MINICORSO IMAGING NON INVASIVO

Malattie del miocardio e del pericardio

Cardiomiopatia da stress (Tako-Tsubo): tra mito e realtà

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No conflict of interest to declare

History

1980 Cebelin & Hirsch introduced the term “stress cardiomyopathy”. They found on autopsy *contraction-band necrosis* in victim of homicidal assault without sustaining internal injuries.

1986 A case report of the Massachusetts General Hospital described a patient who developed heart failure as a result of severe emotional stress (NEJM 1986)

1989 Iga et al. reported a case of pheochromocytoma with reversible left ventricular (LV) dysfunction and concluded that high catecholamine concentrations can directly damage the myocardium.

1990 Sato et al. First described this reversible condition as “takotsubo-like LV dysfunction”.

1997 Pavin et al. revived the term *“stress cardiomyopathy*”. Emotional stress might cause LV dysfunction in the absence of myocardial ischemia.

1998 Brandspiegel HZ et al. A broken heart. *Circulation* 1998 *98:1349*

Why Not Just Call It Tako-Tsubo Cardiomyopathy

A Discussion of Nomenclature

75 individual descriptive names !!

Apical ballooning

- Apical ballooning syndrome
- Acute left ventricular apical ballooning syndrome
- Left ventricular apical ballooning syndrome
- Transient left ventricular apical ballooning syndrome
- Primary apical ballooning
- Transient apical ballooning
- Transient apical ballooning syndrome
- Transient cardiac apical ballooning syndrome
- Transient left apical ballooning syndrome
- Transient cardiac ballooning
- Left apical ballooning syndrome
- Acute apical ballooning syndrome
- Cardiac apical ballooning syndrome
- Apical ballooning
- Apical ballooning without apical ballooning
- Apical ballooning cardiomyopathy
- Reversible apical ballooning of left ventricle
- Left ventricular ballooning syndrome
- Mid-ventricular variant of transient apical ballooning
- Mid-ventricular ballooning syndrome
- Transient left ventricular mid-portion ballooning
- Transient mid-ventricular ballooning
- Transient mid-ventricular ballooning cardiomyopathy
- Transient left ventricular non-apical ballooning
- Reverse or inverted left ventricular apical ballooning syndrome
- Inverted left ventricular apical ballooning syndrome
- Transient basal ballooning

Tako-tsubo

- Takotsubo cardiomyopathy
- Takotsubo-like cardiomyopathy
- Takotsubo syndrome
- Takotsubo disease
- Takotsubo left ventricular dysfunction
- Takotsubo-like left ventricular dysfunction
- Takotsubo-like transient biventricular dysfunction
- Takotsubo-like transient left ventricular ballooning
- Takotsubo-shaped cardiomyopathy
- Takotsubo-shaped hypokinesia of left ventricle
- Takotsubo-type cardiomyopathy
- Takotsubo transient left ventricular apical ballooning
- Mid-ventricular takotsubo cardiomyopathy
- Mid-ventricular form of takotsubo cardiomyopathy
- Inverted takotsubo contractile pattern
- Inverted takotsubo cardiomyopathy
- Inverted takotsubo pattern
- Atypical takotsubo cardiomyopathy
- Reverse takotsubo syndrome
- Atypical basal type takotsubo cardiomyopathy

Stress cardiomyopathy

- Acute stress cardiomyopathy
- Human stress cardiomyopathy
- Acute & reversible cardiomyopathy provoked by stress
- Stress-induced cardiomyopathy
- Stress-induced takotsubo cardiomyopathy
- Stress-induced apical ballooning syndrome
- Stress-related left ventricular dysfunction
- Stress-related cardiomyopathy
- Stress-related cardiomyopathy syndrome
- Stress takotsubo cardiomyopathy
- Emotional stress-induced ampulla cardiomyopathy
- Mid-ventricular stress cardiomyopathy
- Atypical transient stress-induced cardiomyopathy
- Stress-induced myocardial stunning
- Emotional stress-induced tako-tsubo cardiomyopathy
- Stress-associated catecholamine induced cardiomyopathy
- Neurogenic stress syndrome
- Other
  - Neurogenic stunned myocardium
  - Adrenergic cardiomyopathy
  - Broken heart syndrome
  - Ampulla cardiomyopathy
  - Ampulla-shaped cardiomyopathy
  - “Chestnut-shaped” transient regional left ventricular hypokinesia
  - Ball-shaped spherical dilation of left ventricular apex
  - The artichoke heart
  - Transient mid-ventricular akinesia
  - Transient antero-apical dyskinesia

……as of October 12, 2012, there are 1,450 entries in PubMed retrievable using the inquiry term “Takotsubo syndrome”

Sharkey SW et al. JACC 2011

la Repubblica.it | Salute

CUORI SPEZZATI

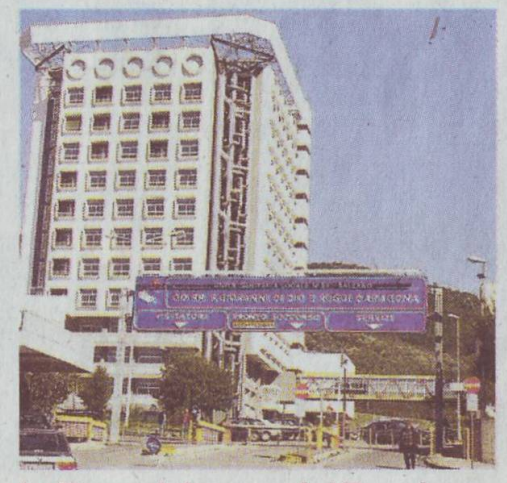
Quando lo stress, le emozioni e i dispiaceri fanno male come un infarto

La conferma arriva dalla medicina: i sentimenti possono davvero deformare il muscolo cardiaco. È la sindrome tako-tsubo, è come un'ischemia e spesso fa finire al pronto soccorso. I sintomi sono gli stessi di un arteria ostruita. Quasi sempre tutto passa senza farmaci

