



Medicina, Cura e Genere

Venerdì 6 maggio 2016

Museo MAGI'900
Pieve di Cento (Bologna)

Cardiomiopatia Tako-Tsubo: solo una malattia della donna?



Roberto Manfredini

Clinica Medica, Università di Ferrara

Playlist

Cardiomiopatia Tako-Tsubo

Ruolo dello stress

Meccanismi patogenetici

Aspetti cronobiologici

Aspetti di genere

Take-home messages

Cardiomiopatia Tako-Tsubo

Ruolo dello stress

Meccanismi patogenetici

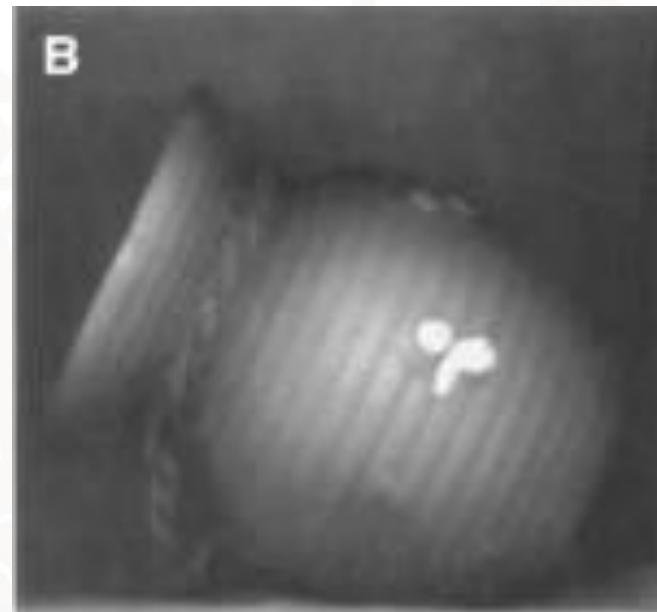
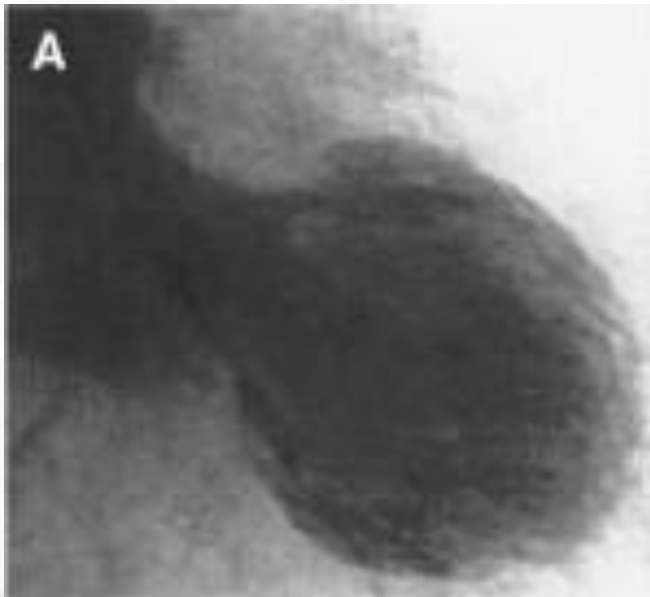
Aspetti cronobiologici

Aspetti di genere

Take-home messages

Cardiomiopatia Tako-Tsubo

Descritta per la prima volta in Giappone nel 1990. Il nome deriva dalle parole Tako (polpo) e Tsubo (giara)



