

16. Kardiologie-Symposium
Das Herzzentrum Hirslanden Zentralschweiz



Takotsubo Syndrome (Broken Heart Syndrome)


PD Dr. med. Jelena-R. Templin-Ghadri
University Heart Center Zurich
Department of Cardiology

Universität Zürich 


19th October 2023

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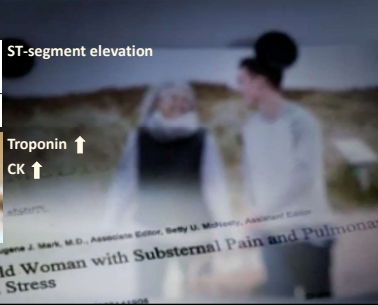
Takotsubo Syndrome after tragic news



ECG ST-segment elevation



Laboratory Troponin ↑
CK ↑



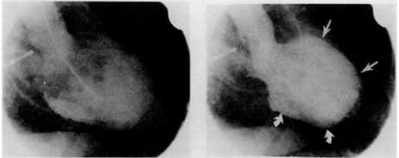
44-Year-Old Woman with Substernal Pain and Pulmonary Edema after Severe Emotional Stress

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Takotsubo Syndrome after tragic news

The NEW ENGLAND JOURNAL of MEDICINE

Case 18-1986 — A 44-Year-Old Woman with Substernal Pain and Pulmonary Edema after Severe Emotional Stress



Skully E et al. *N Engl J Med.* 1986

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Takotsubo Syndrome: First Report

佐藤 光, 立石博信, 内田俊明, ほか: 多枝spasmにより特異な左心室造影像「ツボ型」を示したstunned myocardium: 見玉和久, 土師一夫, 堀 正二・編: 臨床からみた心筋細胞障害 虚血から心不全まで, 科学評論社, 1990, p56-64

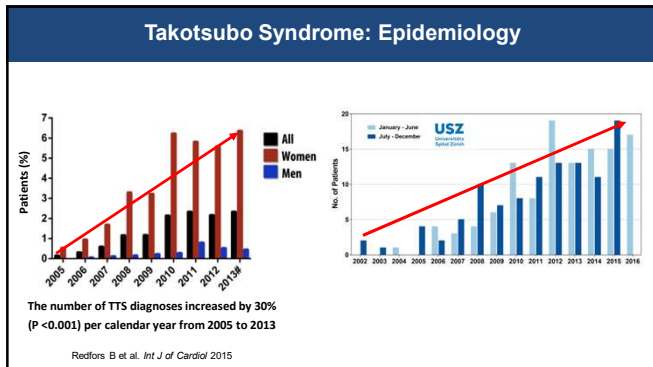



Interview with Dr. H. Sato (left) 2006

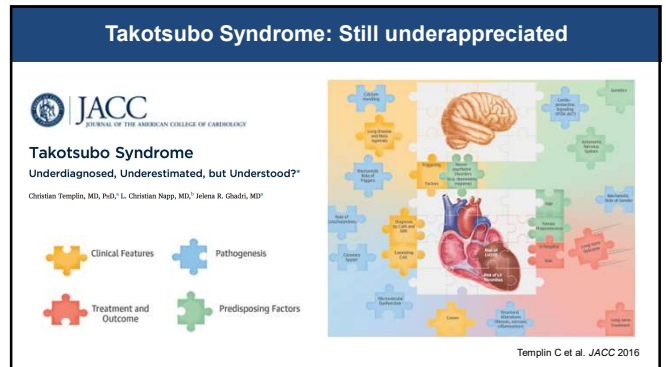


(参考文献3ホームページより引用)

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Takotsubo Syndrome: ESC Guidelines STEMI & Non-STEMI

ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Stress induced (Takotsubo) cardiomyopathy is a recently recognized syndrome, which may be difficult to differentiate from STEMI as symptoms and findings, ranging from slight chest pain to cardiogenic shock, may mimic an acute myocardial infarction but the ECG changes at presentation are usually modest and do not correlate with the severity of ventricular dysfunction. It is often triggered by physical or emotional stress and characterized in its typical form by transient apical or mid-wall ventricular dilation and dysfunction. Because there is no specific test to rule out myocardial infarction in this setting, emergency angiography should not be delayed and in the absence of myocardial infarction will show neither significant culprit coronary artery stenosis nor microvascular disease. The diagnosis is confirmed by the finding, on imaging, of transient apical to mid-ventricular ballooning with compensatory basal hyperkinesis, and by disproportionately low plasma levels of cardiac biomarkers with respect to the severity of ventricular dysfunction and, eventually, by recovery of left ventricular function.¹⁴

