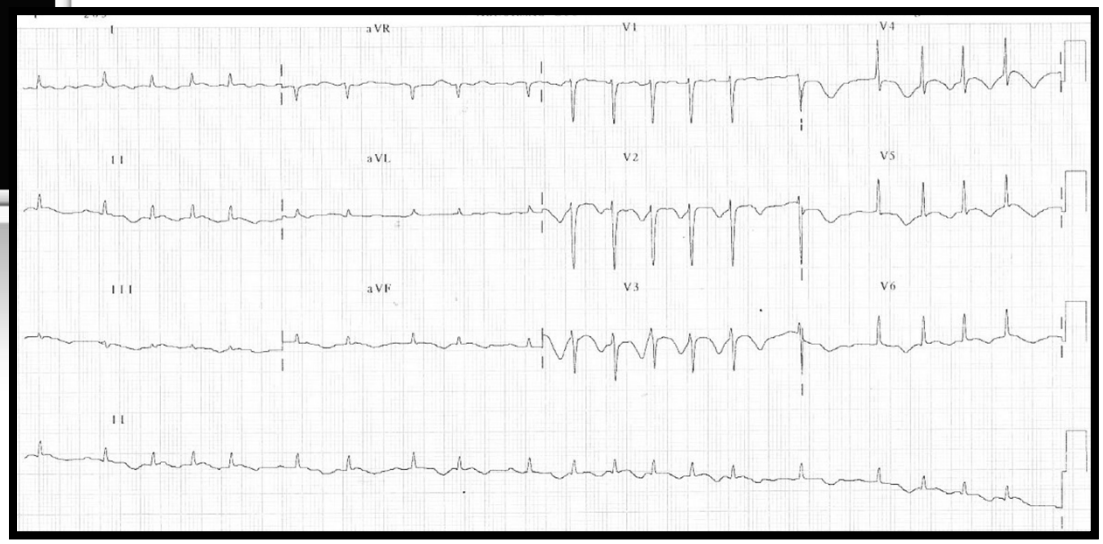


Case 5

Complication Case
77/F
Stressful event : Biliary sepsis and ERCP procedure

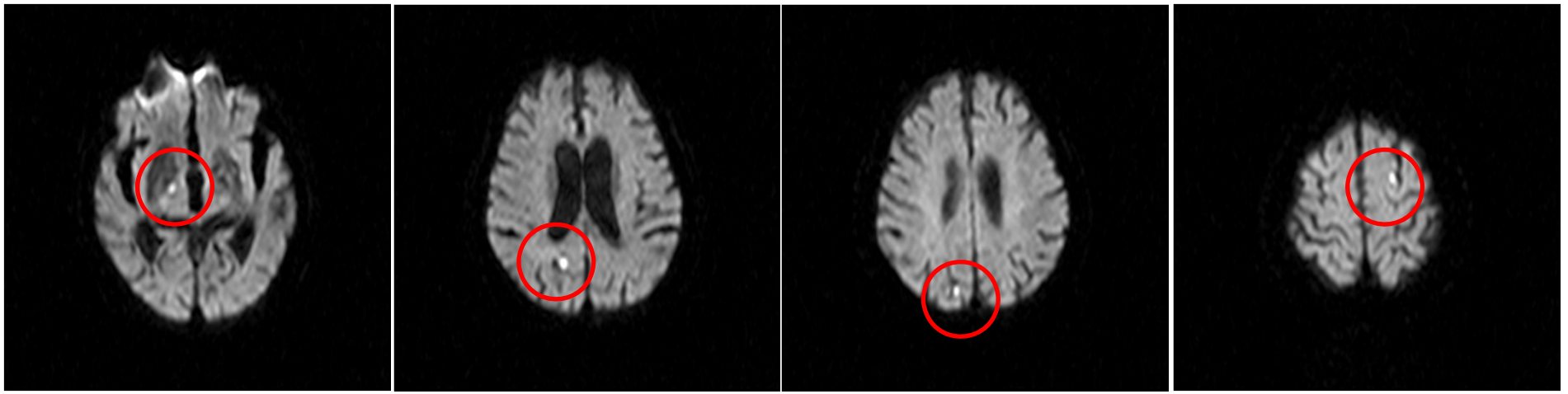


ECG: prolongation of QT interval
