Takotsubo syndrome

May 31, 2020 by Josh Farkas

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pathophysiology
Takotsubo syndrome - EMCrit Project

- Probably results from severe catecholamine surges affecting the myocardium.
- Epinephrine may have the greatest effect in apical regions of the heart where beta-adrenoreceptor density is highest (Keramida et al 2020 [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7160490/]).

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**epidemiology**

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**primary Takotsubo syndrome (initial presenting problem)**

- Underlying etiology in ~1-2% of patients who present with chest pain and troponin elevation.
- In large series, ~90% of patients are women and the mean age is ~65 YO.
- Identifiable stressors are present in 70% of cases (physical or emotional). However, this leaves about 30% of patients with no identifiable stressor.
  - (Lack of an identifiable stressor doesn't exclude Takotsubo syndrome.)
- Prior history of Takotsubo cardiomyopathy increases risk of future episodes.

**secondary Takotsubo syndrome**

- *Extremely common in ICU*, affecting perhaps ~20% of patients in one series (Park et al 2005 [https://pubmed.ncbi.nlm.nih.gov/16002949/]).
- May result from a wide variety of stressors:
  - Post-cardiac arrest
  - Infection
  - Respiratory failure (especially asthma or COPD with excess beta-2 agonists)
  - Autonomic instability, catecholamine excess
  - Poisoning (e.g., sympathomimetic overdose), withdrawal
  - Neurologic disorders (e.g., subarachnoid hemorrhage, status epilepticus, stroke)
  - Surgery
  - Endocrine abnormalities (e.g., pheochromocytoma, thyrotoxicosis, adrenal crisis)
  - Brain death (may limit candidacy for cardiac donation)

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**symptoms**

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- Overall, symptoms are usually more prominent with primary Takotsubo syndrome. In secondary Takotsubo syndrome, these symptoms may often be camouflaged by features of the primary illness (e.g., intubation, sedation).

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https://emcrit.org/ibcc/takotsubo/
• (1) **Anginal chest pain** (diaphoresis, chest pressure, etc.)
• (2) **Arrhythmia** (including polymorphic ventricular tachycardia, VF, AF, bradycardia, asystole).
  • Syncope or palpitations
  • Cardiac arrest
• (3) **Heart failure**
  • Dyspnea, pulmonary edema
  • Cardiogenic shock (in intubated ICU patients, this may be the initial presentation.)

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**EKG**

 eso/utve

> **Caution!** EKG can't reliably differentiate Takotsubo cardiomyopathy versus occlusive MI. That being said, there are some characteristic EKG features which are worth being aware of (especially the diffuse T-wave inversion (TWI) pattern).

**rhythm**

• Atrial fibrillation can occur (although this is nonspecific and can complicate most forms of critical illness).
• Malignant arrhythmia can occur (either Torsade de Pointes or monomorphic ventricular tachycardia).

**intervals**

• QT prolongation is often pronounced (QTc > 500ms) and this predisposes to TdP or VF.
• LBBB may be seen.

**morphology #1: typically begins with anterior STE (anterior MI mimic)**

• STE
  • Usually most notable in V3-V6, but STE in II is also characteristic (this suggests Takotsubo, but can also result from wraparound LAD occlusion).
  • STE has lower magnitude than is typically seen with an anterior occlusive MI.
• Hyperacute T-waves may be seen.
• Features that may support Takotsubo (rather than anterior MI)
  • Absence of pathological Q waves
  • Absence of reciprocal ST depression
  • Lack of STE in aVR or V1
    • STD in aVR suggests Takotsubo.
    • Absence of STE in V1 suggests Takotsubo.

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Sam Ghali, M.D.
@EM_RESUS

**#ECG** of elderly man with Takotsubo Cardiomyopathy aka
"Broken Heart Syndrome"

Mimics **#STEMI**. Diagnosis best confirmed in Cath Lab! **#FOAMed**

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https://emcrit.org/ibcc/takotsubo/
**morphology #2: TWI often appears on day 1-3**

- Diffuse TWI is often seen in a large number of leads (V2-V6, I, II).
- Magnitude and number of leads with TWI is typically *greater* than with MI.
  - Takotsubo may cause bizarre, wide TWI which resembles a subarachnoid hemorrhage T-wave pattern (and this is probably the same underlying physiology).
- Evolution may include development of some ST depression.