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Tako- Tsubo cardiomyopathy, also called apical ballooning, is an emotional stress-related cardiomyopathy of undetermined aetiology characterized by chest pain, elevated cardiac enzymes, normal coronary angiography and an acute transient LV (more frequently apical) dysfunction that mimics MI. Although usually the wall motion abnormalities do not match a territory of coronary perfusion, a coronary aetiology must be excluded by coronary angiogram. An incidence of 2% in patients admitted for ACS has been reported, but this may represent an underestimation.^{10,12,13} An incidence of 5.9% was documented among post-menopausal women admitted with suspected ACS.¹⁰ Three-quarters of patients with Tako-Tsubo cardiomyopathy have higher serum catecholamine levels, and a vascular dysfunction leading to microvascular spasm has been proposed as an underlying mechanism.¹¹ There is a lack of consensus on the diagnostic criteria as well as therapy.^{14,15}

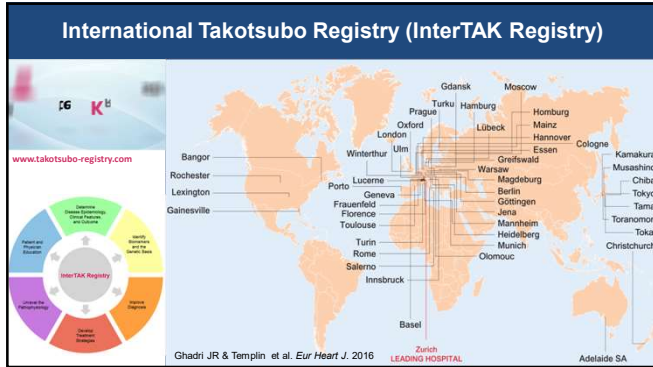
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Takotsubo Syndrome: Overall notion

	Previous notion
Terminology	Takotsubo cardiomyopathy
Epidemiology	Rare disease Japan Asian descent Women Elderly
Triggering factors	Emotional triggers Negative life events Absence of psychotropic drugs Absence of neurological injury
Morphological variants	Apical Ballooning
Coronary artery disease	Absence of coronary artery disease
Outcome	Benign prognosis

USZ Universität Salzburg
Cammann VL. Curr Atheroscler Rep. 2021

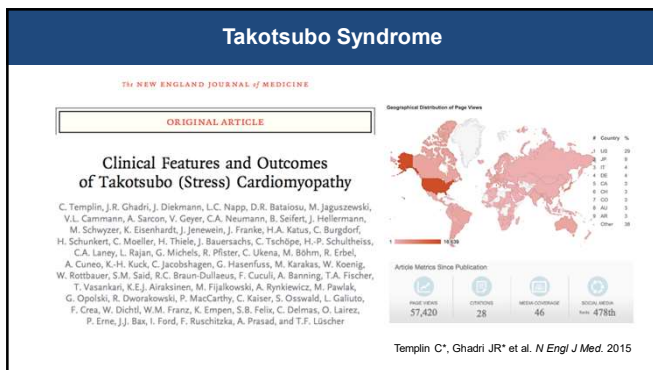
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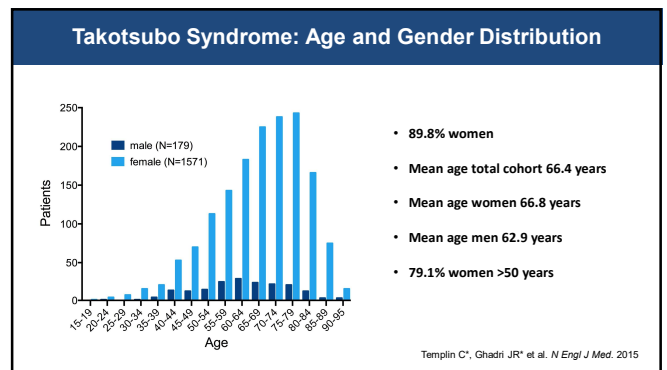
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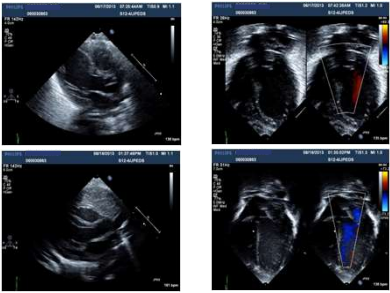


