Takotsubo syndrome

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FACC, FESC
Definition

• Takotsubo
• Apical ballooning
• Broken heart syndrome
• Stress cardiomyopathy
• Cathecholaminergic cardiomyopathy
Epidemiology

- 1990 first report by Japanese
- Unknown prevalence
- Increase in reported incidence
- 90% postmenopausal women- 10% men and younger women
- Primary
- Secondary –undelying medical conditions activating sympathetic NS
- 1-2% of ACS
Endocrine
- Phaeochromocytoma, thyrotoxicosis (endogenous and iatrogenic), SIADH, Addisonian crisis, multiple endocrine neoplasia 2A syndrome, hyperglycaemic hyperosmolar state, hyponatraemia, severe hypothyroidism, Addison’s disease, adrenocorticotropin hormone deficiency, autoimmune polyendocrine syndrome II

Neurological and neurosurgical
- Acute neurosurgical emergencies (e.g. subarachnoid haemorrhage, acute head injury, acute spinal injury)
- Acute neuromuscular crises, especially if involving acute ventilatory failure (e.g. acute myasthenia gravis, acute Guillain–Barré syndrome)
- Epileptic seizures, limbic encephalitis, ischaemic stroke, posterior reversible encephalopathy syndrome

Respiratory
- Acute exacerbation of asthma or COPD (especially with excessive use of inhaled beta2-agonists)
- Acute pulmonary embolism
- Acute pneumothorax
- Obstetric, e.g. miscarriage, labour, emergency Caesarean section

Psychiatric
- Acute anxiety attack/panic disorder
- Attempted suicide
- Drug-withdrawal syndromes
- Electroconvulsive therapy
- Gastrointestinal, e.g. acute cholecystitis, biliary colic, acute pancreatitis, severe vomiting, severe diarrhoea, pseudomembranous colitis
- Peritonitis

Infection
- Severe sepsis
- Babesiosis

Cardiological
- Dobutamine stress echocardiography
- Radiofrequency arrhythmia ablation
- Pacemaker implantation
- Electrical DC cardioversion for atrial fibrillation
- Post-cardiac arrest including ventricular fibrillation

Haematological
- Blood transfusions
- Thrombotic thrombocytopenic purpura

Surgical
- Many cases have been reported during induction of general anaesthesia or during non-cardiac surgery or interventional procedures under local or general anaesthesia (e.g. cholecystectomy, hysterectomy, rhinoplasty, Caesarean section, radiofrequency liver ablation, radiotherapy, colonoscopy, difficult urinary catheterization, carotid endarterectomy)

Medication and illicit drugs
- Epinephrine injection
- Nortriptryline overdose, venlafaxine overdose, albuterol, flecainide, metoprolol withdrawal, 5-fluorouracil, duloxetine
- Cocaine abuse
Acute Heart Failure Association diagnostic criteria

• Transient RWMA often but not always precipitated by an emotional (women) or physical (men) trigger.
• RWMA usually extend beyond a single coronary artery distribution
• Absence of culprit coronary lesion-ruptured plaque, thrombi, dissection-
• New and reversible ECG changes-ST elevation, ST depression, T wave inversion, QT prolongation, LBBB-. ECG abn may persist for 6-12 months.
• Significantly elevated BNP or NT- proBNP. May persist for 6-12 months.
• Mild elevation of cardiac troponins-disparity with the degree of LV dysfunction.
• Recovery of LV function in 3-6 months.
Mayo clinic diagnostic criteria

- Transient RWMA > single coronary; rarely focal, diffuse
- No CAD; if present not correlating with RWMA
- ECG changes or Tn elevation
- No myocarditis or pheochrocytoma
Of the 1750 patients studied, 179 patients were male (10.2%, dark blue), while 1571 were female (89.8%, light blue). Male patients were younger than females (62.9±13.1 vs. 66.8±13.0 years, P<0.001). 1384 patients were women older than 50 years (79.1%).
Triggering factors (N=1750)

- 36.0% Physical triggers
- 27.7% Emotional triggers
- 7.8% Both physical and emotional triggers
- 28.5% No evident trigger
Physical triggers (N=630, 36.0%)

- 20.2% Acute respiratory failure
- 18.4% Post-surgical/fracture
- 15.5% Central nervous system conditions
- 8.1% Infection
- 1.3% Malignancy
- 36.5% Others
Emotional triggers (N=485, 27.7%)

