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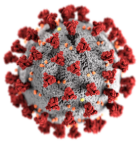
vACCine covid-19  monitoring readinESS

EVENT DEFINITION FORM

Event: Stress Cardiomyopathy
Outcome/covariate: **outcomes**
Version: **1.0**
Status: *Final*

Contributing authors

Authors	Role	Date
Ilse Kelters	Medical/drafting v0.1	June 24, 2020
Miriam Sturkenboom	epidemiological	Jun 28, 2020
Ilse Kelter s	Codes	July 2020
Miriam Sturkenboom	Code review	August 13, 2020
Leila Belbachir	Medical review	August 20
Miriam Sturkenboom	Adding algorithm	August 21, 2020
Corinne Willame	Concept set proposal in algorithm	September 02, 2020
Miriam Sturkenboom	Final codes	February 14, 2021
Carlos Durán	Rev. Narrow/Broad assignment	March 24, 2021
Miriam Sturkenboom	Insertion of codes used for final report	August 20, 2021

1. Event definition

Signs and symptoms:

- Acute chest pain
- Dyspnoea
- Syncope
- New ECG changes
- Sudden elevation of cardiac biomakers
- Induced by physical stress

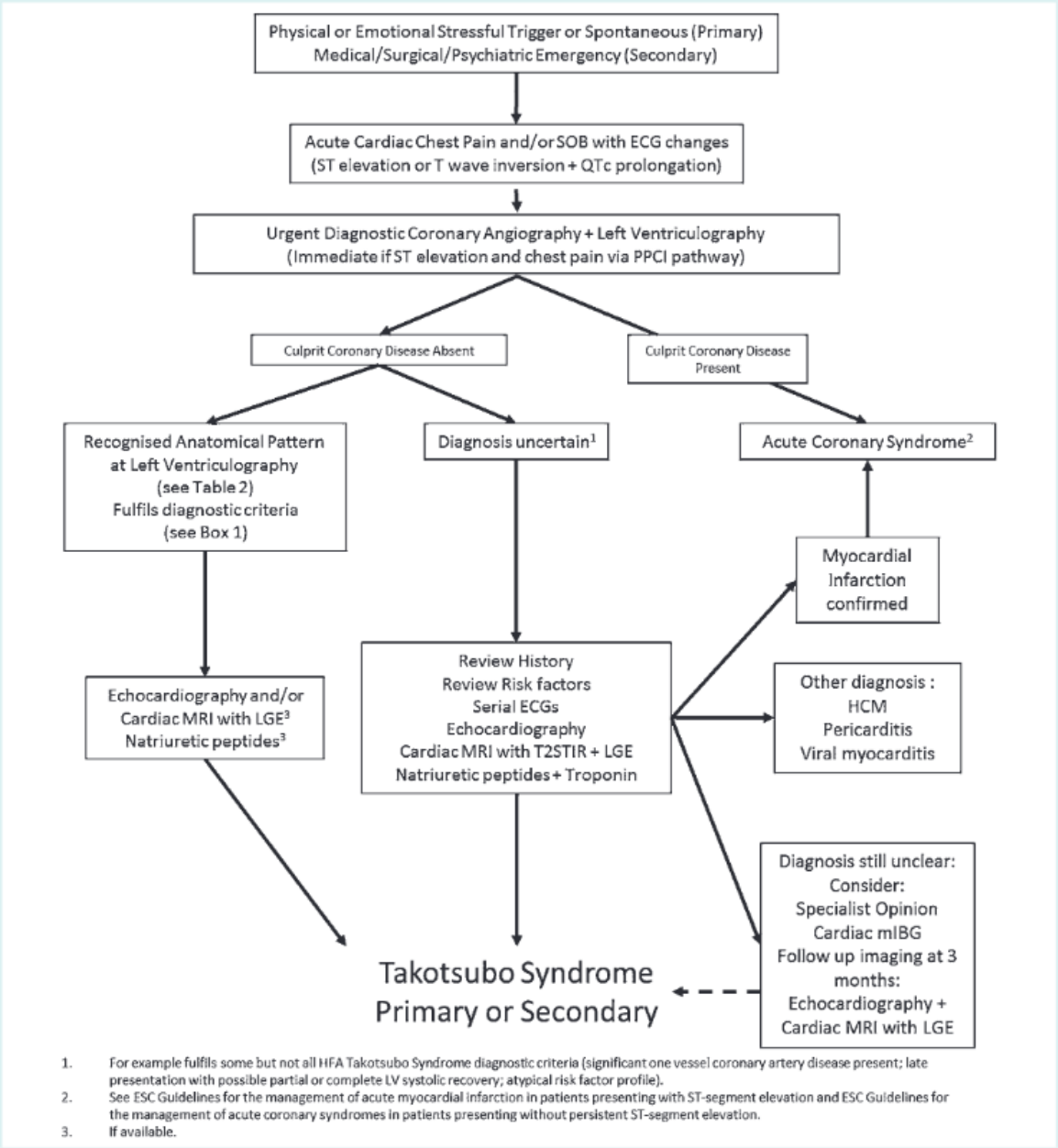
Diagnosis of stress cardiomyopathy is difficult because of its clinical phenotype may closely resemble AMI regarding ECG and abnormalities and biomarkers. Two additional features that are helpful in distinguishing TTS from acute MI are QTc prolongation > 500 ms during the acute phase and the recovery of LV function over 2 – 4 weeks. There are rare cases described where MI and TTS coexist, e.g. MI-induced TTS or TTS with secondary plaque rupture, but this occurs where the acute regional wall motion abnormalities are more extensive than the culprit coronary artery territory, and fulfil the pattern and definition of TTS (Ghardi et al.)