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Takotsubo Syndrome: Baby TTS

Index event

Follow-up



Female premature born baby,
1060 gram
27.6 weeks' gestation born to a
31-year-old caucasian mother

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Takotsubo Syndrome: Presenting symptoms

	Chest pain	Dyspnea	Syncope	Card. shock	Cardiac arrest
Tsuchihashi et al.	67%	7%	NA	5%	NA
Kurusu et al.	63%	20%	6.7%	NA	NA
Seth et al.	25%	58.3%	8.3%	NA	8.3%
Desmet et al.	62%	38%	7.6%	7.6%	NA
Sharkey et al.	100%	5%	NA	55%	5%
Wittstein et al.	95%	NA	NA	26.3%	NA
Eitel et al.	88%		4%	NA	1%
Schneider et al.	72%	16%	3%	1.8%	NA
Templin et al.	75.9%	46.9%	7.7%	9.9%	8.6%

NA=not available

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Takotsubo Syndrome: ECG features on admission

modified
Templin C*, Ghadri JR* et al. *N Engl J Med.* 2015

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Triggering factors of Takotsubo Syndrome

Triggering factors (N=1750)

- 36.0% Physical triggers
- 27.7% Emotional triggers
- 7.5% Both physical and emotional triggers
- 28.8% No evident trigger

Templin C*, Ghadri JR* et al. *N Engl J Med.* 2015
Schlossbauer S et al. & Templin C. *Praxis (Bern 1994)* 2016

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Takotsubo Syndrome: "Happy Heart Syndrome"

Table 1 Happy heart events (n = 20)

Patient 1	Birthday party
Patient 2	Son's wedding
Patient 3	Meeting after 50 years with friends from high school
Patient 4	Preparing 50th wedding anniversary (pleasant anticipation)
Patient 5	Positive job interview
Patient 6	Wedding
Patient 7	Favourite driver won race car competition
Patient 8	Becoming grandmother
Patient 9	Surprise farewell celebration
Patient 10	Son's company opening
Patient 11	Favourite rugby team won game
Patient 12	Emotional opening during a friend's birthday
Patient 13	Celebrating 80th birthday
Patient 14	Winning several jackpots at the casino
Patient 15	Celebration of normal PET-CT scan
Patient 16	Visiting opera with her family
Patient 17	Family party
Patient 18	Unexpected visit from favourite nephew
Patient 19	Grandchildren visiting from London (abroad)
Patient 20	Becoming great grandmother

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Takotsubo Syndrome: Different Types & Ejection Fraction

Type	Admission	60-day follow-up	P-value
Apical	~45%	~55%	P=0.001
Midventricular	~45%	~55%	P=0.51
Basal	~45%	~55%	P=0.029
Focal	~45%	~55%	P=0.029

Templin C, Ghadri JR et al. *N Engl J Med.* 2015; Ghadri JR et al. & Templin C. *JAMA Cardiology* 2016

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Takotsubo Syndrome: Confirming focal Takotsubo by cardiac MRI

Courtesy of PD Dr. Robert Manka, University Hospital Zurich

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Takotsubo Syndrome: Atypical Forms

Patients with atypical TTS are characterized by:


- Younger age of onset
- Neurologic disorders ↑
- ST-segment depression ↑
- More preserved LVEF
- Lower BNP values on admission

Type	Mean LVEF (%)
Midventricular	42.9%
Basal	43.9%
Focal	50.8%

Ghadri JR et al. & Templin C. *JAMA Cardiology* 2016


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Takotsubo Syndrome: Case & Clinical pitfall



Knee arthroscopy

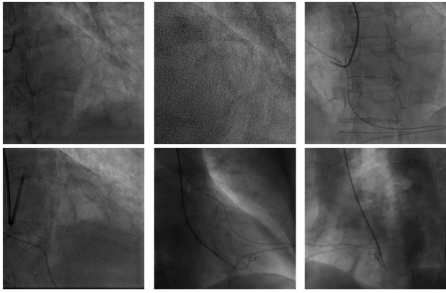
- 66-year old female
- history of panic disorder
- CvrRf: smoking
- PEA during anaesthesia
- cardiopulmonary resuscitation with 30 chest compressions