- 22.1% Grief/loss
- 22.1% Panic/fear/anxiety
- 16.1% Interpersonal conflict
- 15.8% Anger/frustration
- 7.6% Financial or employment problems
- 16.3% Others
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Takotsubo Cardiomyopathy</th>
<th>Acute Coronary Syndrome</th>
<th>P Value†</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total Cohort (N=1750)</td>
<td>Matched Cohort (N=455)</td>
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<tr>
<td>Female sex — no. (%)</td>
<td>1571 (89.8)</td>
<td>411 (90.3)</td>
<td>1.00</td>
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<tr>
<td>Age — yr</td>
<td>66.4±13.1</td>
<td>67.7±12.5</td>
<td>0.19</td>
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<td>Chest pain — no./total no. (%)</td>
<td>1229/1619 (75.9)</td>
<td>322/438 (73.5)</td>
<td>&lt;0.001</td>
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<tr>
<td>Dyspnea — no./total no. (%)</td>
<td>760/1620 (46.9)</td>
<td>208/439 (47.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Median troponin (IQR) — factor × ULN‡</td>
<td>7.70 (2.22–24.00)</td>
<td>7.68 (2.38–24.21)</td>
<td>0.62</td>
</tr>
<tr>
<td>Median creatine kinase (IQR) — factor × ULN</td>
<td>0.85 (0.52–1.48)</td>
<td>0.87 (0.55–1.42)</td>
<td>&lt;0.001</td>
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<tr>
<td>Median brain natriuretic peptide (IQR) — factor × ULN</td>
<td>6.12 (2.12–15.70)</td>
<td>5.89 (1.68–13.92)</td>
<td>&lt;0.001</td>
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<td>ST-segment change — no./total no. (%)</td>
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<tr>
<td>Elevation</td>
<td>690/1578 (43.7)</td>
<td>185/420 (44.0)</td>
<td>0.03</td>
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<tr>
<td>Depression</td>
<td>121/1578 (7.7)</td>
<td>35/420 (8.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>Heart rate — beats/min</td>
<td>87.5±21.8</td>
<td>87.3±21.8</td>
<td>&lt;0.001</td>
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<td>Systolic blood pressure — mm Hg</td>
<td>130.6±28.8</td>
<td>131.8±31.4</td>
<td>0.96</td>
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<td>Left ventricular ejection fraction — %¶</td>
<td>41.1±11.8</td>
<td>40.7±11.2</td>
<td>&lt;0.001</td>
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<td>Left ventricular end diastolic pressure — mm Hg</td>
<td>21.3±8.0</td>
<td>22.1±7.7</td>
<td>0.001</td>
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<td>Coexisting medical condition — no./total no. (%)</td>
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<tr>
<td>Coronary artery disease</td>
<td>245/1597 (15.3)</td>
<td>96/455 (21.1)</td>
<td>&lt;0.001</td>
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<tr>
<td>Neurologic or psychiatric disorder</td>
<td>714/1525 (46.8)</td>
<td>252/452 (55.8)</td>
<td>&lt;0.001</td>
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<tr>
<td>Acute neurologic disorder</td>
<td>143/1528 (9.4)</td>
<td>41/452 (9.1)</td>
<td>&lt;0.001</td>
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<tr>
<td>Past or chronic neurologic disorder</td>
<td>293/1512 (19.4)</td>
<td>98/452 (21.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>Acute psychiatric disorder</td>
<td>149/1525 (9.8)</td>
<td>57/452 (1.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Past or chronic psychiatric disorder</td>
<td>444/1512 (29.4)</td>
<td>165/451 (36.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
A

P<0.001

Patients (%)

0-29%  30-44%  45-54%  ≥55%

LVEF on admission (%)

Takotsubo cardiomyopathy (N=443)
Acute coronary syndrome (N=295)

B

LVEDP (mmHg)

LVEF (%)
C

LVEF (%)

P<0.001

Admission  In-hospital recovery  60-day follow-up
(N=1179)  (N=671)  (N=290)
Figure 3. Kaplan–Meier Estimates of 10-Year Outcome Events.