Peak **CK-MB 58** IU/L, **TnT 0.981** ng/mL



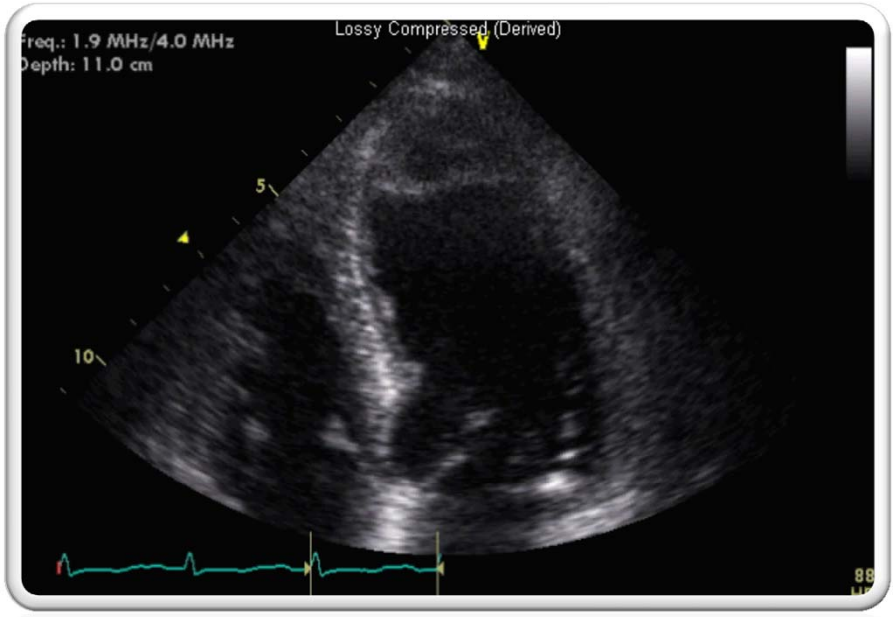
Case 5

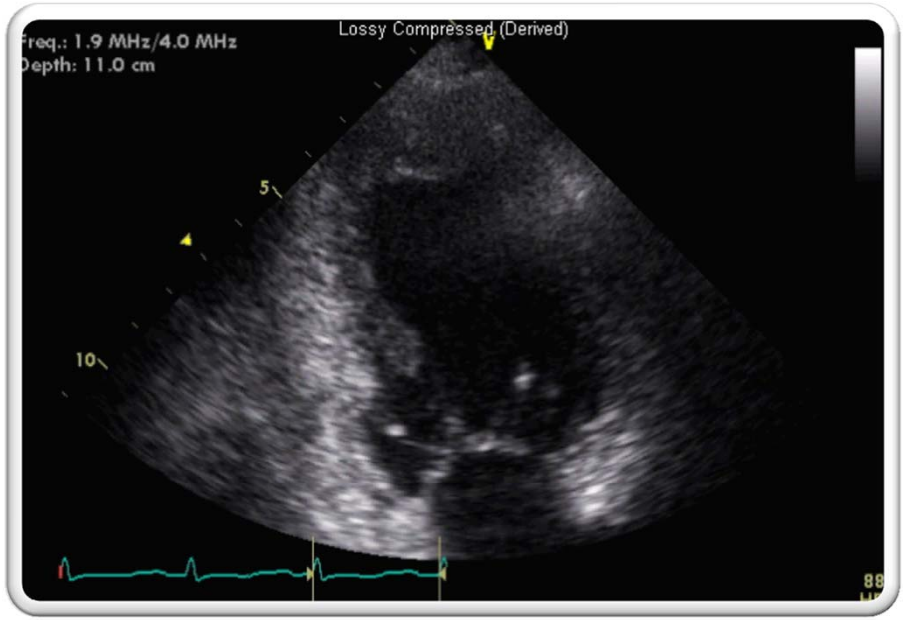
- Multiple Cb infarction and check the MRI (diffusion image)