- hsTNT: (0.010 to **0.177ng/ml**, cut-off 0.014ng/ml)
- Myoglobin: (33 to **61 ng/ml**, cut-off 58 ng/ml)
- CK: remained normal

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Takotsubo Syndrome: Case Presentation



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Myocardial Infarction, Takotsubo Syndrome or both?

- hsTNT decreased to 0.101 and 0.029ng/ml within 24 hour
- NT-pro BNP increased to 331 and 1338ng/l

incomplete knowledge and diagnostic work up may lead to a false diagnosis and contribute to a wrong and underestimated incidence of TTS!

Diagnosis: midventricular Takotsubo syndrome with concomitant significant coronary lesion

UniversitätsSpital Zürich 23.10.2023 Seite 20

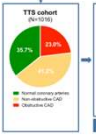
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Takotsubo Syndrome and Coronary Artery Disease


InterTAK Registry
Patients diagnosed with TTS between 2002 and 2017 (N=1145)

Exclusion (N=126):
No angiography (N=115)
Coronary disease not defined (N=11)

TTS cohort (N=1019)



TTS, obstructive CAD (N=457)




Zurich ACS Registry
(N=2346)

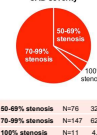
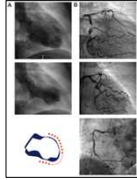
ACS cohort (N=2346):
NSTEMI (61.2%), STEMI (38.8%)

Matched for Age and Sex

TTS, obstructive CAD

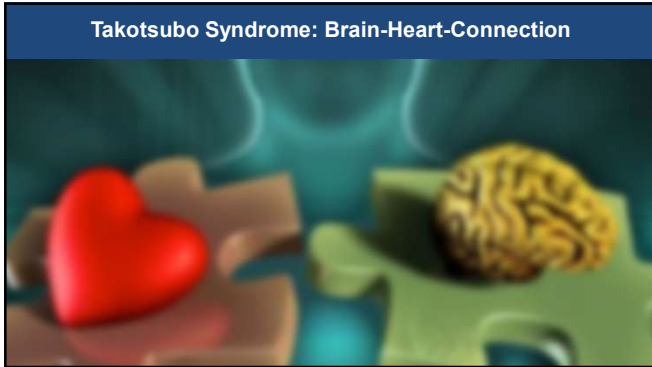


CAD severity

USZ UniversitätsSpital Zürich Napp LC et al. & Templin C. Eur Heart J. 2019

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Takotsubo Syndrome: Brain-Heart-Connection

European Heart Journal ESC
European Society of Cardiology

Altered limbic and autonomic processing supports brain-heart axis in Takotsubo syndrome

Christian Templin^{1,4†}, Jürgen Häggg^{2†}, Carina Klein², Marlene S. Topka², Thierry Hiestand¹, Rena A. Levinson¹, Stjepan Jurisic¹, Thomas F. Lüscher^{3,4}, Jelena-Rima Ghadri^{1‡}, and Lutz Jäncke^{3,4‡}

Parasympathetic Network

Sympathetic Network

Default mode Network

Whole brain level

→ decreased communication between brain regions associated with emotional processing and the autonomic nervous system, which controls the unconscious workings of the body, compared to the healthy people.

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Takotsubo Syndrome: Brain-Heart-Connection

JAMA

**For Broken Heart Syndrome,
Brain May Hold the Key**

Sancar F. et al. 2019

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Takotsubo Syndrome: Brain-Heart-Connection