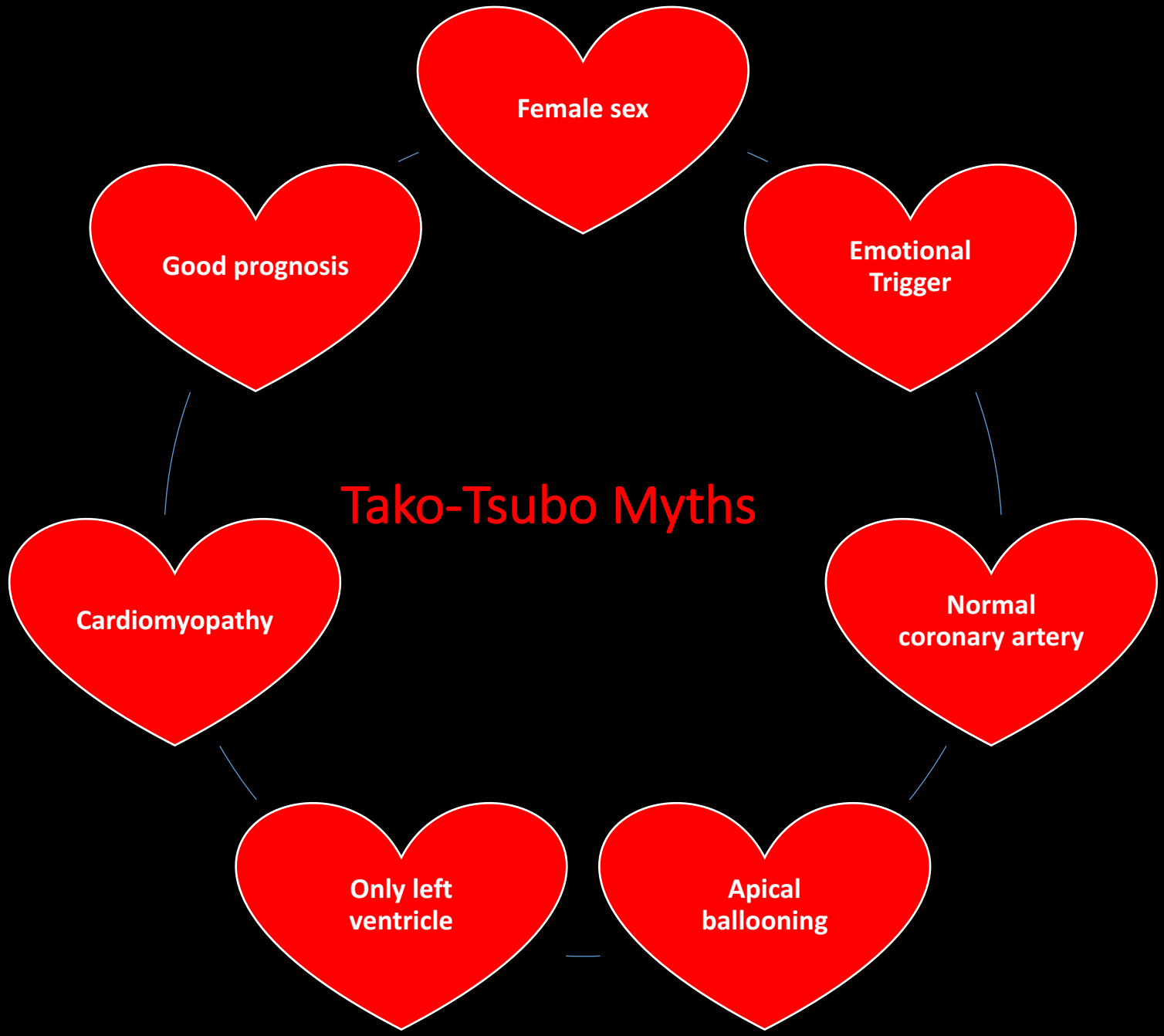
Tako-Tsubo, il «crepacuore» delle donne

Luciana Mauro

Potremmo chiamarla «sindrome da crepacuore», ma i giapponesi che per prima l'hanno scoperta la definiscono «Sindrome Tako-Tsubo». Recenti studi condotti dal dottor Rodolfo Citro, esperto di imaging cardiaco e di ecocardiografia come dirigente medico presso il Dipartimento Torre Cuore dell'Azienda Ospedaliera Universitaria Ruggi d'Aragona, spiegano che la "cardiomiopatia da stress" colpisce il 90% delle donne ed è preceduta da emozioni forti (perdita di un caro o finanziaria, paure, litigi, stati d'ansia, notizie di tradimenti etc), oppure da stress fisici, nella maggior parte dei casi di tipo medico. Gli studi di Citro, condotti con le Università di Pavia e di Ferrara e presentati al congresso dell'American Heart Association, rilevano che la sindrome Tako-Tsubo è prevalente nei mesi estivi, al contrario dell'infarto miocardico, invece prevalente d'inverno. «La patologia è subdola - spiega lo specialista - perchè si presenta come un infarto ma non lo è, anche se mette a dura prova la soravvivenza del paziente».



La Torre del cuore del Ruggi
Da qui gli studi sulla «Tako-Tsubo»


Female sex
Emotional Trigger
Normal coronary artery
Apical ballooning
Only left ventricle
Cardiomyopathy
Good prognosis
Tako-Tsubo Myths

Female sex (post-menopausal)

Demographic, clinical and echocardiographic features in patients with TTS with and without RVi.

Variables	Overall population (n = 424)
Medical history	
Age, yrs	69.1 ± 11.5
Male sex, n (%)	33 (7.8)
Hypertension, n (%)	257 (60.6)
Diabetes, n (%)	47 (11.1)
Hypercholesterolemia, n (%)	152 (35.8)
Smoking, n (%)	92 (19.3)
Menopause, n (%)	365 (93.4)
History of CAD, n (%)	73 (17.2)
COPD, n (%)	56 (13.2)
Cancer, n (%)	43 (10.1)
Psychiatric disorders, n (%)	70 (16.5)
Overall comorbidities, n (%)	0.96 ± 1.13
CCI	3.7 ± 1.9

Citro et al. Int. Journal of Cardiol. 2016

Table 1. Clinical and Demographic Characteristics of the Study Population

	Overall Population (n = 227)	Patients With Major Complications (n = 59)	Patients Without Major Complications (n = 168)	p Value
Age, yrs	66.2 ± 12.2	67.5 ± 14.5	65.8 ± 11.4	0.372
Age ≥ 75 yrs	65 (28.6)	25 (42.4)	40 (23.8)	0.011
Female	205 (90.3)	54 (91.5)	151 (89.9)	0.804
Body surface area, m^2	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	0.054
Medical history				
Hypertension	137 (60.4)	33 (55.9)	104 (61.9)	0.442
Hypercholesterolemia	88 (38.8)	20 (33.9)	68 (40.5)	0.438
Diabetes mellitus	25 (11.0)	10 (16.9)	15 (8.9)	0.096
Smoking	47 (20.7)	15 (25.4)	32 (19.0)	0.351
Menopause	180 (87.8)	46 (85.1)	134 (88.7)	0.477

Citro et al. JACC Imaging. 2014

Male vs Female

Variables	Male	Female	P value
Age, yy	68.0 ± 15.6	69.2 ± 11.04	0.496
Apical form, n	89%	91%	0.678
Identifiable Trigger	75%	77%	0.716
Emotional Trigger	36%	55%	0.016
Major Cardiac Events	21%	20%	0.934
LVEF	37.08 ± 6.9	36.55 ± 7.1	0.659
Overall complications	21%	22%	0.544
Hypertension	50%	62%	0.132
Diabetes	9%	11%	0.734
Hypercholesterolemia	27%	38%	0.147
Coronary artery disease	16%	18%	0.758

Unpublished data

Emotional trigger

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Age ≥ 75 yrs	65 (28.6)	25 (42.4)	40 (23.8)	0.011
Female	205 (90.3)	54 (91.5)	151 (89.9)	0.804
Body surface area, m^2	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	0.054
Other symptoms	10 (4.4)	6 (10.2)	4 (2.4)	0.021
Systolic blood pressure, mm Hg	131.1 ± 25.6	129.6 ± 32.6	131.6 ± 23.1	0.606
Diastolic blood pressure, mm Hg	77.4 ± 12.8	76.7 ± 14.1	77.7 ±12.4	0.619
Heart rate, beats/min	84.8 ± 16.1	88.8 ± 20.5	83.4 ± 14.1	0.031
Presence of identifiable trigger events	187 (82.4)	48 (81.4)	139 (82.7)	0.843
Emotional trigger	133 (58.6)	31 (52.5)	102 (60.7)	0.286
Physical trigger	54 (23.8)	17 (28.8)	37 (22.0)	0.190

Citro et al. JACC Imaging. 2014

Table 1. Demographic and Clinical Characteristics of the Study Population

Characteristic	Overall Population (N = 190)	Age <65 (n = 78)	Age 65–74 (n = 61)	Age ≥75 (n = 51)	P-Value*
Trigger events, n (%)	137 (72.1)	63 (80.8)	39 (63.9)	35 (68.6)	.07

12

Demographic, clinical and echocardiographic features in patients with TTS with and w

Variables	Overall population (n = 424)
Presenting features	
SBP, mmHg	125.2 ± 23.8
DBP, mmHg	74.5 ± 13.4
Heart rate, bpm	86.0 ± 18.3
Chest pain, n (%)	304 (71.7)
Dyspnea, n (%)	42 (9.9)
Chest pain and dyspnea, n (%)	32 (7.5)
Emotional trigger event	228 (53.8)
Physical trigger event, n (%)	102 (24.1)
Length of hospitalization, days	6.8 ± 4.3

Citro et al. Int. Journal of Cardiol. 2016

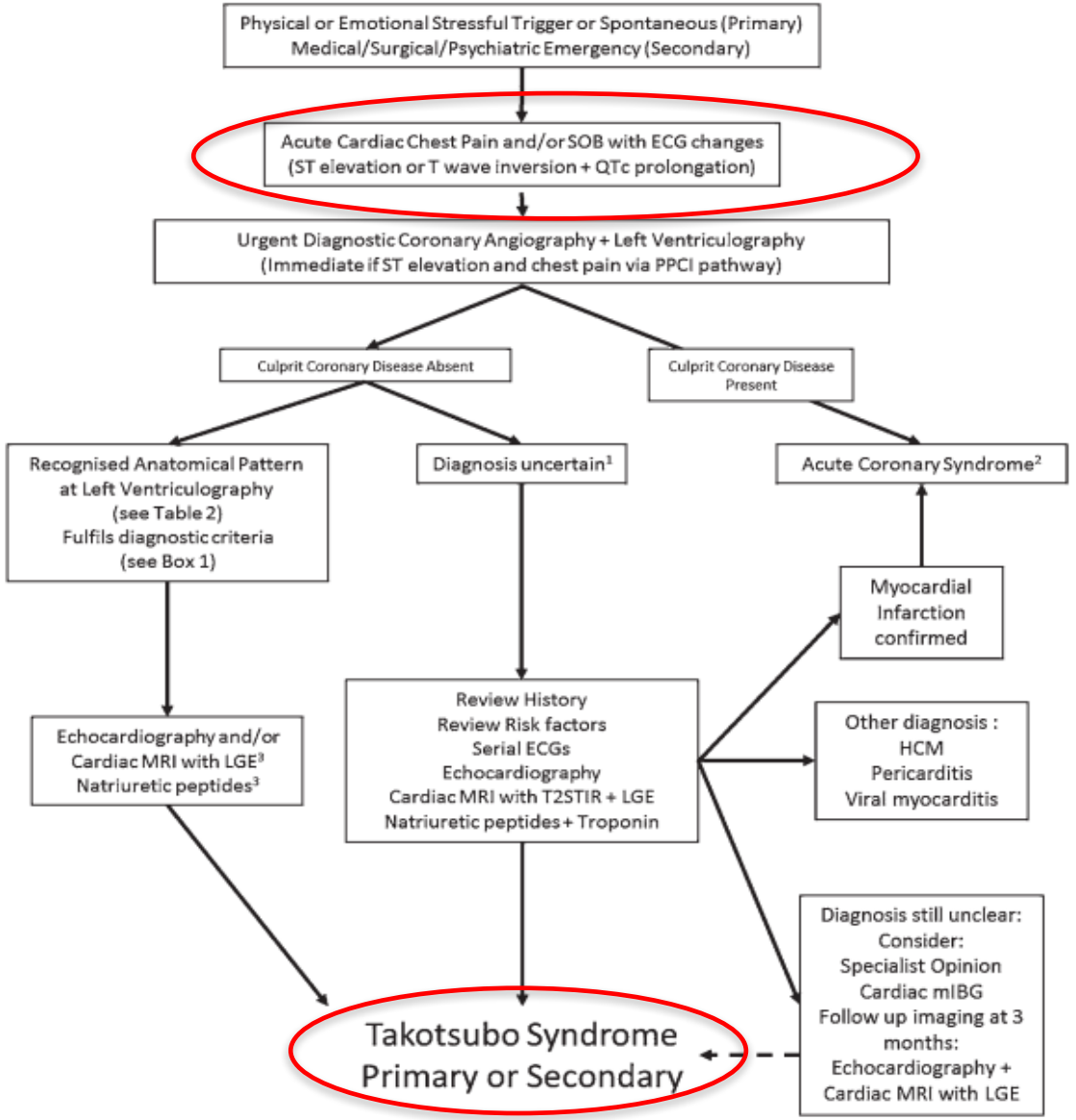
An identifiable trigger events was detected in 72 to 82% of patients with TTS
An emotional trigger is identified in 53 to 58 % of cases