Case 5

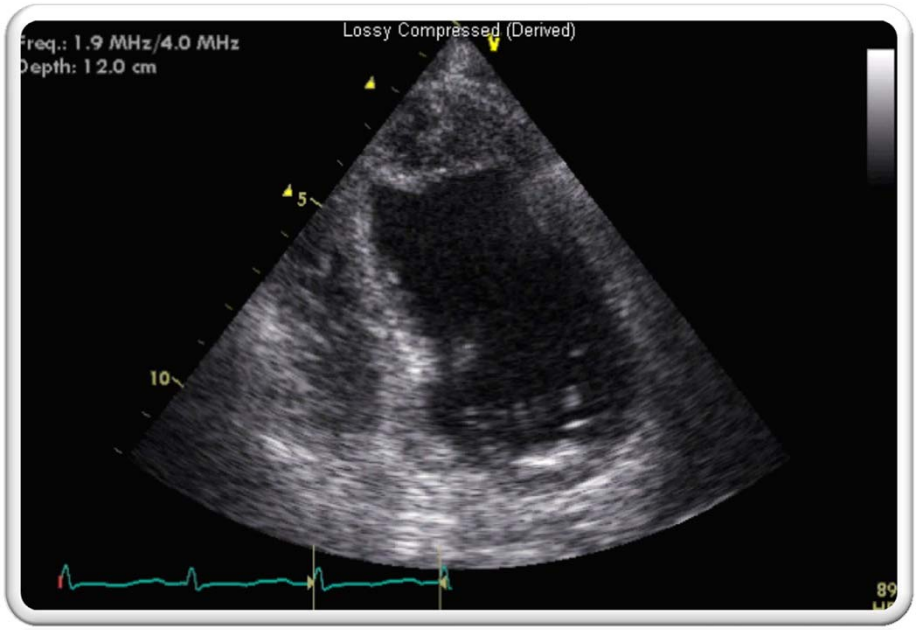
F/u Echocardiography

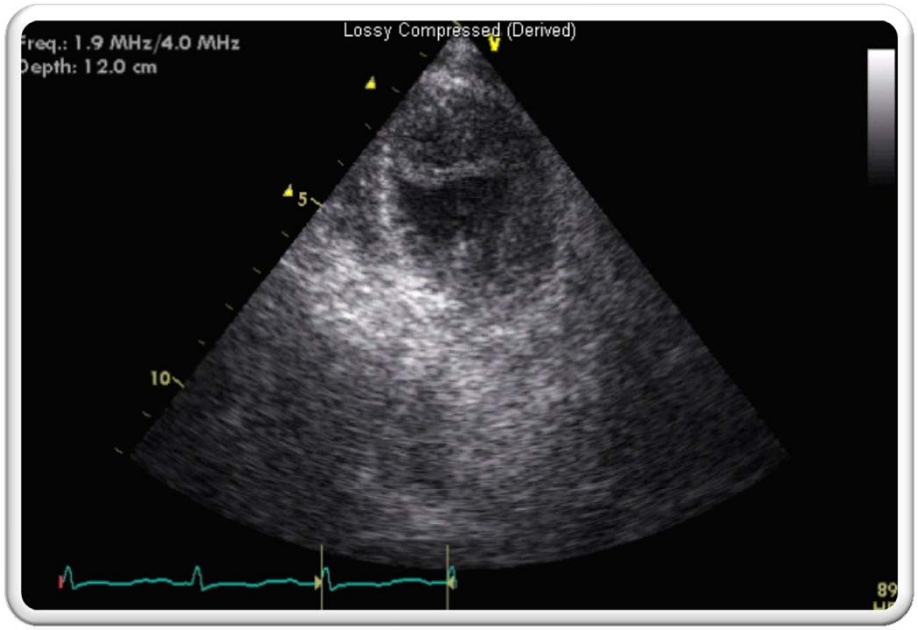




Case 5

F/u echo, large thrombus(mural)





Management

- There are **no specific treatments**
- When shock occurs, intraaortic balloon pumping is established as additional support for the circulation
- Arrhythmia resulting from QT prolongation is commonly observed
  : do not administer antiarrhythmics prophylactically
- Administration of magnesium sulfate is effective for ventricular tachycardia in the acute phase of takotsubo cardiomyopathy if the QT interval is prolonged
- Do not administer β-adrenoceptor blockers,
  : Can prolong the QT interval and
  leave unopposed the potentially adverse effects of high local concentrations of catecholamines at α-adrenoceptors.

Management

- Thrombosis in takotsubo cardiomyopathy cases, which might reflect vasoconstrictor, platelet activation, or prothrombotic effects of extremely high epinephrine levels.

- Because apical ballooning increases the risk of cardiac rupture, it is still **controversial** whether treatment with aspirin or heparin is indicated

- Epinephrine promotes platelet activation by stimulating platelet α_2 – adrenoceptors provides additional rationale for treatment with a combined **α– and β–blocker**

Management

- **Estrogen treatment** is beneficial in preventing the animal model of takotsubo cardiomyopathy
  - treatment might be considered in **elderly women** who have suffered an episode of takotsubo cardiomyopathy
  - clinical trials of estrogen administration in takotsubo cardiomyopathy patients **have not been performed.**

- Hypotension d/t dynamic outflow tract obstruction(caused by hyperkinesis of the basal LV segments and systolic anterior motion of the mitral valve)
  → intravenous inotropic agents would be contraindicated;