Shown are the proportions of patients with any major adverse cardiac and cerebrovascular event (MACCE), which was a composite of death from any cause, recurrence of takotsubo cardiomyopathy, stroke or transient ischemic attack (TIA), or myocardial infarction (MI).
pathophysiology

• Vascular
  • Spasm
  • Aborted MI with recanalization
  • Abrupt increase in afterload

• Myocardial
  • Acute LVOT obstruction
  • Catecholamine-induced myocardial stunning
Anatomic variations

• Apical -hypokinesis +basal hypercontractility  (75-80%)
• Mid left ventricular –hypokinesis+basal and apical hypercontractility (10-15%)
• Inverted or basal –hyponikesis+apical hypercontractility  (5%)
• Rare forms
  • Biventricular apical dysfunction (more severe form)
  • Isolated RV involvement
symptoms

• Chest pain
• Sob
• Syncope (VT, LVOT obstruction)
• Palpitations
• Shock
diagnosis

• ECG abnormal >95%
  • ST elevation/depression, Q, LBBB <12h
  • QT prol/ T inversion 24-48 h

• Urgent coronary angiography-ventriculography (bystander CAD 10%)

• Biomarkers (troponin, BNP)

• Echo (MR, LVOTO, RV involvement, thrombus)

• CMR (edema +, LGE -, dd myocarditis)

• MIBG ( reduced in affected area, nl perfusion, dd AMI)
<table>
<thead>
<tr>
<th></th>
<th>Takotsubo syndrome</th>
<th>Myocardial infarction</th>
<th>Myocarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of wall motion abnormality</td>
<td>Concentric mid- and apical LV wall</td>
<td>Follows expected epicardial coronary artery distribution</td>
<td>Usually global unless regional edema/LGE is severe</td>
</tr>
<tr>
<td>Myocardial edema</td>
<td>Typically transmural in a concentric mid and apical LV wall distribution</td>
<td>Subendocardial or transmural at sites of wall motion abnormalities</td>
<td>Subepicardial, mid-myocardial or transmural</td>
</tr>
<tr>
<td>Left ventricular impairment</td>
<td>Yes: typically impaired ejection fraction with elevated indexed end systolic volume &gt; 33% of patients</td>
<td>Yes: typically impaired ejection fraction with elevated indexed end systolic volume May be seen, particularly if right coronary artery territory involved</td>
<td>Yes, but may show only mild/borderline low normal ejection fraction Rarely impacts on right ventricular function</td>
</tr>
<tr>
<td>Right ventricular impairment</td>
<td></td>
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<td></td>
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<tr>
<td>LGE</td>
<td>Maybe (10%-40%)</td>
<td>Yes</td>
<td>Often</td>
</tr>
<tr>
<td>Site of LGE</td>
<td>Concentric transmural mid and apical LV wall</td>
<td>Typically subendocardial or transmural in recognized epicardial coronary artery distribution</td>
<td>Mid-myocardial or subepicardial in a focal non-coronary artery distribution</td>
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<tr>
<td>Type of LGE</td>
<td>Low-intensity LGE</td>
<td>Bright LGE</td>
<td>Low-intensity or Bright LGE</td>
</tr>
<tr>
<td>Microvascular obstruction</td>
<td>No</td>
<td>Maybe</td>
<td>No</td>
</tr>
<tr>
<td>Resolution at 3 months</td>
<td>Yes</td>
<td>No</td>
<td>Potentially but may show residual myocardial fibrosis and impairment</td>
</tr>
</tbody>
</table>

Int Heart J 2018; 59: 250-255)
| Gender and age | 90% female. Majority >50 years and post-menopausal. | No sex prevalence. More frequent in the young. |
| Preceding events | Stressor trigger identifiable in ~70% of cases. | Symptoms and signs of infection often present (fever, chills, headache, muscle aches, general malaise, cough, nausea, vomiting, diarrhoea). |
| Cardiac symptoms | Chest pain, dyspnoea, palpitations. | Chest pain, dyspnoea, peripheral oedema, fatigue, and palpitations. |
| Clinical signs | Pericardial rub rare. | Pericardial rub may be present. |
| ECG at admission | ST changes such as ST-segment elevation or non-ST-segment elevation. Deep T wave inversion, QT prolongation. Rarely normal. | ST-segment elevation or depression, negative T-wave, bundle branch block, atrioventricular block, low voltage, and/or ventricular arrhythmias. Normal in several cases. |
| Cardiac enzymes | Low/moderate troponin rise. Discrepancy between the large amount of dysfunctional myocardium and peak troponin level. | Frequently significant troponin rise, proportional to the hypokinetic area. Normal in several cases. |
| Other biomarkers | C-reactive protein (CRP) mildly elevated unless infective trigger. BNP moderately or significantly elevated. | Erythrocyte sedimentation rate and CRP elevated. BNP basically elevated. Acute viral serology may be detected. |
| Echocardiography | Apical ballooning, anatomical variants, 'circumferential pattern', left ventricular outflow tract obstruction (LVOTO), right ventricular (RV) involvement, transient mitral regurgitation. | Localized or diffuse wall motion abnormalities of LV and/or RV dilatation, increased wall thickness, pericardial effusion. |
| Cardiac magnetic resonance imaging | High T2 signal intensity (oedema), late gadolinium enhancement (LGE) usually absent acutely. If present acutely patchy LGE which usually resolves at follow-up. Absence of typical infarct LGE pattern. | High T2 signal intensity (oedema), LGE with non-ischaemic distribution (often epicardial). Absence of typical infarct LGE pattern. |
| Histological findings | Contraction band necrosis. | Infiltration of many inflammatory cells. Interstitial oedema. |
| Viral genome, separation of virus, or identification of virus by antibody titre | Rare and usually absent where measured. | Often positive. |
| Prognosis | 50% of cases have acute complications, 4–5% mortality. | Variable but majority full recovery. Highest mortality with fulminant myocarditis. |
| Therapy | Supportive. | Supportive. Immunosuppression in severe cases if giant cell myocarditis suspected. |
Complications-1