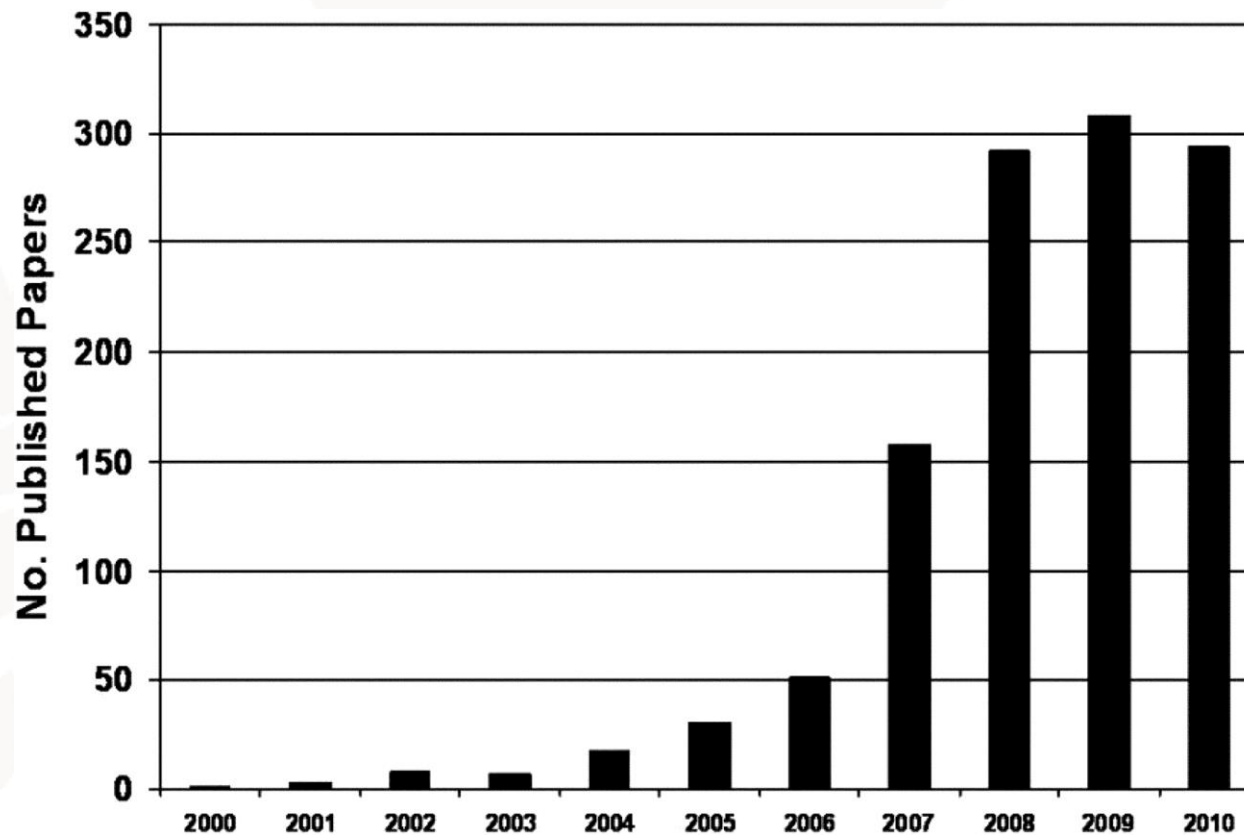
Altre definizioni

- Stress-induced cardiomyopathy
- Transient left ventricular apical ballooning syndrome
- Apical ballooning syndrome
- Ampulla cardiomyopathy
- Broken Heart Syndrome



Argomento 'hot' per la ricerca

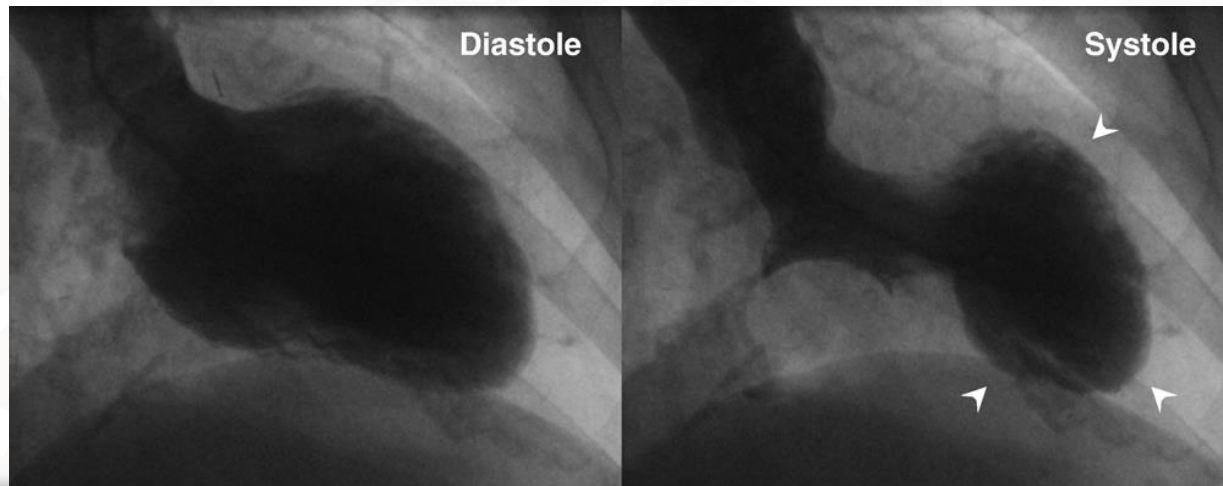
PubMed (April 30, 2016): 2929



Sharkey et al, *Circulation* 2011

Cardiomiopatia Tako-Tsubo

Disfunzione transitoria delle sezioni apicale e medio-ventricolare del ventricolo sx, in assenza di malattia coronarica significativa, e spesso scatenata da uno stress (emotivo o fisico).