  To reduce outflow obstruction,
  short-acting β–blockers and intravenous fluids could be used cautiously to decrease contractility and increase cavity size, respectively

Management

Subacute and long-term care

- Empirical approach, treating individuals with takotsubo cardiomyopathy as those with other causes of cardiomyopathy (with angiotensin-converting enzyme inhibitors and β-blockers) at least until left ventricular systolic function recovers

- Long-term β-blocker and combined α– and β-blocker are attractive therapies given the putative association between takotsubo cardiomyopathy and a catecholamine surge

- Such strategies have been advocated if patients have no contraindications, but few trial data show efficacy of these strategies

Conclusion

- Takotsubo cardiomyopathy is important in the differential diagnosis of acute coronary syndrome.

- **Variants of this cardiomyopathy are increasingly recognized**.

- The pathophysiologic mechanism is unknown.
- Stress cardiomyopathy is a form of **myocardial stunning**, but with cellular mechanisms different to those caused by transient episodes of ischemia secondary to coronary stenosis.

- The cause of myocardial stunning is multifactorial.
  And **catecholamine excess likely has a central role.**

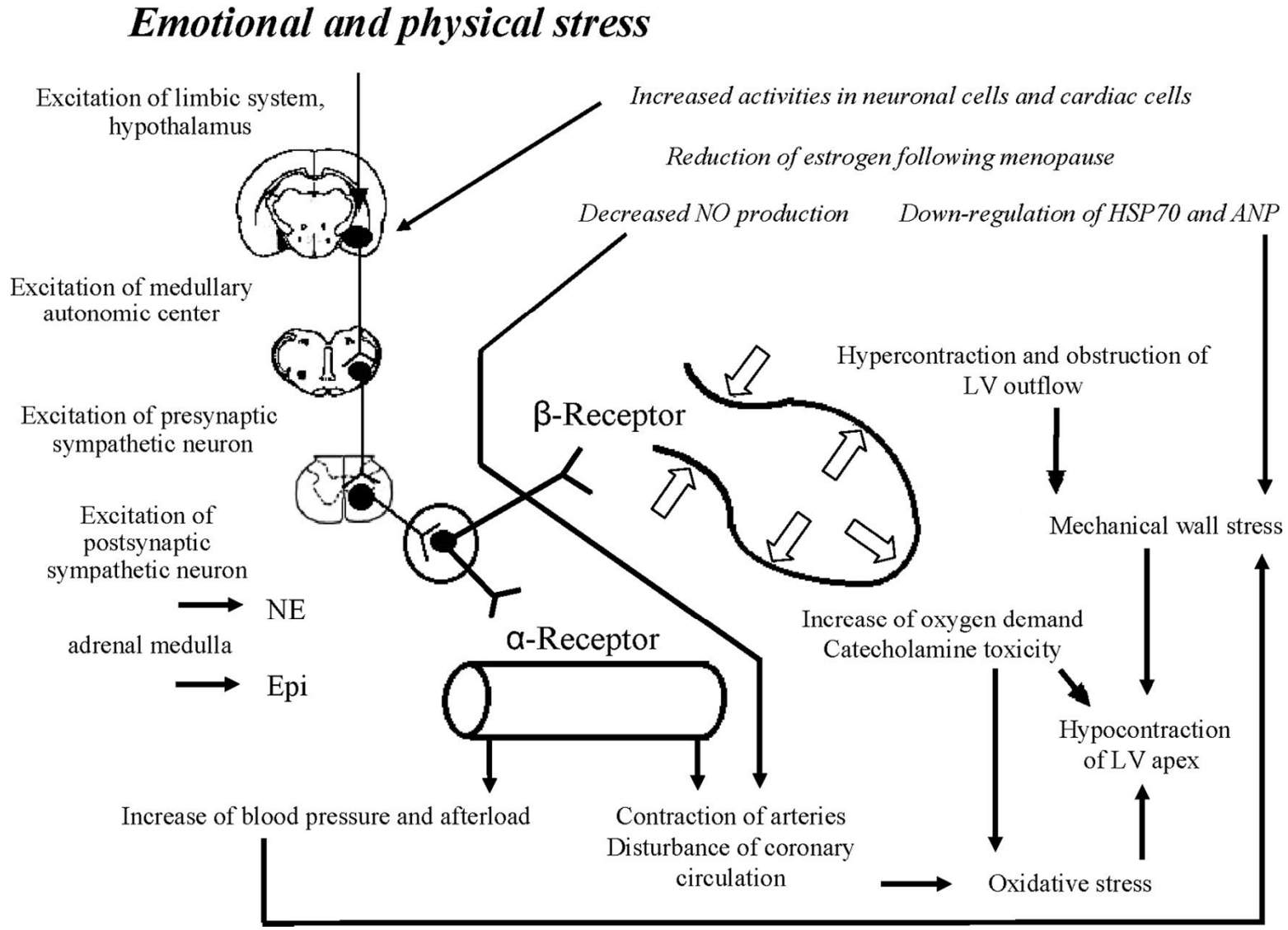
Conclusion

- Takotsubo cardiomyopathy is **not rare**, likely will lead to a higher reported incidence.
- Diagnosis of takotsubo cardiomyopathy has important implications for clinical management at presentation and afterward.
- The long term prognosis is generally favorable;
  however, a small subset has potentially life-threatening complications during the initial presentation.

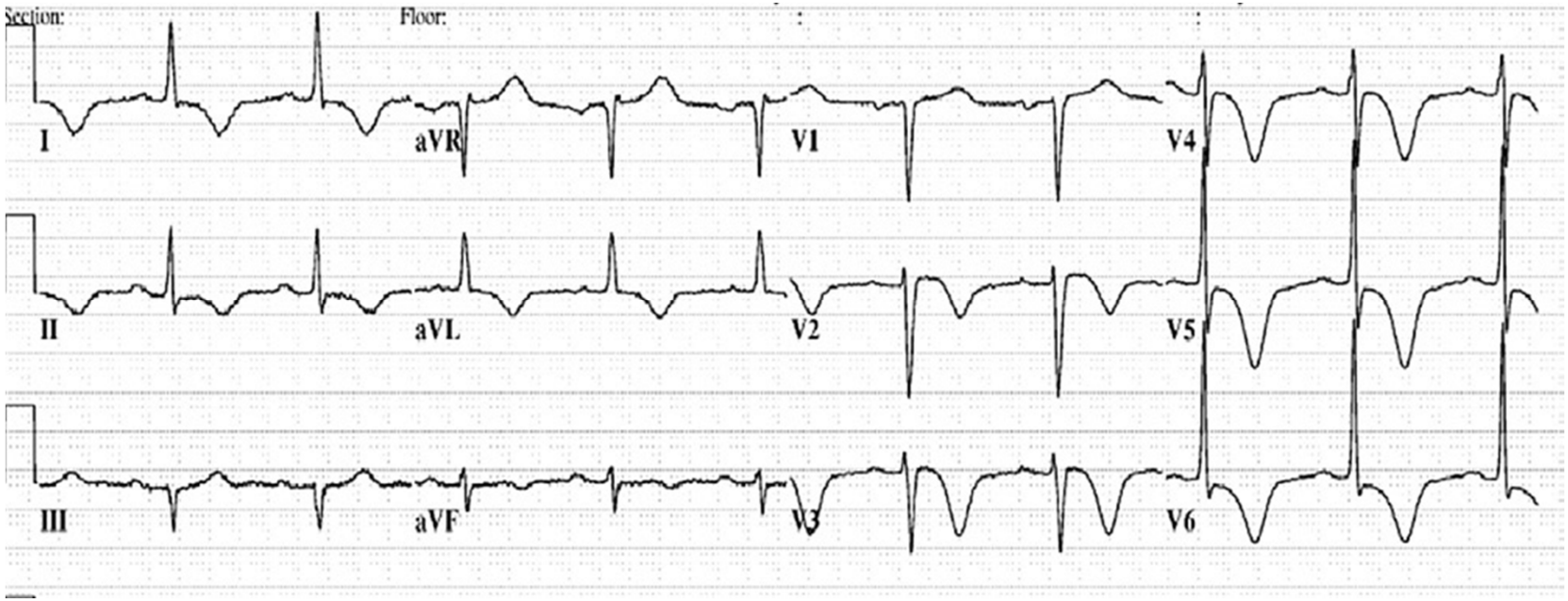
Thank you for your attention

- I'm very stressful status
- Concentration of Catecholamine is increasing in my blood at now
- I don't want to get a Takotusbo CMP

Backup Slide



Akashi et al., Takotsubo Cardiomyopathy Circulation, 2008



- Diffuse T-wave inversion with QT prolongation

Management

Acute care

- **Initial clinical management** of patients with takotsubo cardiomyopathy is **similar** to that of patients with **acute coronary syndrome**

- The diagnosis must be confirmed with coronary artery and left ventricular imaging
- Hypotension occurs frequently

- Acute pump failure may require **intravenous pressor support**,
  but given the evidence of catecholamine excess in the origin of this syndrome,
  mechanical support with an **intra-aortic balloon pump** may be preferred.