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Evolution of EKG changes in a patient with stress cardiomyopathy.

*Durán-Cambra A et al. Ann Noninvasive Electrocardiol 2014*
classic pattern

- Classic pattern is akinesia of the apex, with hypercontractility of the base.
- Classic "apical ballooning pattern" – may mimic LAD-distribution ischemia.
  - If circumferential wall motion abnormalities are present and extend beyond any single coronary artery territory, this argues against MI. However, echocardiographic differentiation with 100% accuracy may not be possible.
- LV outflow tract obstruction (LVOTO) with systolic anterior motion of the mitral valve may occur due to basilar hyperkinesis.
  - This is important to recognize, as it has hemodynamic implications for management (more on this below).

variant patterns in up to 40%

- Include:
  - (1) Mid-ventricular wall variant – hypokinesis only of the mid-ventricular region with normal apical function.
  - (2) Basal ("Reversed") variant – basal hypokinesis, with normal function of the apex.
  - (3) Focal variants – most often isolated anterolateral segment dysfunction (closest echocardiographic mimic of an occlusive MI).
  - (4) Global hypokinesis – this is fortunately rare.
- It's possible that these different echocardiographic patterns may represent different stages in the evolution of Takotsubo syndrome (see video above).
  - Initially, the apex is involved the most.
  - At a later timepoint, the apex has recovered. Meanwhile, a secondary stress cardiomyopathy has developed in the basal myocardium.

RV involvement

- ~15-30% of cases may involve the RV.
- This is a poor prognostic sign.

Ivan Stankovic, MD, PhD
@Ivan_Echocardio

In up to 1/4 of cases of stress cardiomyopathy (takotsubo), apical ballooning also involves the right ventricular apex.

#POCUS #FOAMed #FoCUS
cardiac MRI

(a) Diagnostic information: May help sort out Takotsubo’s cardiomyopathy versus MI & myocarditis based on absence of late gadolinium enhancement (LGE)

- MI typically shows late gadolinium enhancement (LGE) in a focal subendocardial or transmural distribution.
- Myocarditis typically shows late gadolinium enhancement (LGE) in a patchy distribution.
- Takotsubo’s cardiomyopathy typically has no late gadolinium enhancement.

(b) Prognostic and management information

- Evaluation for mural thrombus.
- Evaluation of LV function.
- Detection of LV outflow tract obstruction.

role of cardiac MR?

- MRI is primarily limited by logistics (e.g., availability of MRI scanner, length of study). As such, MRI has the greatest value in patients whose EKGs don’t mandate urgent catheterization (e.g., presentation with a diffuse T-wave inversion pattern, rather than ST elevation).
- MRI is more valuable in patients with poor transthoracic echo windows.
- MRI may have greater ability to differentiate from myocarditis or MI, compared to echocardiography.

labs

Laboratory studies aren’t useful for the immediate diagnosis of Takotsubo’s cardiomyopathy (in real time). That being said...

troponin

- Elevated in 90% of cases of Takotsubo cardiomyopathy.
- Disproportionately low compared to magnitude of wall motion abnormality.

BNP

- Elevated in ~80% of patients.
- The diagnostic value of BNP is highly dubious, since it is extremely nonspecific (especially among critically ill patients, most of whom will have an elevated BNP).

diagnostic approach

differential diagnosis

- Any other cause of acute systolic heart failure (e.g., viral myocarditis, postpartum cardiomyopathy, hyperthyroidism)
- Myocardial infarction
  - Occlusive myocardial infarction
  - Non-occlusive myocardial infarction
  - Demand (type II) myocardial infarction in the context of chronic systolic failure
- Apical hypertrophic cardiomyopathy

Excellent Echo
@excellentecho

https://emcrit.org/ibcc/takotsubo/
Did you think this was takotsubo? It's actually an LAD infarction. These can look similar on echo, so be careful!