Cardiomiopatia Tako-Tsubo

- Fino al 2% delle sospette sindromi coronariche acute (SCA) (donne 6-9%, uomini 0.5%)
- Più frequente nelle donne (~90%), >80% dei casi in postmenopausa
- Mortalità intra-ospedaliera: 1-2%
- Recupero della funzione del Vsx: 1-4 sett.
- Recidive (10% ad un follow-up di 4 anni)

Cardiomiopatia Tako-Tsubo

Ruolo dello stress

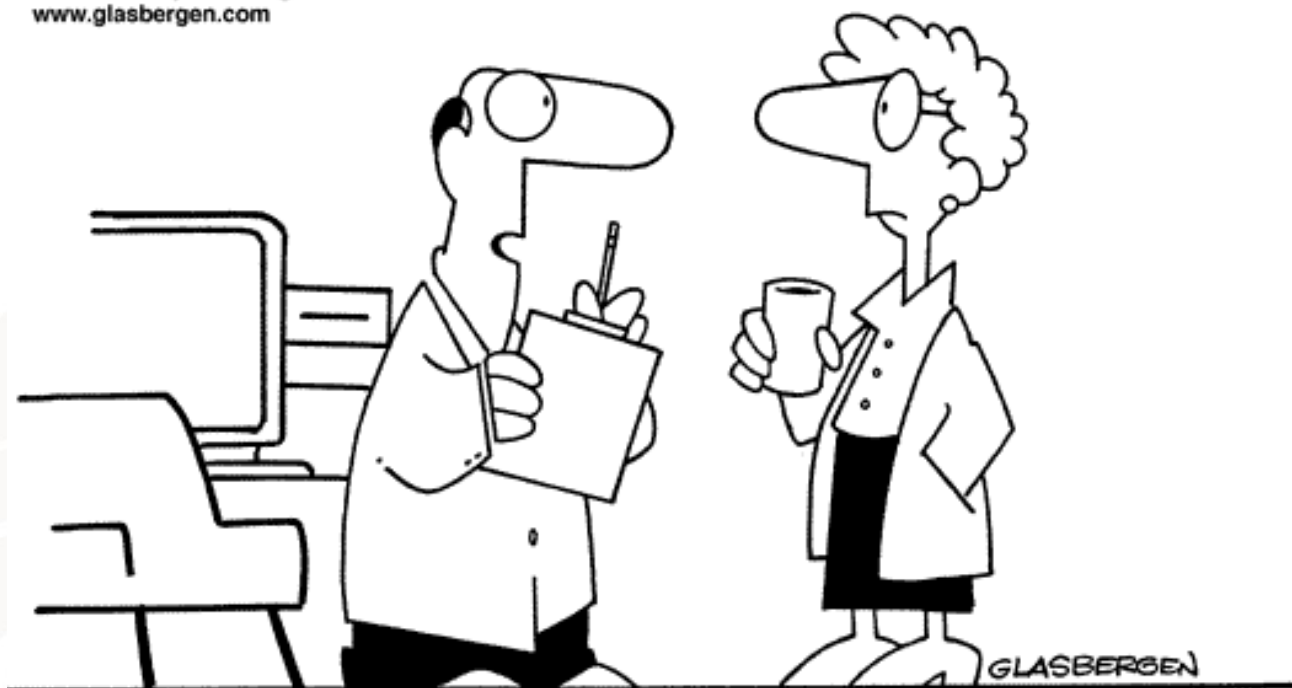
Meccanismi patogenetici

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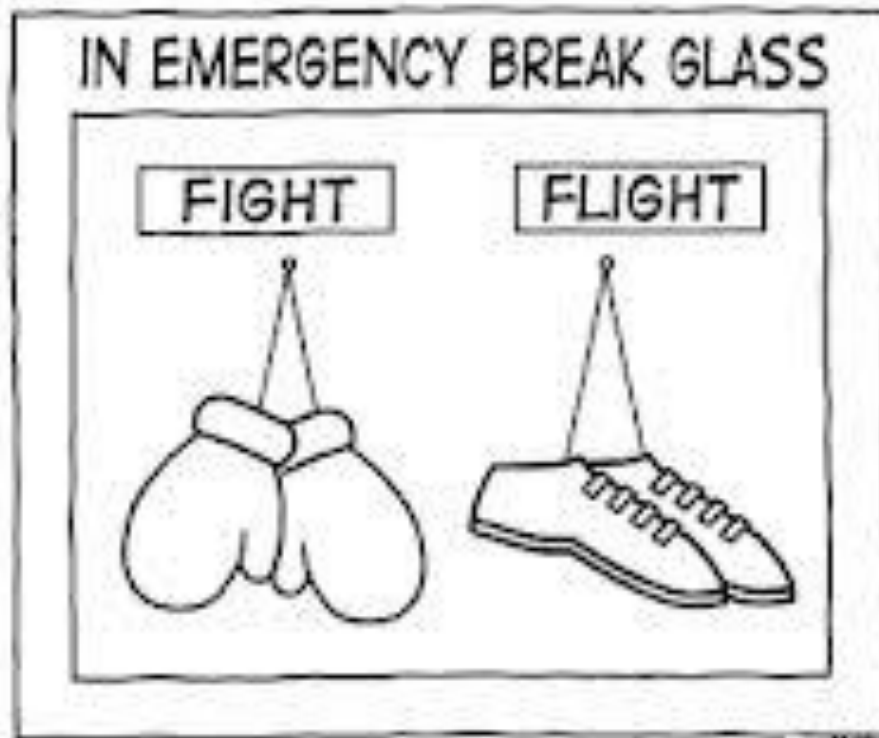
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“According to the latest research, the average human body is 20% water and 80% stress.”



Fight or Flight



J. de Charro

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Triggers ‘emotivi’

- Morte, malattia grave o grave lesione riguardante un membro della famiglia, un amico, il proprio animale
- Cattive notizie (diagnosi di grave malattia, divorzio di un familiare)
- Grave litigio
- Aggressione
- Coinvolgimento in azione legale