European Journal of Heart Failure (2015)
doi:10.1002/ejhf.424

REVIEW

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

Alexander R. Lyon[1,2,*], Eduardo Bossone[3], Birke Schneider[4], Udo Sechtem[5], Rodolfo Citro[6], S.Richard Underwood[1,2], Mary N. Sheppard[7], Gemma A. Figtree[8,9], Guido Parodi[10], Yoshihiro J. Akashi[11], Frank Ruschitzka[12], Gerasimos Filippatos[13], Alexandre Mebazaa[14], and Elmir Omerovic[15]



Takotsubo Syndrome Diagnostic Algorithm

Table 1 Triggers for secondary Takotsubo syndrome

Endocrine
e.g. 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
Nortriptyline overdose, venlafaxine overdose, albuterol, flecanide, metoprolol withdrawal, 5-fluorouracil, duloxetine
Cocaine abuse

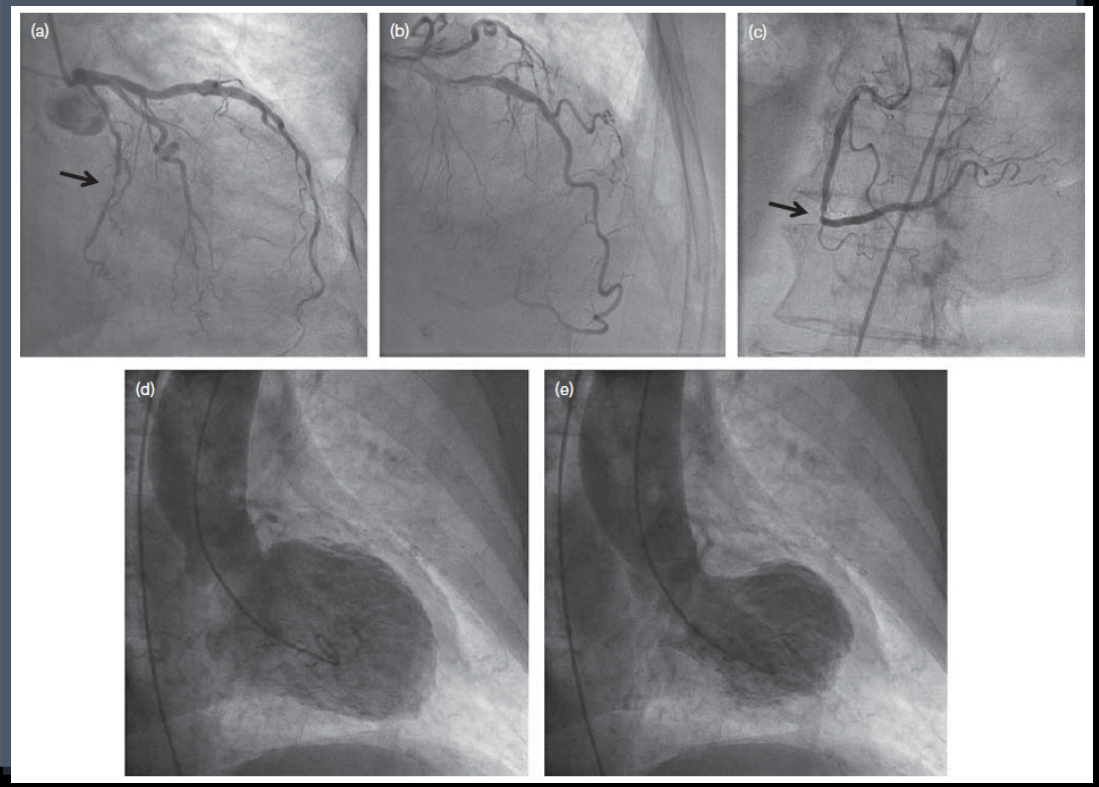
Box 1 Heart Failure Association diagnostic criteria for Takotsubo syndrome

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]

Normal coronary artery

Tako-tsubo cardiomyopathy and coronary artery disease: a possible association

Guido Parodi[a], Rodolfo Citro[b], Benedetta Bellandi[a], Stefano Del Pace[a], Fausto Rigo[d], Marco Marrani[a], Gennaro Provenza[e], Mario Leoncini[f], Joerge A. Salerno Uriarte[g], Francesco Bovenzi[h] and Eduardo Bossone[c], on behalf of the Tako-tsubo Italian Network (TIN)

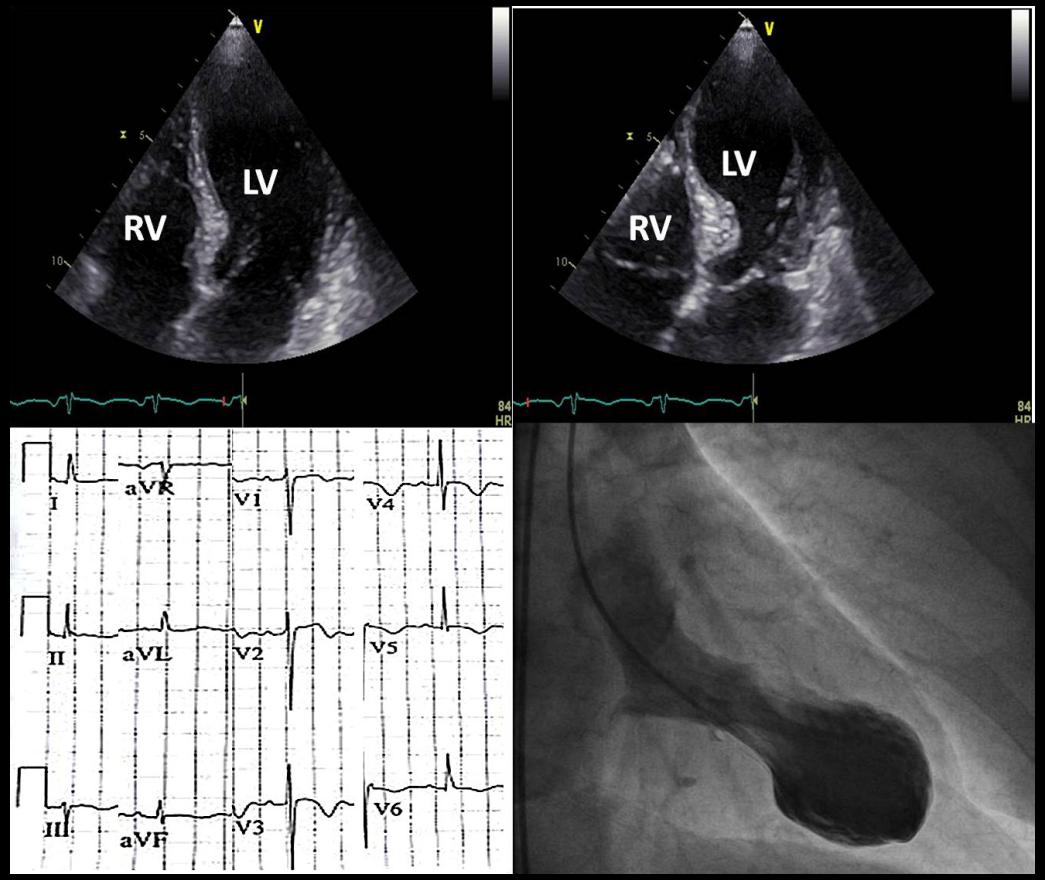


Coexistent significant coronary artery narrowing in about 10% of pts.