• Acute
  • AHF  12-45%
  • RVF  18-34%
  • LVOT obstruction  10-25%
  • MR  14-25%
  • Shock  6-20%

• Arrhythmias
  • AF  5-15%
  • VT  4-9%
  • Bradycardia  2-5%

• Thrombus  2-8%
• Tamponade  <1%
• Ventricular wall rupture  <1%
Complications-2

- In-hospital mortality: 1-4.5%
- Recurrence: 5-22% (3 months-10yrs)
- 5-year mortality: 3-17%
AHF

• Predictors
  • Age
  • EF at presentation
  • Admission and peak troponin
  • Physical trigger

• Supportive therapy
  • Inotropes
  • Ventilation
  • IABP
LVOTO

- 20-140mmHg gradient
  - Significant > 25mm
  - High risk > 40mm
- Apical stunning + basal hypercontraction
- MR, shock
- Inotropes, nitrates worse
- B-blockers better, a-1 agonist (phenylephrine) better
- levosimendan?
MR

• SAM/LVOT obstruction
• Apical tethering sublvular apparatus
• More often AHF or shock
Chronic phase
shock

- LVOTO
- MR
- RV failure
arrhythmias

- AHF
- QT
- Rarely remote (LVEF recovery)
thrombus

• Embolism
• Usually 2-5 days symptom onset
• May occur 14 days symptom onset
• Anticoagulation for 3 months
• Usually resolves in 2 weeks
RV (1/3)

- Age
- EF
- AHF
- Pleural effusion
- Longer stay
- Prognosis
Wall rupture

• 2-8 days symptom onset
• LVOTO
• Persistent ST elevation
Risk stratification (1 major or 2 minor)

• High risk-major factors
  • Age>75
  • SBP<110 mmHG
  • Pulm edema
  • VT, VF, syncope
  • LVEF<35%
  • LVOTO>40mmHg
  • MR
  • Apical thrombus
  • VSD or free wall rupture

• High risk-minor factors
  • Age: 70-75
  • Physical trigger
  • ECG: QT>500ms, Q, pers ST elevation
  • LVEF:35-45%
  • BNP>600 pg/ml, NT-proBNP>2000pg/ml
  • Bystander CAD (10-15%)
  • RV involvement
Treatment

- B-blockers (EF<45%)
- ACE-inhibitors (EF<45%)
- Anticoagulants (thrombus, AF)
- Secondary treat underlying condition
GENERAL

• Usually transient and benign
• If shock look for LVOT obstruction
• thrombus→anticoagulation (3 months)
• ↓↓ EF anticoagulation
• LV usually recovers within 1-4 weeks
• In hospital mortality 4%
• 2% /year recurrence rate (? prevention)
Non-invasive cardiac imaging evaluation of patients with chronic systolic heart failure: a report from the European Association of Cardiovascular Imaging (EACVI)

<table>
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<tr>
<th>Condition</th>
<th>Echo</th>
<th>CMR</th>
<th>SPECT</th>
<th>PET</th>
<th>CT</th>
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<tbody>
<tr>
<td>Myocarditis</td>
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<td>Sarcoidosis</td>
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<td>Hypertrophic CMP</td>
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<td>ARVC</td>
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European Heart Journal (2014) 35, 3417–3425
# Unclassified CMs

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<td>cardiomyopathy</td>
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<td>α-dystrobrevin</td>
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