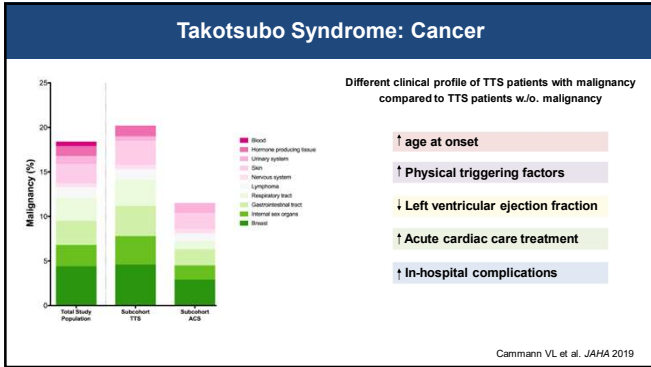
The New York Times

Broken-Heart Syndrome Is Not All in the Head

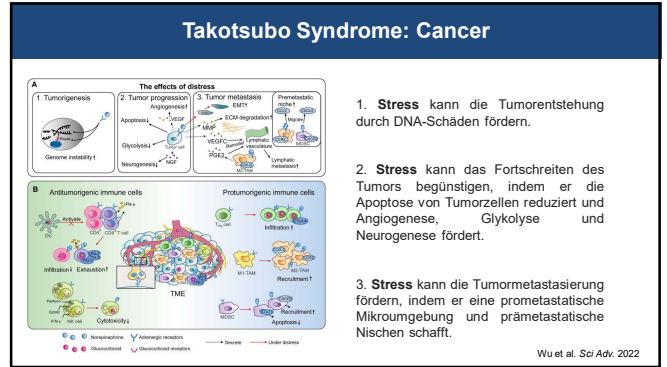
by Gretchen Reynolds March 19, 2019

.....The scans suggest that **broken-heart syndrome probably begins in the brain** with its reactions — or overreactions — to stress, says Christian Templin, the professor of cardiology at University Hospital Zurich who led the study. It's unclear if stress changed the brains of people with Takotsubo in ways that then led to heart damage or if their brains were instead predisposed to handle stress poorly. Nor is it clear how the disturbed brain remakes the heart. But, Templin says, "stress hormones are released, which might affect cardiovascular response." The study underlines the fact that our brains and hearts are connected even more intimately than scientists have believed, Templin says. Biochemical cross talk between them affects both. Grief can break a body, so no one should hesitate to seek help in handling stress.....