Non culprit lesion!

Coronary Artery Disease 2013, 24:527–533

Apical ballooning



STATE-OF-THE-ART REVIEW ARTICLE

Standard and Advanced Echocardiography in Takotsubo (Stress) Cardiomyopathy: Clinical and Prognostic Implications

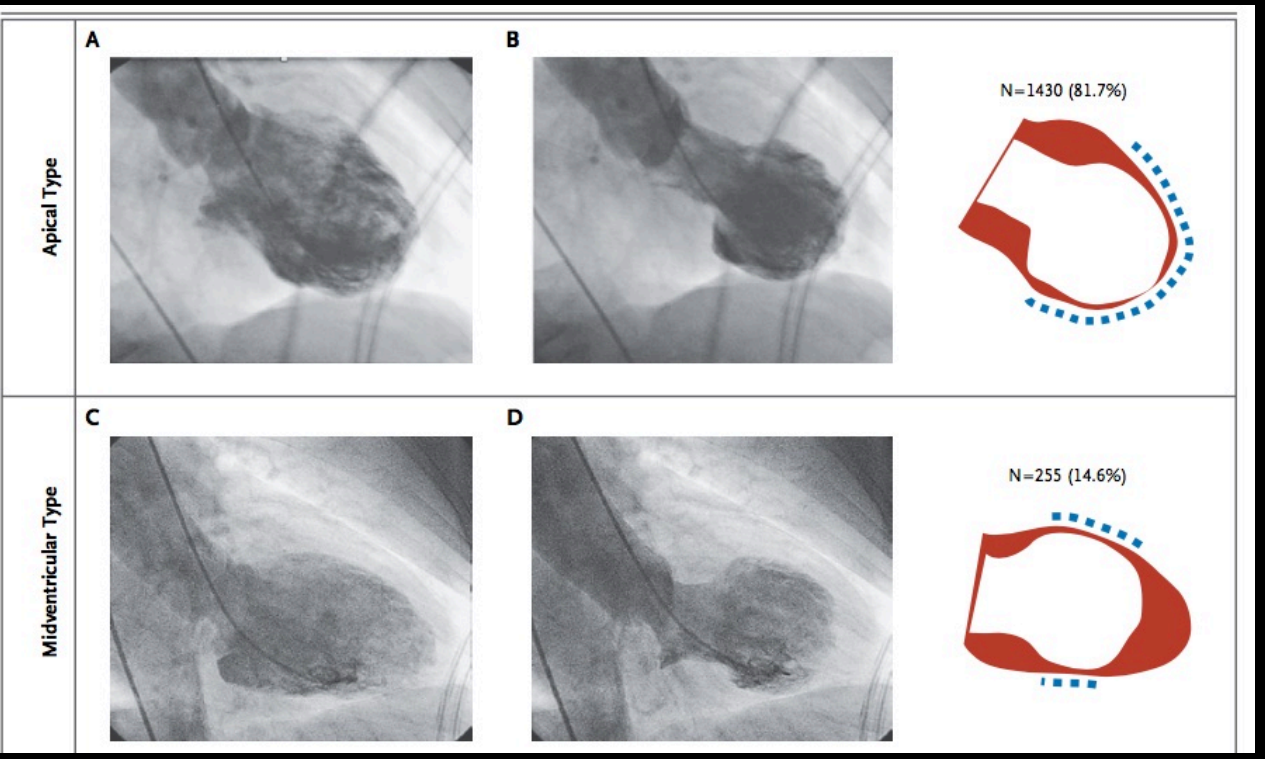
Rodolfo Citro, MD, PhD, FESC, Alexander R. Lyon, MD, PhD, FESC, Patrick Meimoun, MD, Elmir Omerovic, MD, Björn Redfors, MD, Thomas Buck, MD, PhD, FESC, FACC, Stamatios Lerakis, MD, Guido Parodi, MD, PhD, Angelo Silverio, MD, Ingo Eitel, MD, Birke Schneider, MD, FESC, Abhiram Prasad, MD, and Eduardo Bossone, MD, PhD, FESC, FCCP, FACC, *Salerno and Florence, Italy; London, United Kingdom; Compiègne, France; Gothenburg, Sweden; Dortmund and Lübeck, Germany; Atlanta, Georgia*

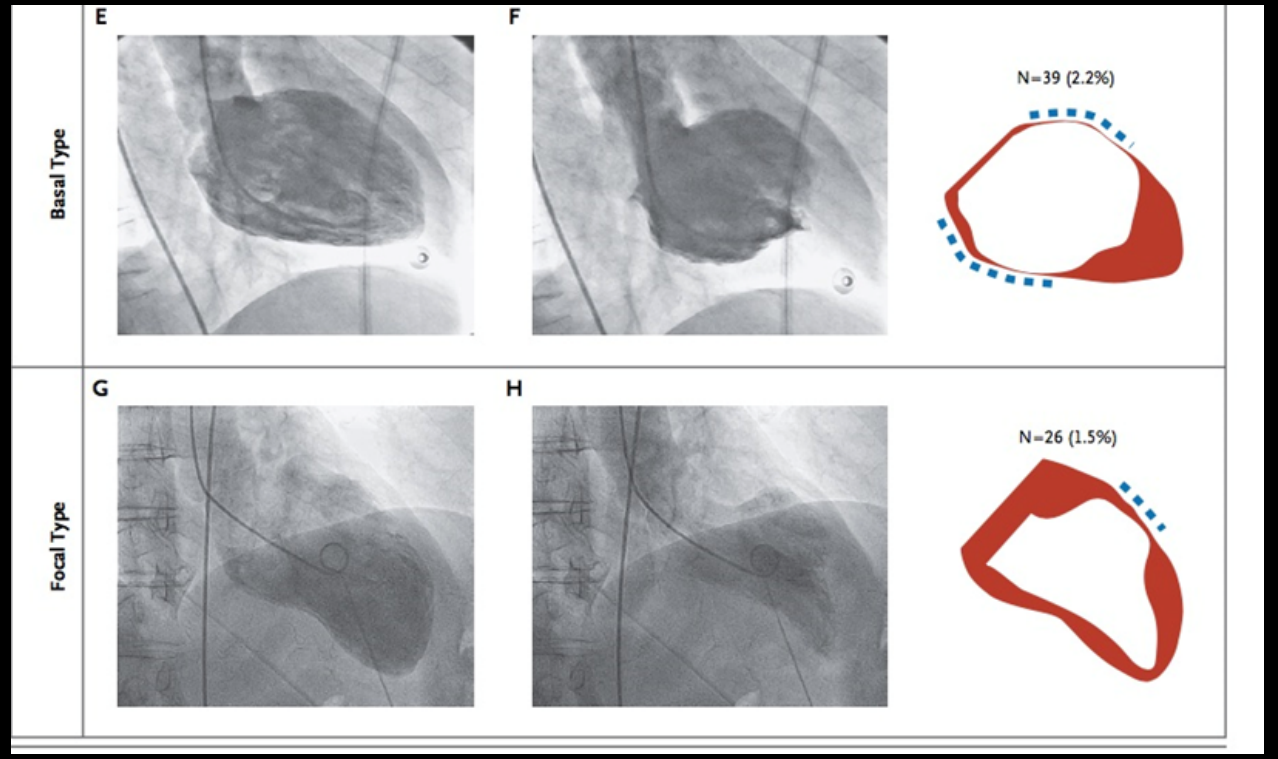
Journal of the American Society of Echocardiography ■ 2014

Table 3 Role of standard echocardiography in TTC

Diagnostic findings
LV morphology
Apical ballooning
Midventricular
Inverted forms
Apical sparing
Basal "reverse"
LV WMAs
Circumferential pattern
Coronary flow in distal LAD
RV involvement
Biventricular ballooning
Possible complications
LVOTO
Moderate to severe MR
Intraventricular thrombus detection
Cardiac rupture