- Hypotension d/t dynamic outflow tract obstruction(caused by hyperkinesis of the basal LV segments and systolic anterior motion of the mitral valve)
  → intravenous inotropic agents would be contraindicated;
  To reduce outflow obstruction,
  short-acting β–blockers and intravenous fluids could be used cautiously to decrease contractility and increase cavity size, respectively
- Peripheral vasoconstrictors such as phenylephrine may be considered if β-blockers and fluid administration are contraindicated or ineffective
- Arrhythmias such as atrial fibrillation, ventricular tachycardia, and ventricular fibrillation are not rare

Table. Patient Clinical and Laboratory Characteristics

	Tsuchihashi et al[1]	Kurowski et al[10]	Kurisu et al[2]	Sharkey et al[8]	Wittstein et al[12]	Inoue et al[11]	Sato et al[4]	Bybee et al[7]	Yoshida et al[13]	Akashi et al[3]
Subjects, n	88	35	30	22	19	18	16	16	15	13
Country	Japan	Germany	Japan	US	US	Japan	Japan	US	Japan	Japan
Series type	Retrospective	Prospective	Retrospective	Prospective	Prospective	Retrospective	Retrospective	Prospective	Prospective	Prospective
Age, y	67±13	72±9	70±8	65±13	61±15	76±8	71±9	71±12	72±7	73±10
Women, %	86	94	93	91	95	94	94	100	80	85
Preceding emotional stressor, %	20	42	17	86	100	11	· · ·	38	40	31
Preceding stressor, %	43	42	17	14	· · ·	39	100	44	40	69
Chest pain, %	67	· · ·	67	91	95	72	100	69	87	54
ST-segment elevation, %	90	69	100	59	11	100	56	81	87	92
ST-segment elevation in precordial leads, %	85	· · ·	97	59	· · ·	100	· · ·	81	· · ·	92
Q waves, %	27	· · ·	· · ·	45	37	56†	· · ·	31	7	· · ·
Mean QTc, ms	· · ·	· · ·	· · ·	· · ·	542*	· · ·	· · ·	501±55	508*	· · ·
Elevation in cardiac enzyme levels, %	56	· · ·	· · ·	· · ·	· · ·	· · ·	56	100	· · ·	85
Initial average LVEF	0.41±0.11	0.5±0.13	0.49±0.12	0.29±0.09	0.20*	· · ·	0.49±0.04	0.4	0.43±0.08	0.42±0.10
Follow-up LVEF	0.64±0.10	0.68±0.12	0.69±0.12	0.63±0.06	0.60*	· · ·	0.66±0.03	0.6	0.76±0.01	0.65±0.08
Time of recovery, d	· · ·	· · ·	11.3±4.3	24±29	21*	· · ·	17.7	8	11±4	17±7
Initial Forrester subset		· · ·		· · ·	· · ·	· · ·	· · ·	· · ·	· · ·	1.9±0.3
Pulmonary edema, %	22	· · ·	3	0	16	28	6	44	· · ·	0
Intraaortic balloon pumping, %	8	· · ·	0	18	16	6	0	6	7	15
Coronary stenosis >50%, %	0	0	0	0	5	0	0	0	· · ·	0
Angiographically normal coronary arteries, %	· · ·	0	83	100	95	100	100	25	100	100
Spontaneous multivessel spasm, %	0	0	10	· · ·	0	0	0	0	0	0
Provocable multivessel spasm, n/n (%)	5/48 (10)	· · ·	6/14 (43)	· · ·	· · ·	· · ·	0/6 (0)	· · ·	1/6 (17)	0/11 (0)
Transient intraventricular pressure gradient, %	18	· · ·	· · ·	23	· · ·	· · ·	· · ·	13	14	· · ·
In-hospital mortality, %	1	3 (9)	0	0	0	6	0	0	0	8
Documented recurrence, n/n (%)	2/72 (3)	2 (6)	0	2/22 (9)	0	· · ·	· · ·	1/16 (6)	· · ·	0

LVEF indicates left ventricular ejection fraction. Values are expressed as mean±SD when appropriate. This table is adapted and modified from Reference 14 with permission.

*Median.

†In precordial leads.