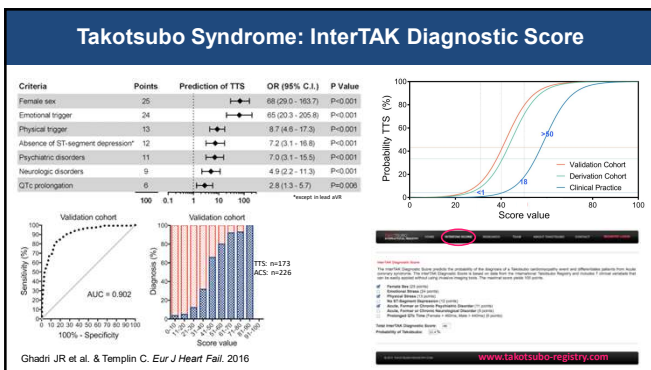
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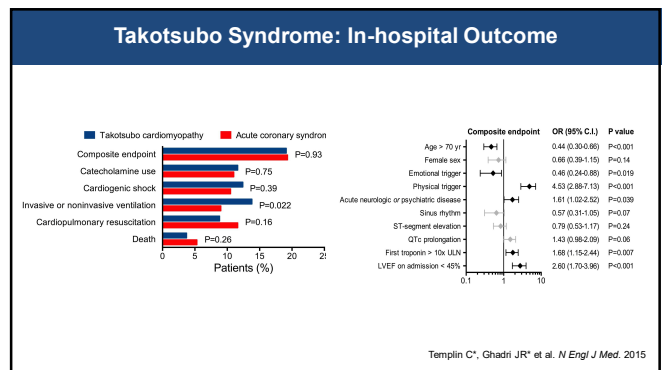
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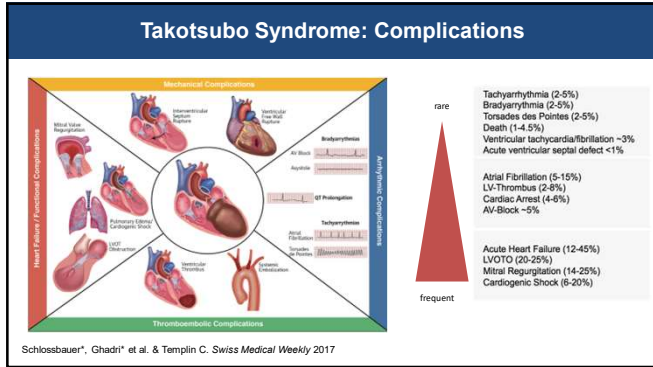
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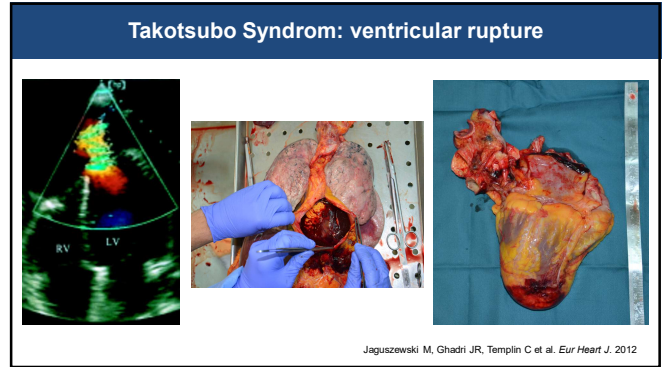
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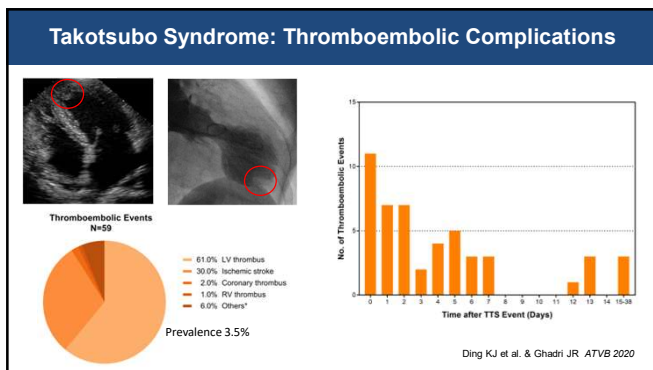
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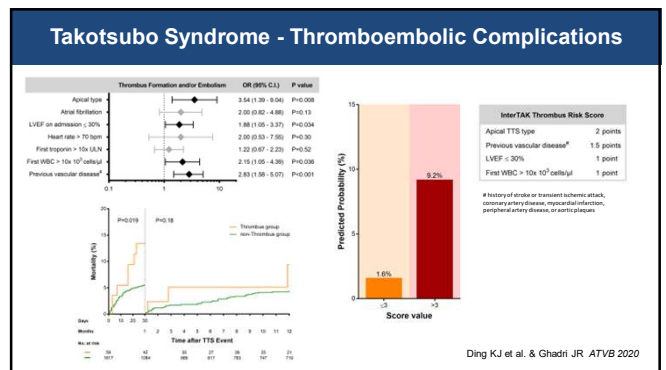
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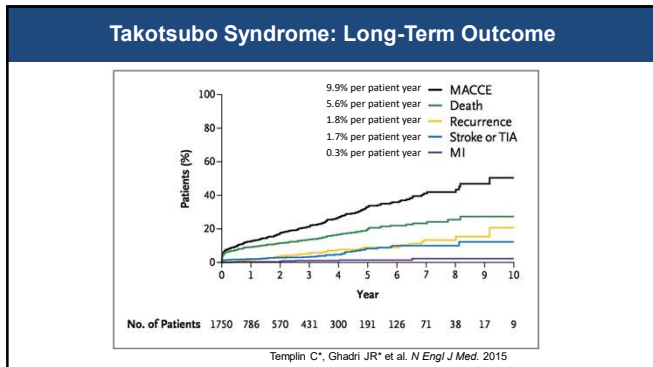
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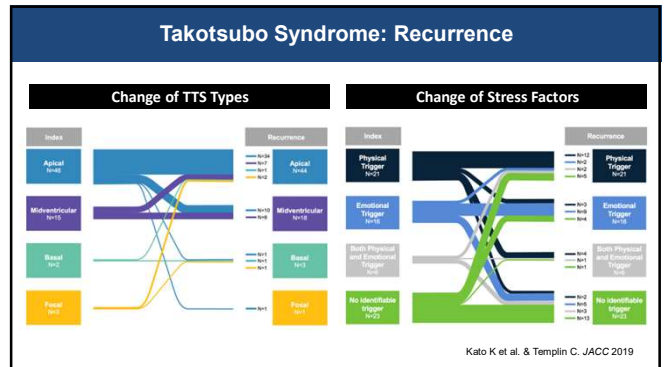
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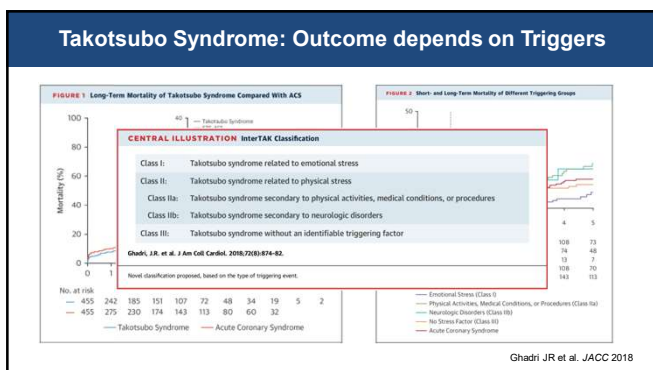
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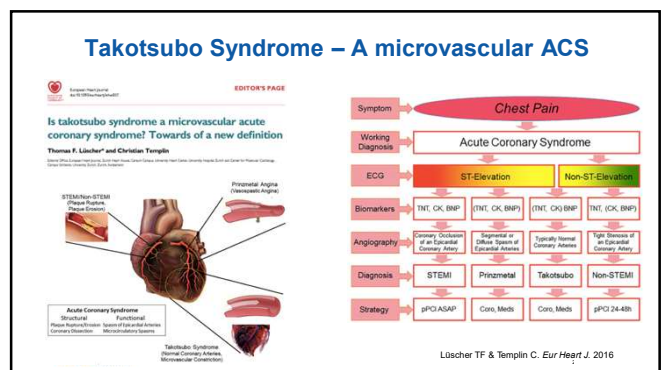
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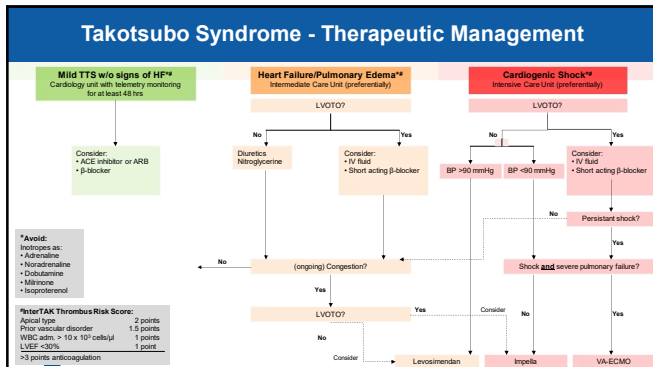
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Takotsubo Syndrome: InterTAK Diagnostic Criteria