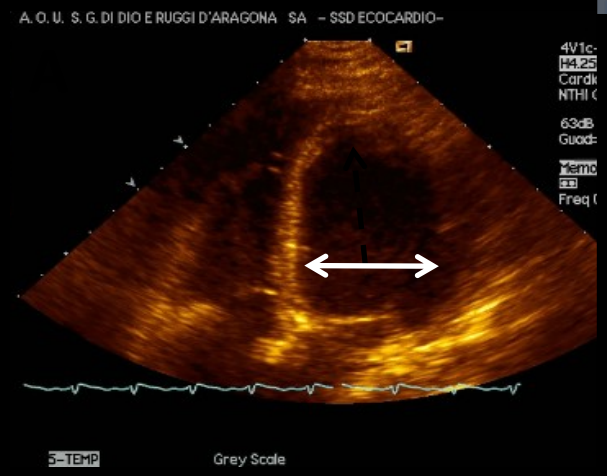
TTS: LV Phenotype



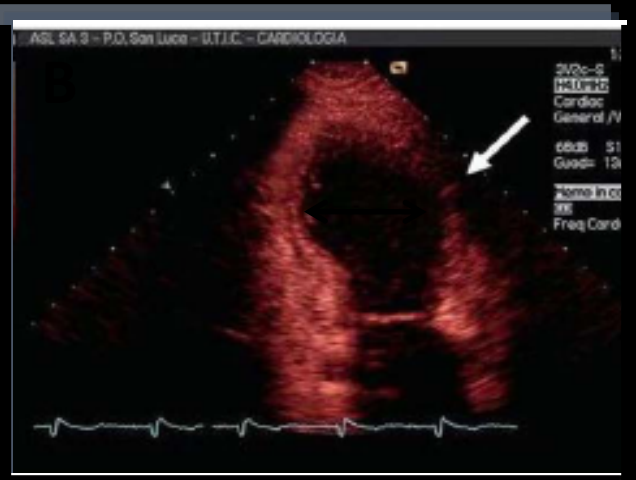


TTS: LV Phenotype

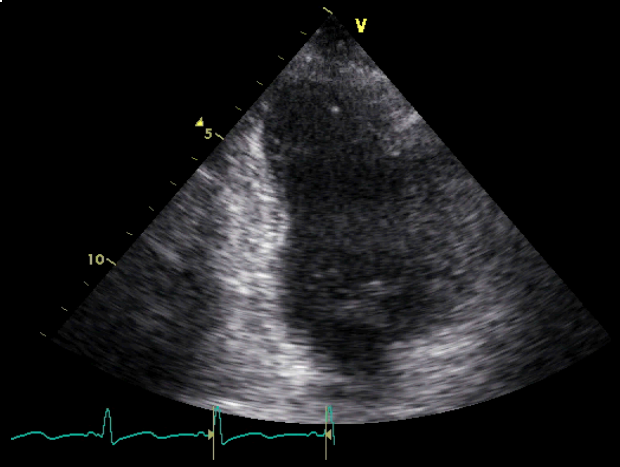
APICAL SPARING



MIDVENTRICULAR BALLOONING



BASAL BALLOONING



Citro R, Heart Failure Clinics 2013

Right ventricular involvment in TTS

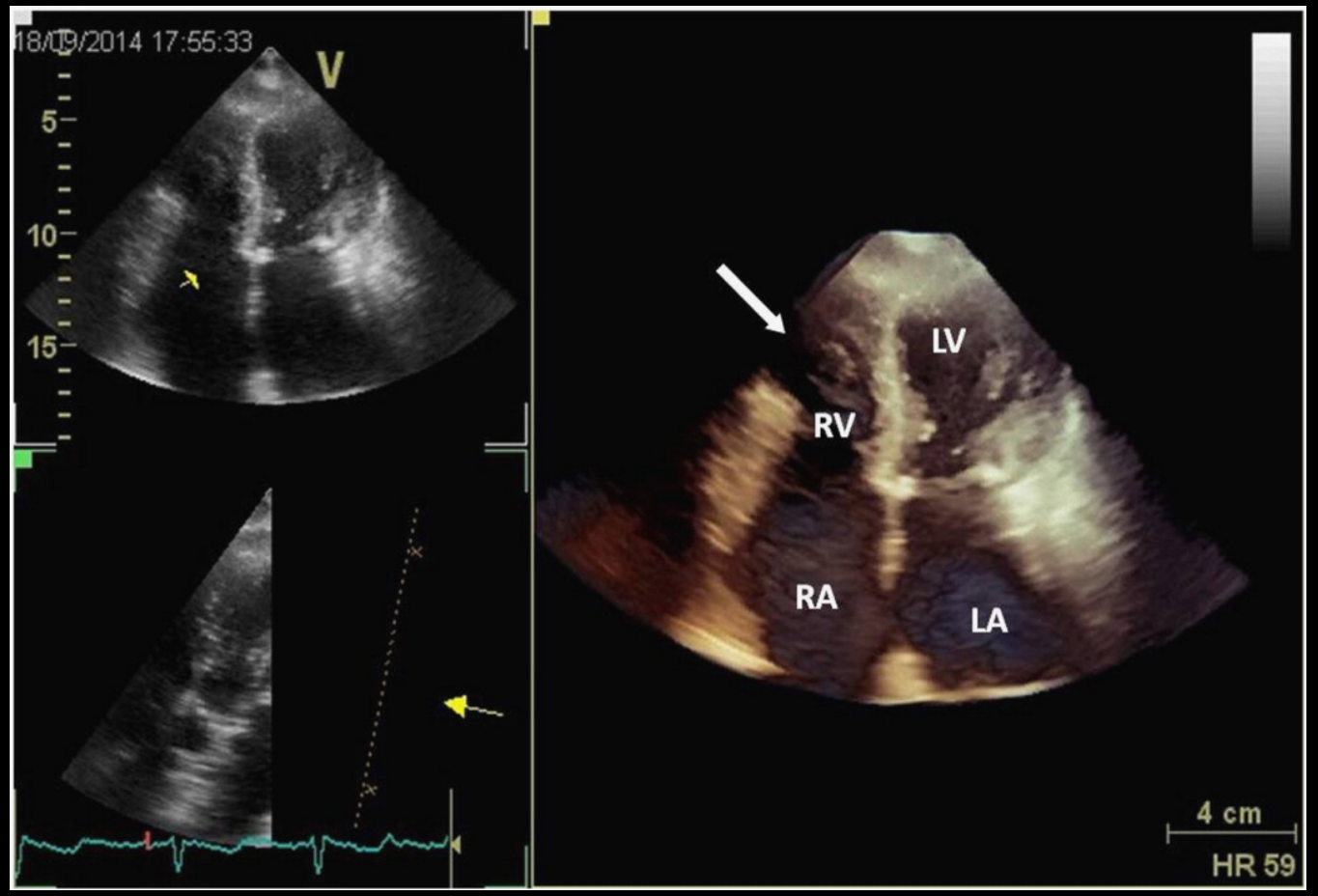
Clinical profile and in-hospital outcome of Caucasian patients with takotsubo syndrome and right ventricular involvement

Rodolfo Citro [a,b,*], Eduardo Bossone [a], Guido Parodi [c], Scipione Carerj [d], Quirino Ciampi [e], Gennaro Provenza [f], Concetta Zito [d], Costantina Prota [a], Angelo Silverio [a], Olga Vriz [g], Antonello D'Andrea [h], Gennaro Galasso [a], Cesare Baldi [a], Fausto Rigo [i], Massimo Piepoli [j], Jorge Salerno-Uriarte [b], Federico Piscione [a], on behalf of the "Takotsubo Italian Network" Investigators (see Appendix)

Int. Journal of Cardiol. 2016

424 pts (mean age 69.1±11.5 yrs; female 92.2%) with diagnosis of TTS : 57 patients (13.4%) with RV involvment

RVi was identified by the detection of severe akinesia or dyskinesia, localized exclusively at the apical and/or mid RV segments (biventricular ballooning), with sparing of the basal segments ("reverse McConnell's sign")

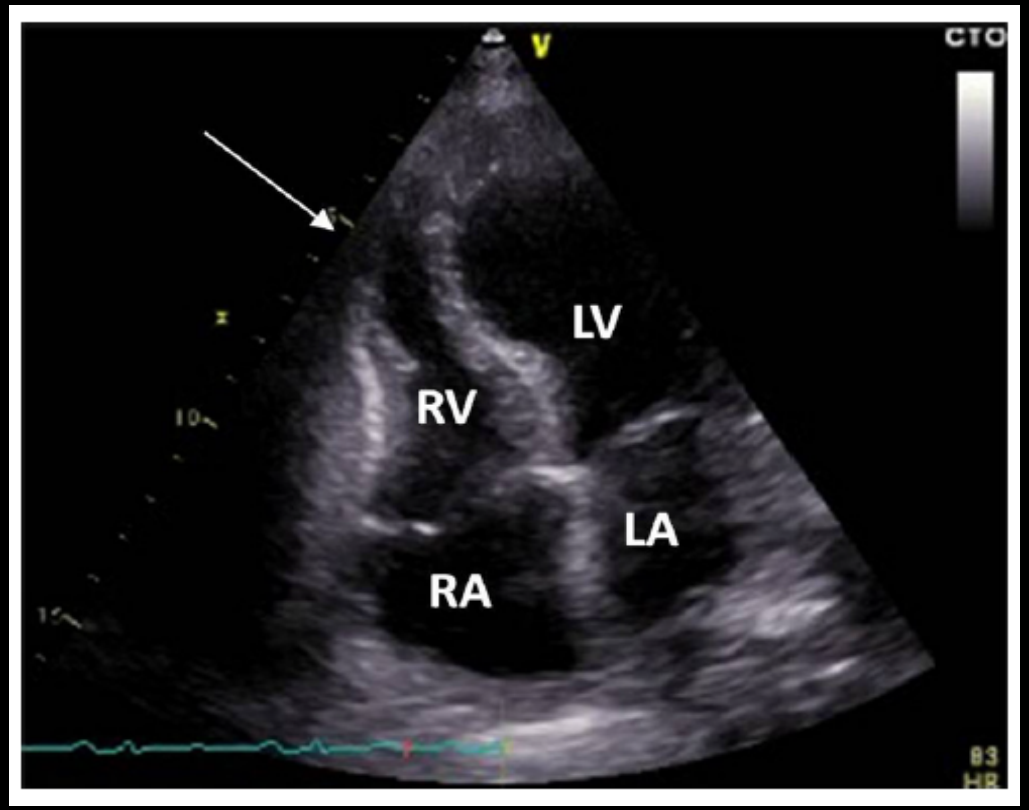


Only left ventricle

Independent Impact of RV Involvement on In-Hospital Outcome of Patients With Takotsubo Syndrome