Table 2. **Reported Complications Associated with the Transient Left Ventricular Apical Ballooning Syndrome**

Left heart failure with and without pulmonary edema
Cardiogenic shock
Dynamic intraventricular obstruction with left ventricular intracavitary pressure gradient generation
Mitral regurgitation resulting from chordal tethering as well as systolic anterior motion of the mitral valve apparatus
Ventricular arrhythmias
Left ventricular mural thrombus formation
Left ventricular free-wall rupture
Death

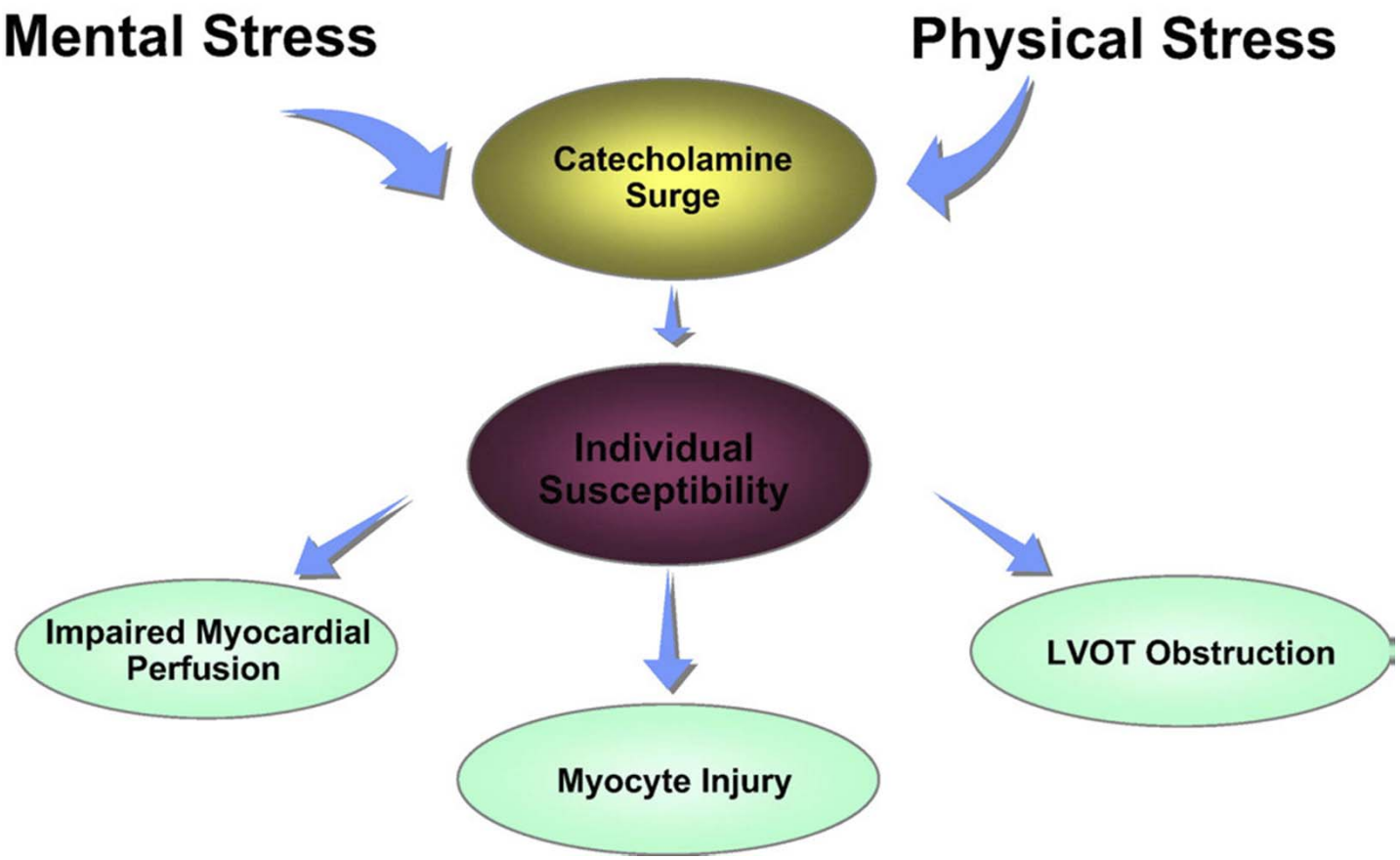

Mental Stress
Physical Stress
Catecholamine Surge
Individual Susceptibility
Impaired Myocardial Perfusion
Myocyte Injury
LVOT Obstruction