**diagnostic approach**

- Differentiation from occlusive MI or acute coronary syndrome
  - If the EKG shows ST elevation, then cardiac catheterization is usually required to exclude occlusive MI.
  - If the EKG *doesn't* show features of occlusive MI, immediate catheterization isn't necessarily required. Close observation may be reasonable, depending on the clinical scenario. A relatively *moderate* troponin elevation in the context of *dramatic* wall motion abnormalities would support Takotsubo cardiomyopathy (as opposed to myocardial infarction).

**treat underlying problem if possible**

- Many patients may have secondary Takotsubo cardiomyopathy, which can result from a variety of emergent problems (listed above in the section on [epidemiology](#epidemiology)).
- Evaluate for an underlying cause and treat if possible.

**anticoagulation?**

**consider anticoagulation for classic apical ballooning form**

- The classical apical ballooning form of stress cardiomyopathy carries a ~5% risk of mural thrombus formation within the apex. This risk isn't fixed, but rather may vary, depending on individual severity and the degree of blood stasis within the cardiac apex.
- Short-term anticoagulation may be considered for patients with a *large apical akinetic zone*.
  - Thrombus formation is greatest within 2-5 days of symptom onset, but has been described up to 14 days after onset. The best way to assess risk may be serial echocardiography to determine when ventricular function improves.
  - There is no high-quality evidence on this. Treatment decisions should be individualized based on clinical judgement, the extent of echocardiographic findings, and bleeding risks.

**arrhythmia management**
patients at risk for wide variety of arrhythmias

- Atrial fibrillation is the most common (~20%).
- Ventricular arrhythmia (2-10%) – may include Torsade de Pointes, ventricular fibrillation.
- Complete heart block can also occur, but seems to be considerably less common.

risk stratification for arrhythmias

- There are no highly reliable predictors.
- Risk may be higher if the following features are present:
  - QTc > 500 ms.
  - QRS duration > 105 ms (Jesel 2018).
  - J-wave (a.k.a. Osborn wave).

management?

- Monitor with telemetry.
- Optimize potassium and magnesium levels (K >3.5 mM, Mg >>2 mg/dL).
- Review the patients’ medication list and discontinue any QT-prolonging medications.
- Avoid iatrogenic catecholamines as able (perhaps even nebulized beta-2 agonists).
- Consider initiation of beta-blocker (see below).
- If arrhythmias do occur, treat them based on usual algorithms. Consider electrophysiology consultation (although ICD implantation is generally not indicated in the acute phase, given the reversibility of the injury).

**treatment if hemodynamically stable**

(beta to contents)| jump

**beta-blocker**

- Beta-blockade is probably advisable if LVEF is reduced and the patient is hemodynamically stable enough to tolerate this.
  - (1) This may reduce stress on myocardium and also reduce incidence of arrhythmias.
  - (2) Given the centrality of excess adrenergic tone in the pathophysiology of this disease, a beta-blocker makes sense.
- Beta-blockade may be especially useful in patients with LV outflow tract obstruction (wherein a reduced heart rate may improve diastolic ventricular filling).
- However – If the LVEF is severely reduced, beta-blockers may carry a risk of precipitating cardiogenic shock. Thus, as in patients with advanced heart failure, these should be used cautiously and up-titrated gradually.

**afterload reduction**

- This may be useful, particularly in patients with hypertension.
- An ACE inhibitor is an attractive option. However, if there are concerns regarding renal function, then a combination of hydrazine plus isosorbide dinitrate may be safer (at least in the short term, until the patient has stabilized).
- Afterload reduction is contraindicated if there is dynamic LV outflow tract obstruction on echocardiogram (LVOTO; more on this below).
  Likewise, overly aggressive afterload reduction could theoretically cause the development of LVOTO, even if it isn’t initially present (LVOTO is a reversible physiologic phenomenon).