TABLE 1 Clinical features and In-Hospital Outcomes of Patients With Apical TTS With and Without RVi

	Patients With RVi (n = 56; 16.5%)	Patients Without RVi (n = 283; 83.5%)	p Value
Age, yrs	67.7 ± 13.6	70.1 ± 10.6	0.145
Male	4 (7.1)	24 (8.5)	0.740
Systolic blood pressure, mm Hg	123.7 ± 20.4	125.2 ± 23.6	0.661
Heart rate, beats/min	89.1 ± 17.6	85.6 ± 18.8	0.203
Chest pain at presentation	42 (75.0)	227 (80.2)	0.371
Dyspnea at presentation	23 (41.1)	38 (13.4)	<0.001
COPD	14 (25.0)	34 (12.0)	0.019
Charlson comorbidity index	4.3 ± 1.9	3.8 ± 1.9	0.050
ST-segment elevation	29 (51.8)	192 (67.8)	0.031
Troponin I, ng/ml	1.5 ± 1.6	4.9 ± 9.9	0.013
Brain natriuretic peptide, pg/ml	1,080.3 ± 775.2	824.4 ± 441.8	<0.001
GFR, ml/min	66.8 ± 24.9	69.2 ± 23.6	0.627
Left ventricular ejection fraction, %	35.2 ± 7.0	36.2 ± 7.4	0.329
Wall motion score index	1.96 ± 0.28	1.84 ± 0.24	0.002
E/e′ ratio	11.7 ± 3.3	10.9 ± 2.6	0.064
Right ventricular fractional area change, %	32.3 ± 5.9	40.0 ± 11.0	<0.001
Systolic pulmonary artery pressure, mm Hg	43.9 ± 15.0	40.0 ± 5.8	0.001
TAPSE, mm	18.7 ± 4.0	20.0 ± 4.1	0.084
Moderate to severe mitral regurgitation	20 (35.7)	47 (16.6)	0.013
Left ventricular outflow tract obstruction	7 (12.5)	17 (6.0)	0.091
In-hospital major adverse events			
Acute heart failure	20 (35.7)	37 (13.1)	<0.001
Cardiogenic shock	3 (5.4)	20 (7.1)	0.779
Death	2 (3.6)	4 (1.4)	0.259

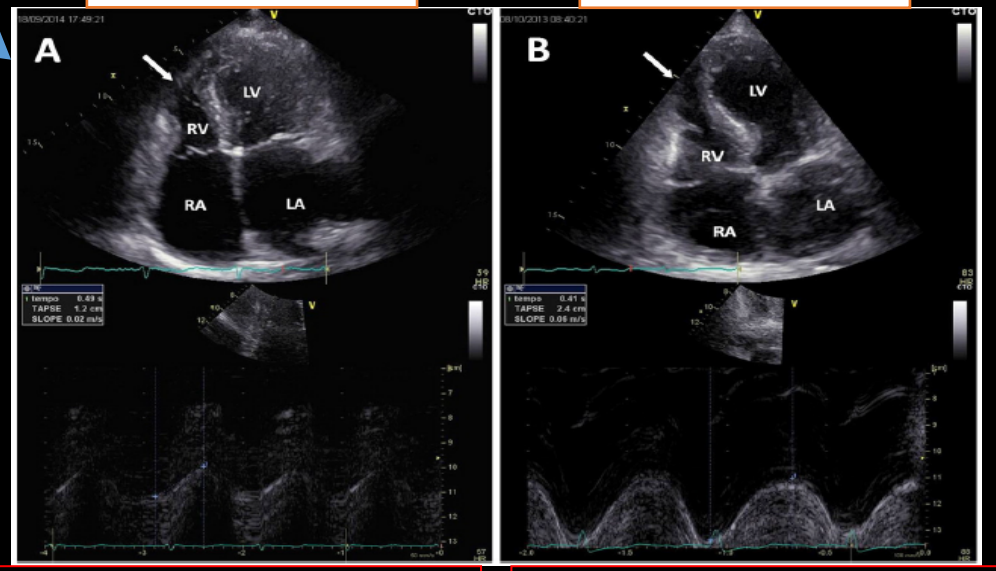


Citro R. et al. JACC Imaging 2015

Right ventricular involvment in TTS

TAPSE : 12 mm

TAPSE : 24 mm



Patient who developed Acute HF during hospitalization

Patient without complications during hospitalization

Hazard ratio (95% CI) for acute heart failure, cardiogenic shock, and in-hospital mortality at univariate and multivariate analysis in TTS patients with RVi.

	Univariate analysis		Multivariate analysis	
Variables	HR (95% CI)	p-value	HR (95% CI)	p-value
Heart rate	1.038 (1.003–1.074)	0.031		
CCI	1.472 (1.078–2.008)	0.015	1.871 (1.202–2.912)	0.006
WMSI	0.393 (0.250–1.108)	0.002		
E/e' ratio	1.315 (1.079–1.601)	0.007		
sPAP	1.067 (1.023–1.114)	0.003	1.059 (1.016–1.104)	0.007
TAPSE	0.836 (0.718–0.974)	0.021	0.728 (0.619–0.855)	< 0.001

Citro et al. Int. Journal of Cardiol. 2016

Is a Cardiomyopathy?

…….more syndrome than cardiomyopathy…….

….sindrome perché non è identificabile una forma paradigmatica ma piuttosto un fenotipo clinico comune nel quale probabilmente convergono molteplici processi fisiopatologici.

Vi sono altresì diversi motivi che non giustificherebbero l'adozione del termine cardiomiopatia:

1) la restitutio ad integrum del miocardio disfunzionante nella fase acuta con il conseguente recupero completo della funzione contrattile a distanza
2) le evidenze fisiopatologiche che sono più a favore di una disfunzione del microcircolo coronarico, attraverso vari meccanismi aventi in comune un aumento di attività delle catecolamine, che a favore di una malattia primitiva del muscolo cardiaco, in genere associata a disordini primitivi del miocardio di origine genetica o sconosciuta

Citro et al. Giornale Italiano di Cardiol. 2016

Good prognosis

Differences in Clinical Features and In-Hospital Outcomes of Older Adults with Tako-Tsubo Cardiomyopathy

Rodolfo Citro, MD, FESC,[*] Fausto Rigo, MD,[†] Mario Previtali, MD,[‡] Quirino Ciampi, MD,[§] Francesco Antonini Canterin, MD,[‖] Gennaro Provenza, MD,[#] Roberta Giudice, MD,[*] Marco Mariano Patella, MD,[**] Olga Vriz, MD,[††] Rahul Mehta,[‡‡] Cesare Baldi, MD,[*] Rajendra H. Mehta, MD, MS, FACC,[§§] and Eduardo Bossone, MD, PhD, FESC, FACC, FCCP[‖‖] on behalf of the Tako-tsubo Italian Network Investigators (see Appendix 1)

Table 3. In-Hospital Complications and Mortality

Complication	Overall Population (N = 178)	<65 (n = 76)	65–74 (n = 54)	≥75 (n = 48)	*P*-Value*
Atrial fibrillation, n (%)	8 (4.5)	2 (2.6)	2 (3.7)	4 (8.3)	.31
Left ventricular apical thrombosis, n (%)	4 (2.2)	1 (1.3)	1 (1.9)	2 (4.2)	.57
Supraventricular tachycardia, n (%)	3 (1.7)	1 (1.3)	1 (1.9)	1 (2.1)	.94
Bradyarrhythmia, n (%)	2 (1.1)	2 (2.6)	0 (0.0)	0 (0.0)	.26
Stroke, n (%)	1 (0.6)	0 (0.0)	1 (1.9)	0 (0.0)	.32
Respiratory arrest, n (%)	1 (0.6)	1 (1.3)	0 (0.0)	0 (0.0)	.51
Acute heart failure, n (%)	28 (15.7)	7 (9.2)	10 (18.5)	11 (22.9)	.10
Ventricular tachycardia or ventricular fibrillation, n (%)	8 (4.5)	1 (1.3)	3 (5.6)	4 (8.3)	.17
Cardiogenic shock, n (%)	11 (6.2)	6 (7.9)	1 (1.9)	4 (8.3)	.29
In-hospital mortality, n (%)	5 (2.8)	1 (1.3)	1 (1.9)	3 (6.3)	.24
Composite adverse events, n (%)	43 (24.2)	13 (17.1)†	12 (22.2)	18 (37.5)	.03
Overall complications, n (%)	56 (31.5)	17 (22.4)†	15 (27.8)	24 (50.0)	.004
Length of hospital stay, days, mean ± SD	7.9 ± 5.7	5.9 ± 3.2	8.6 ± 6.0	9.6 ± 7.2	.10

* Difference between the three age groups according to analysis of variance.
† $P < .05$ versus ≥ 75 according to post hoc analysis.