Table 2
Characteristics of LV thrombus formation and function

First author	Case no	Age gender	Location of TF	Morphology of thrombus	Diagnosis of TS and TF	Recognition of TF (days)	Resolution of TF (days)	LVEF in the acute phase (%)	Wall motion abnormalities	LVD Recovery (days)	CE events
Barrera-Ramirez	1	64 F	LV apex	Mural	Echo	0	90	40	Apical akinesis	90	—
Yasuga	2	76 F	LV apex	NA	Echo	6	14	Na	Apical hypo-akinesis	90	—
Tibrewala	3	64 F	LV apex	Mural	VG+echo	0	30	25 (†)	Apical dyskinesis	90	—
Calastra	4	64 F	LV apex	NA	MRI	NA	30	NA	Apical akinesis	30	—
Grabosky	5	85 F	NA	NA	VG+echo	NA	NA	30	Mid-apical hypokinesis	Few Weeks	Stroke
Grabosky	6	64 F	LV apex	Round-shaped	VG+echo	0	NA	45	Mid-apical hypokinesis	Few Weeks	Stroke
Robles	7	74 F	LV apex	NA	VG+echo	0	60	40	Apical akinesis	60	—
Singh	8	74 M	LV apex	Oval-shaped	Echo+MRI	14 (#)	40	30	Apical hypokinesis	40	—
Nerella	9	43 F	LV apex	Mural	Echo	5	NA	25	Apical akinesis	8	Renal infarct
Yoshida	10	51 M	LV apex	Mural	Echo	0	14	48	Apical akinesis	8	—
Korosoglou	11	74 F	LV apex	Mural	Echo+MRI	0	12	33	Apical akinesis	12	—
Kimura	12	54 F	LV apex	Giant	VG	1–2	7	NA	Apical akinesis	14	—
Santos	13	47 F	LV apex	NA	VG+echo	NA	7	40	Apical akinesis	Few weeks	—
de Gregorio	14	74 F	LV apex	Round-shaped (*)	Echo	0	14	45	Apical akinesis	14	Minor stroke
Andò	15	57 F	LV apex	Mural	Echo+VG	NA	NA	NA	Mid-apical akinesis	NA	Leg ischemia

*Multiple masses, the biggest one was mobile; #The diagnosis of TS was made by VG; †The reported value was 20–30%.
CE, cardioembolic; LV, left ventricle/ventricular; LVD, LV dysfunction; LVEF, LV ejection fraction; MRI, cardiac magnetic resonance imaging; NA, not available/reported; TS, Takotsubo-like; VG, ventriculography.

Table 1. Proposed Mayo Clinic Criteria for Diagnosis of Takotsubo Cardiomyopathy

1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments, with or without apical involvement. Regional wall motion abnormalities extend beyond a single coronary vascular bed.* A preceding physical or emotional stressor is often present.
2. No obstructive coronary disease or acute plaque rupture (determined angiographically).†
3. New electrocardiographic abnormalities (ST-segment elevation, T-wave inversion, or both) or modest elevation in cardiac troponin level.
4. No pheochromocytoma or myocarditis. For such patients, the diagnosis of takotsubo cardiomyopathy should be made cautiously, and a clear, stressful, precipitating event must be sought.

*A rare exception to these criteria is regional wall motion abnormality that is limited to 1 coronary territory. †A patient with obstructive coronary atherosclerosis may also have takotsubo cardiomyopathy development. However, this is very rare (based on our experience and the medical literature). Adapted with permission, from Prasad et al. (21).

Case 1

- 81/F
- C/C : G-weakness
- She came to our ER d/t general weakness. She have vascular dementia and hypertension.
- Stressful event : none
- ECG : deep T wave inversion, prolongation of QT interval (QTc 545msec)
- Cardiac enzyme :

  CK: 82 IU/L, CK-MB 6 IU/L, TnT 0.188ng/mL

Management

Subacute and long-term care

- In-hospital death is rare
- Complete recovery of left ventricular systolic function is necessary to confirm the diagnosis of takotsubo cardiomyopathy.
- The recovery time varies and can be as short as several days or as long as several weeks
- Empirical approach, treating individuals with takotsubo cardiomyopathy as those with other causes of cardiomyopathy (with angiotensin-converting enzyme inhibitors and β-blockers) at least until left ventricular systolic function recovers
- Left ventricular thrombus and systemic thromboembolism have been reported. Anticoagulation therapy, at least until recovery of the wall motion abnormality, should be considered for those with clinically significant apical hypokinesis or akinesis that persists 2 to 3 days after presentation

- Long-term β-blockade and combined α– and β-blockade are attractive therapies given the putative association between takotsubo cardiomyopathy and a catecholamine surge
- Such strategies have been advocated if patients have no contraindications, but few trial data show efficacy of these strategies