Box 1 Heart Failure Association diagnostic criteria for Takotsubo syndrome

1. Transient regional wall motion abnormalities of LV or RV myocardium which are frequently, but not always, preceded by a stressful trigger (emotional or physical).
2. The regional wall motion abnormalities usually[a] extend beyond a single epicardial vascular distribution, and often result in circumferential dysfunction of the ventricular segments involved.
3. The absence of culprit atherosclerotic coronary artery disease including acute plaque rupture, thrombus formation, and coronary dissection or other pathological conditions to explain the pattern of temporary LV dysfunction observed (e.g. hypertrophic cardiomyopathy, viral myocarditis).
4. New and reversible electrocardiography (ECG) abnormalities (ST-segment elevation, ST depression, LBBB[b], T-wave inversion, and/or QTc prolongation) during the acute phase (3 months).
5. Significantly elevated serum natriuretic peptide (BNP or NT-proBNP) during the acute phase.
6. Positive but relatively small elevation in cardiac troponin measured with a conventional assay (i.e. disparity between the troponin level and the amount of dysfunctional myocardium present).[c]
7. Recovery of ventricular systolic function on cardiac imaging at follow-up (3–6 months).[d]

[a]Acute, reversible dysfunction of a single coronary territory has been reported.
[b]Left bundle branch block may be permanent after Takotsubo syndrome, but should also alert clinicians to exclude other cardiomyopathies. T-wave changes and QTc prolongation may take many weeks to months to normalize after recovery of LV function.
[c]Troponin-negative cases have been reported, but are atypical.
[d]Small apical infarcts have been reported. Bystander subendocardial infarcts have been reported, involving a small proportion of the acutely dysfunctional myocardium. These infarcts are insufficient to explain the acute regional wall motion abnormality observed.

(Diagnostic criteria From: Lyon et al.)



Takotsubo Syndrome Diagnostic Algorithm

(From: Lyon et al.)

Stress cardiomyopathy

Table 2 Anatomical variants of Takotsubo syndrome

Variant	Estimated prevalence
Apical with or without MLV variant (typical)	75–80%
MLV	~10–15%
Inverted or basal	~5%
Biventricular	Clinical <0.5%; CMR 33%
Right ventricular	Unknown
Apical tip sparing	Unknown
Possible atypical variants	
Global	Unknown
Focal	Unknown

CMR, cardiac magnetic resonance; MLV, mid-left ventricular;

(From: Lyon et al.)

2. Synonyms / lay terms for the event

Takotsubo syndrome
Takotsubo cardiomyopathy
Tako-Tsubo cardiomyopathy
Stress cardiomyopathy
Stress-induced cardiomyopathy
Apical ballooning syndrome
Ampullary-shaped cardiomyopathy
'broken heart syndrome'
Transient left ventricular dysfunction

3. Laboratory tests that are specific for event

1. Cardiac biomarkers: cardiac troponin, BNP, NT-proBNP, creatine kinase, creatine kinase MB isoform. Other biomarkers are only used in research studies and not in the routine practice (e.g. serum catecholamines, neuropeptide-Y and serotonin).