**treatment if hemodynamically unstable**

(beta to contents)| jump

**hemodynamic management of unstable patients with LV outflow tract obstruction (LVOTO)**

- LVOTO occurs when the base of the heart contracts vigorously, causing the turbulent flow of blood in the aortic outflow tract to pull the anterior leaflet of the mitral valve anteriorly (causing mitral regurgitation). This may occur in the classic (apical) variant of Takotsubo cardiomyopathy.
- LVOTO is important to recognize, because these patients respond differently to treatments compared to most patients with heart failure:
• Afterload reduction (e.g., nitroglycerine) and diuretics will make LVOTO worse!
• Beta-blockade and fluid loading may improve LVOTO.
• Hypotension in the context of LVOTO may respond to a pure vasoconstrictor (e.g., phenylephrine). In contrast, inotropic agents may exacerbate LVOTO.

• Key interventions for unstable patients with LVOTO are generally:
  - Fluid resuscitation if there is evidence of hypovolemia.
  - Vasoconstriction with phenylephrine as needed to support the mean arterial pressure.
  - Cautious beta-blockade, especially if there is substantial tachycardia (e.g., esmolol infusion) (Santoro 2016 [https://pubmed.ncbi.nlm.nih.gov/26946520/]). If this is tolerated, it may be transitioned to longer-acting beta-blockers.

**Hemodynamic management of unstable patients without LV outflow tract obstruction (LVOTO)**

• Overall, this is similar to the management of other patients with severe systolic heart failure (discussed further in the chapter on decompensated heart failure [https://emcrit.org/pulmcrit/heart-failure/]).
• Inotropes are a double-edged sword here (Ansari 2018 [https://pubmed.ncbi.nlm.nih.gov/29554866/]):
  - Inotropes may improve cardiac output and organ perfusion. However, increased inotropy can potentially cause LVOTO physiology, exacerbating matters (Sattar 2020 [https://pubmed.ncbi.nlm.nih.gov/32042529/]).
  - The pathophysiological cause of Takotsubo cardiomyopathy is excess sympathetic tone, so inotropes could potentially exacerbate this.
  - Inotrope use could theoretically increase the risk of ventricular arrhythmia.
  - Overall – the lowest possible dose of inotrope should be used which maintains systemic perfusion. When possible, volume resuscitation and phenylephrine may be used to support perfusion, without increasing stress on the myocardium.
• In severe shock, mechanical support (e.g., ECMO or LVAD) may be used as a bridge to recovery.

**Prognosis**

• In-hospital mortality is 2-5%, so this isn’t a benign entity.
• LVEF generally recovers by 12 weeks, sometimes much faster. However, mild cardiac dysfunction can persist (Scally 2018 [https://pubmed.ncbi.nlm.nih.gov/29128863/]).

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**EM Ottawa**
@emergmedottawa

Focus on POCUS: Heartbreaker. Cardiac Echo in the ED. Female in her 60’s presents to the emergency department on her 7th post-operative day feeling nauseous, vomiting, weak and dizzy. What’s your call? emottawablog.com/2017/12/focus-... cc: @DDxDino @RobSuttle @DrRitcey @LumpyPoetMD
To keep this page small and fast, questions & discussion about this post can be found on another page [here](https://emcrit.org/emcrit/takotsubo/).

Failure to recognize LV outflow tract obstruction in patients with apical hypokinesis. (LV outflow tract obstruction has major implications for hemodynamic management.)

Diagnostic confusion between Takotsubo cardiomyopathy versus occlusive MI. These entities can look nearly identical on EKG and echocardiography, so when in doubt consult with cardiology and consider catheterization.

Premature prognostication of cardiac function in patients with Takotsubo cardiomyopathy (the ejection fraction may look awful, but patients can still have a dramatic recovery).

Going further:

- [Takotsubo's Cardiomyopathy](https://rebelem.com/rebel-core-cast-20-0-takotsubos-cardiomyopathy/) (RebelEM, by Anand Swaminathan)
- [Takotsubo Cardiomyopathy](https://www.wikem.org/wiki/Takotsubo_cardiomyopathy) (WikEM)