Table 1 International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)

- Patients show **transient**^a left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS).^b
- An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
- Neurologic disorders** (e.g. subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as **pheochromocytoma** may serve as triggers for takotsubo syndrome.
- New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.
- Levels of **cardiac biomarkers** (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
- Significant coronary artery disease is not a contradiction in takotsubo syndrome.
- Patients have no evidence of infectious myocarditis.^c
- Postmenopausal women are predominantly affected.

^aWall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.
^cCardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and confirm diagnosis of takotsubo syndrome.

Ghadri JR et al. *Eur Heart J* 2018

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Takotsubo Syndrome: Change of Knowledge

	Previous notion
Terminology	Takotsubo cardiomyopathy
Epidemiology	Rare disease
	Japan
	Asian descent
	Women
	Elderly
Triggering factors	Emotional triggers
	Negative life events
	Absence of pheochromocytoma
	Absence of neurologic injury
Morphological variants	Apical Ballooning
Coronary artery disease	Absence of coronary artery disease
Outcome	Benign prognosis

USZ Universitätsspital Zürich
Cammann VL et al. *Curr Atheroscler Rep*. 2021

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Vielen Dank!

PD Dr. med. Jelena-Rima Ghadri, FESC, FHFA
Department of Cardiology
University Heart Center
University Hospital Zurich
Switzerland
e-mail: jelena-rima.templin-ghadri@usz.ch

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