Citro R et al JAGS 2011

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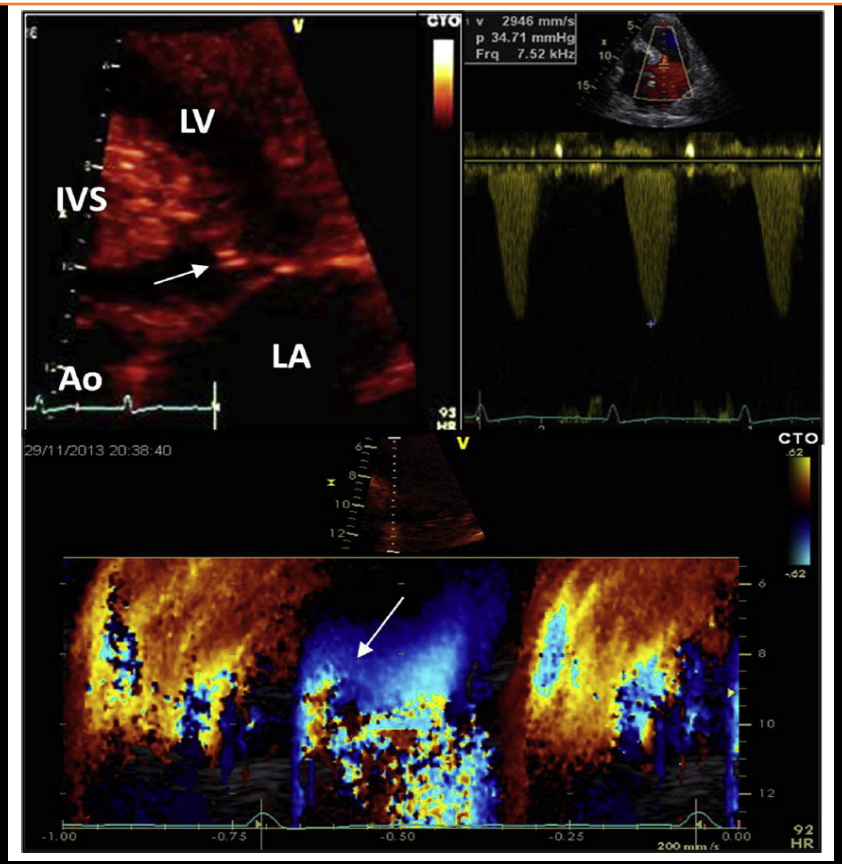
Table 4. Univariate and Multivariate Predictors of In-Hospital Events

	Hazard Ratio (95% Confidence Interval) *P*-Value	
Variable	Univariate Analysis	Multivariate Analysis
Aged ≥ 75	2.72 (1.39–5.31) .003	2.45 (1.28–5.82) .04
Presence of triggers	1.22 (0.57–2.57) .60	–
ST-segment elevation on admission	1.33 (0.68–2.58) .39	–
Peak troponin I, ng/mL	1.00 (0.99–1.00) .68	–
Glomerular filtration rate, mL/min*	0.98 (0.96–0.99) .02	–
Beta-blockers	0.60 (0.31–1.15) .13	–
Left ventricular ejection fraction on admission	0.88 (0.82–0.94) <.001	0.87 (0.81–0.95) <.001

Citro R et al JAGS 2011

TTS: Left ventricular outflow tract obstruction

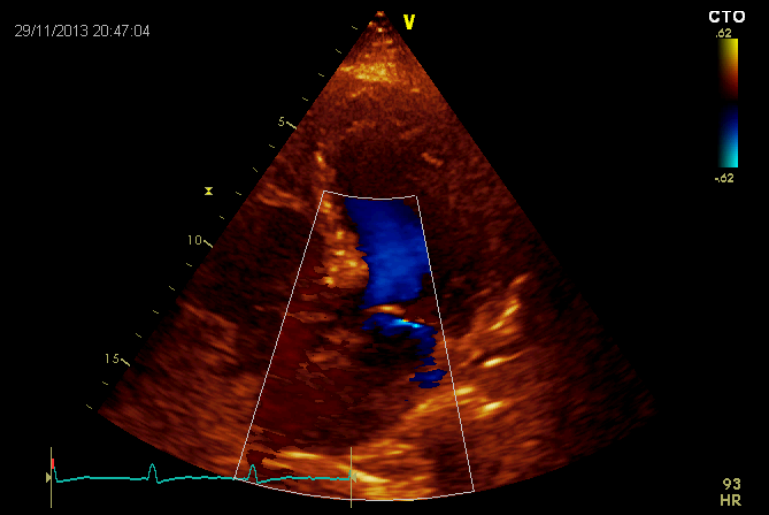


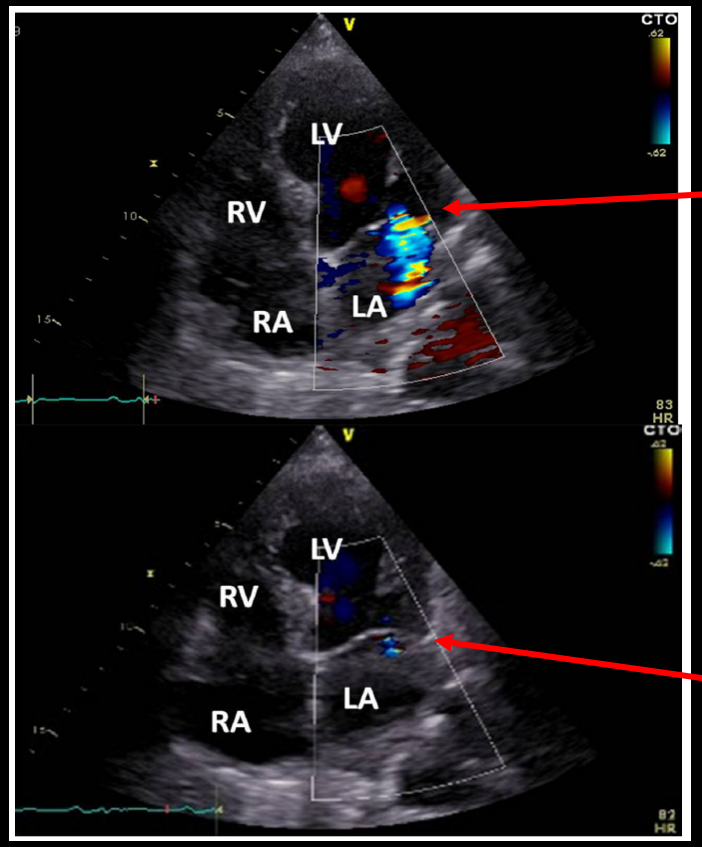
Variables	Overall population (n = 227)	Patients with major complications (n=59)	Patients without major complications (n=168)	P value
LV outflow tract obstruction	29 (12.8)	14 (23.7)	15 (8.9)	0.006

Citro R, et al. JACC Imaging. Feb 2014

Citro R, Lyon AR, Meimoun P, et al. JASE 2014

TTS: Reversible moderate to severe mitral regurgitation





Acute phase

Recovery

Variables	Overall population (n = 227)	Patients with major complications (n=59)	Patients without major complications (n=168)	P value
Moderate to severe MR	49 (21.5)	29 (49.1)	20 (11.9)	<0.001

Citro R, et al. JACC Imaging. Feb 2014

Citro R, Lyon AR, Meimoun P, et al. JASE 2014.

ORIGINAL RESEARCH

Echocardiographic Correlates of Acute Heart Failure, Cardiogenic Shock, and In-Hospital Mortality in Tako-Tsubo Cardiomyopathy

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Overall population 227 pts: Major adverse events in 59 pts

Table 5. Hazard ratio (95% CI) for the major adverse events (acute heart failure, cardiogenic shock, and in-hospital mortality) in univariate and multivariate models.