4. Diagnostic tests that are specific for event

1. Coronary angiography

The coronary arteries are angiographically normal, in contrast to STEMI or NSTEMI. Coronary angiography with left ventriculography is considered the gold standard diagnostic tool to exclude or confirm TTS (Ghadri et al.)

2. Ventriculography

Mostly done by catheterization or echocardiography, where variety of LV regional wall motion abnormalities does correlate with more than one coronary artery territory.

3. 12-lead ECG
4. Cardiac Magnetic Resonance with late gadolinium enhancement (LGE)
5. Coronary computed tomography angiography

5. Drugs that are used to treat event

- Catecholamines, beta-2-agonists (when haemodynamic unstable)
- Beta-blocker: metoprolol, carvedilol
- ACE-inhibitor
- Low Molecular Weight Heparin (if apical thrombus is present)

6. Procedures used specific for event treatment

1. Haemodynamic monitoring; continuous ECG monitoring
2. Mechanical support: LVAD, ECMO, IABP

7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

Out of hospital - emergency room

8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA:

ICD 9
429.83: Takotsubo syndrome

9. Proposed codes by Codemapper

Coding system	Code	Code name	Concept	Concept name	Algorithm
ICD10/CM	I51.81	Stress induced cardiomyopathy	C1719472	Stress induced cardiomyopathy	Narrow
ICD10/CM	I51.81	Takotsubo syndrome	C1739395	Takotsubo Cardiomyopathy	Narrow
ICD9CM	429.83	Takotsubo syndrome	C1739395	Takotsubo Cardiomyopathy	Narrow
RCD2	G554500	Takotsubo syndrome	C1739395		Narrow
RCD2	G554511	Stress cardiomyopathy			Narrow
SCTSPA	441541008	miocardiopatía de takotsubo	C1739395	Takotsubo Cardiomyopathy	Narrow
SNOMEDCT_US	441541008	Takotsubo cardiomyopathy	C1739395	Takotsubo Cardiomyopathy	Narrow

Stress cardiomyopathy

10. Algorithm proposal

Broad algorithm:

- Concept set = (Stress_cardiomyopathy) in any provenance, no prior codes
- Index date: first occurrence of any of the concept set

Narrow algorithm:

- Concept set = (Stress_cardiomyopathy) from ER/Outpatient with beta-blocker afterward (no prior codes)
- Index date: first occurrence of any of the concept set

11. Background rates

There are not so many published incidence data, as the disease is only recently recognized. Minhas et al. reported on a significant increase in the incidence of TS from 2006 to 2012[1]. In that study, the incidence of TS increased almost 20 times during the time-period. Similarly, a study by Murugiah et al. showed that hospitalization rates for TS are increasing. In that study, the incidence of primary TS increased from 2.3 hospitalizations per 100,000 person-years in 2007 to 7.1 in 2012[2]. Jabri et al reported an increase of stress cardiomyopathy during the COVID-19 pandemic[3].

12. References

Ghadri JR, Wittstein IS, Prasad A, et al. International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology. Eur Heart J. 2018;39(22):2032-2046. doi:10.1093/eurheartj/ehy076

Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on Takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2016;18(1):8-27. doi:10.1002/ejhf.424

[1] Minhas AS, Hughey AB, Kolias TJ. Nationwide trends in reported incidence of takotsubo cardiomyopathy from 2006 to 2012. *Am J Cardiol.* 2015;116:1128–1131. doi: 10.1016/j.amjcard.2015.06.042

[2] Murugiah K, Wang Y, Desai NR, Spatz ES, Nuti SV, Dreyer RP, et al. Trends in short- and long-term outcomes for takotsubo cardiomyopathy among medicare fee-for-service beneficiaries, 2007 to 2012. *JACC Heart Fail.* 2016;4:197–205. doi: 10.1016/j.jchf.2015.09.013.

[3] Jabri A, Kalra A, Kumar A, et al. Incidence of Stress Cardiomyopathy During the Coronavirus Disease 2019 Pandemic. *JAMA Netw Open.* 2020;3(7):e2014780. doi:10.1001/jamanetworkopen.2020.14780