Variables	Wald Chi-square	P-value	HR	95% CI	Wald Chi-square	P-value	HR	95% CI
Age ≥ 75	7.162	0.007	2.353	1.257-4.403	4.270	0.039	2.818	1.055-7.529
Heart rate	4.492	0.034	1.020	1.001-1.038				
Chest pain with dyspnea	9.552	0.002	3.477	1.578-7.664				
BNP	3.385	0.049	1.002	1.000-1.004				
LVEF	15.398	< 0.001	0.892	0.842-0.944	18.400	<0.001	0.923	0.890-0.958
E/e' ratio	23.345	< 0.001	1.266	1.150-1.393	6.410	0.011	1.131	1.028-1.244
sPAP	23.549	< 0.001	1.086	1.050-1.122				
Moderate to severe MR	23.532	< 0.001	5.916	2.885-12.133	5.049	0.025	3.254	1.163-9.109
RV involvement	11.957	0.001	3.845	1.792-8.250				
LVOT obstruction	7.992	0.005	3.173	1.425-7.067				

BNP: brain natriuretic peptide; LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow tract; MR: mitral regurgitation; RV: right ventricular; sPAP: pulmonary artery systolic pressure.

Citro R, et al. J Am Coll Cardiol Img 2014;7:119–29

Clinical Characteristics and Outcome of Left Ventricular Ballooning Syndrome in a European Population

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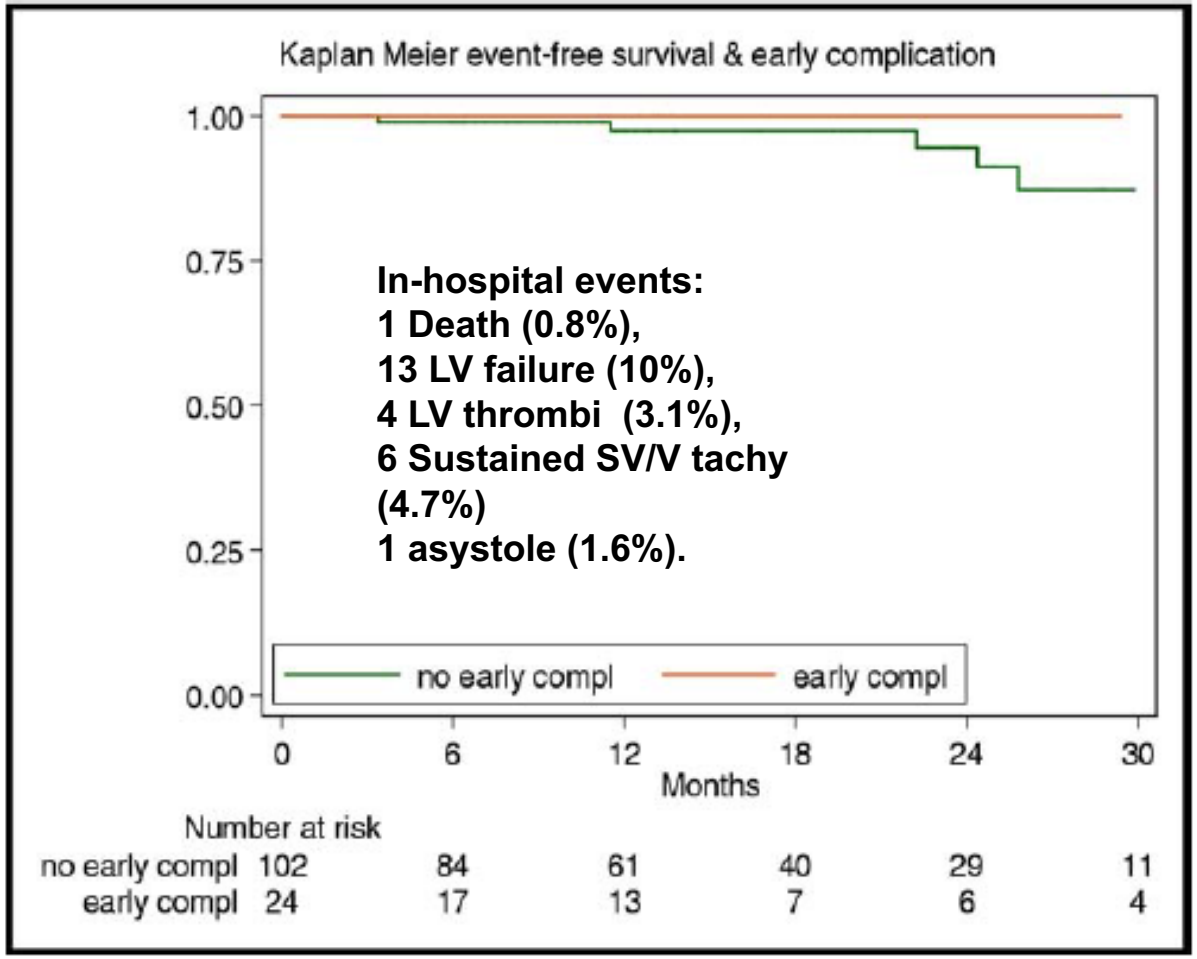
Am J Cardiol 2011



In-hospital events:
1 Death (0.8%),
13 LV failure (10%),
4 LV thrombi (3.1%),
6 Sustained SV/V tachy (4.7%)
1 asystole (1.6%).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Takotsubo Cardiomyopathy		Acute Coronary Syndrome	P Value†
	Total Cohort (N=1750)	Matched Cohort (N=455)	Matched Cohort (N=455)	
Female sex — no. (%)	1571 (89.8)	411 (90.3)	411 (90.3)	1.00
Age — yr	66.4±13.1	67.7±12.5	68.7±12.3	0.19
Treatment — no./total no. (%)				
Catecholamine	212/1735 (12.2)	53/455 (11.6)	50/455 (11.0)	0.75
Invasive or noninvasive ventilation	301/1735 (17.3)	63/455 (13.8)	41/455 (9.0)	0.02
Cardiopulmonary resuscitation	149/1735 (8.6)	40/455 (8.8)	53/455 (11.6)	0.16
In-hospital outcomes — no./total no. (%)				
Cardiogenic shock	170/1716 (9.9)	55/445 (12.4)	48/455 (10.5)	0.39
Death	72/1750 (4.1)	17/455 (3.7)	24/455 (5.3)	0.26

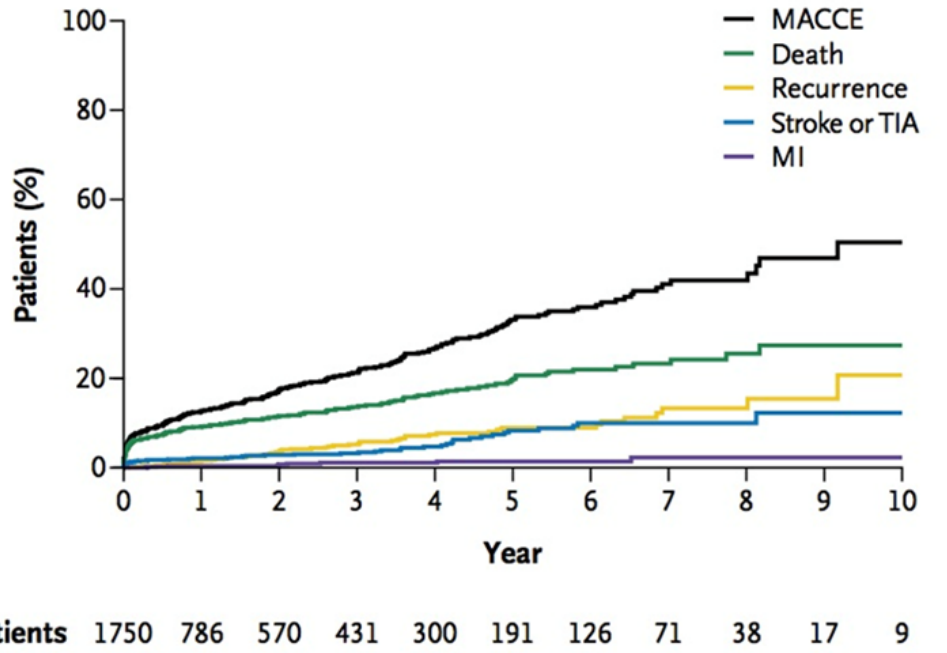


Figure 3. Kaplan–Meier Estimates of 10-Year Outcome Events.

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).

Templin C et al. NEJM 2015

Take home messages

- La TTS non colpisce esclusivamente le donne (F:M 9:1) dopo la menopausa (circa 10 % in epoca pre-menopausa).
- Il trigger event non è solo emotivo, ma può essere una patologia medico-chirurgica acuta o può anche non essere evidente.
- Può coesistere una coronaropatia anche significativa (circa 10% dei casi).
- Esistono diversi fenotipi oltre al classico «apical left ventricular ballooning» (circa 15-20% di forme «atipiche»)
- Può essere interessato anche il ventricolo destro («biventricula ballooning» in circa il 10-15%)
- La prognosi non è sempre benigna (soprattutto nei pazienti anziani, con più comorbidità, con interessamento del ventricolo destro, con insufficienza mitralica moderata severa in fase acuta ed ostruzione all' efflusso ventricolare sinistro)

Grazie da Salerno