- Incidente d’auto
- Trasloco
- Perdita economica (affari, gioco, licenziamento)
- Disastri naturali (terremoti..)
- Party a sorpresa
- Public speaking



57-year-old African American woman, presenting with severe dyspnea following the shooting death of her son. Discharged on day 6.

Happiness Can Break Your Heart: A Rare Case of Takotsubo Cardiomyopathy After Good News

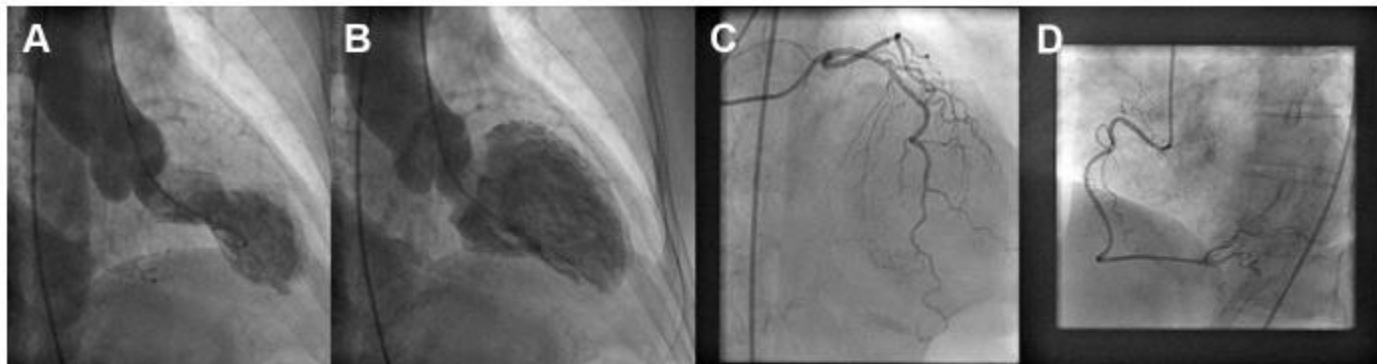


Figure 2. Right anterior oblique projection of left ventriculogram showing an ejection fraction of 65%, with apical akinesis and hyperdynamic basal segments consistent with Takotsubo cardiomyopathy during (A) systole and (B) diastole. Angiographic images demonstrating no obstructive coronary artery disease in the (C) left and (D) right coronary systems.

86-year-old retired teacher recognized with a prestigious lifetime teaching award, with many of her former students present at the ceremony.



European Heart Journal
doi:10.1093/eurheartj/ehv757

CLINICAL RESEARCH

Heart failure/cardiomyopathy

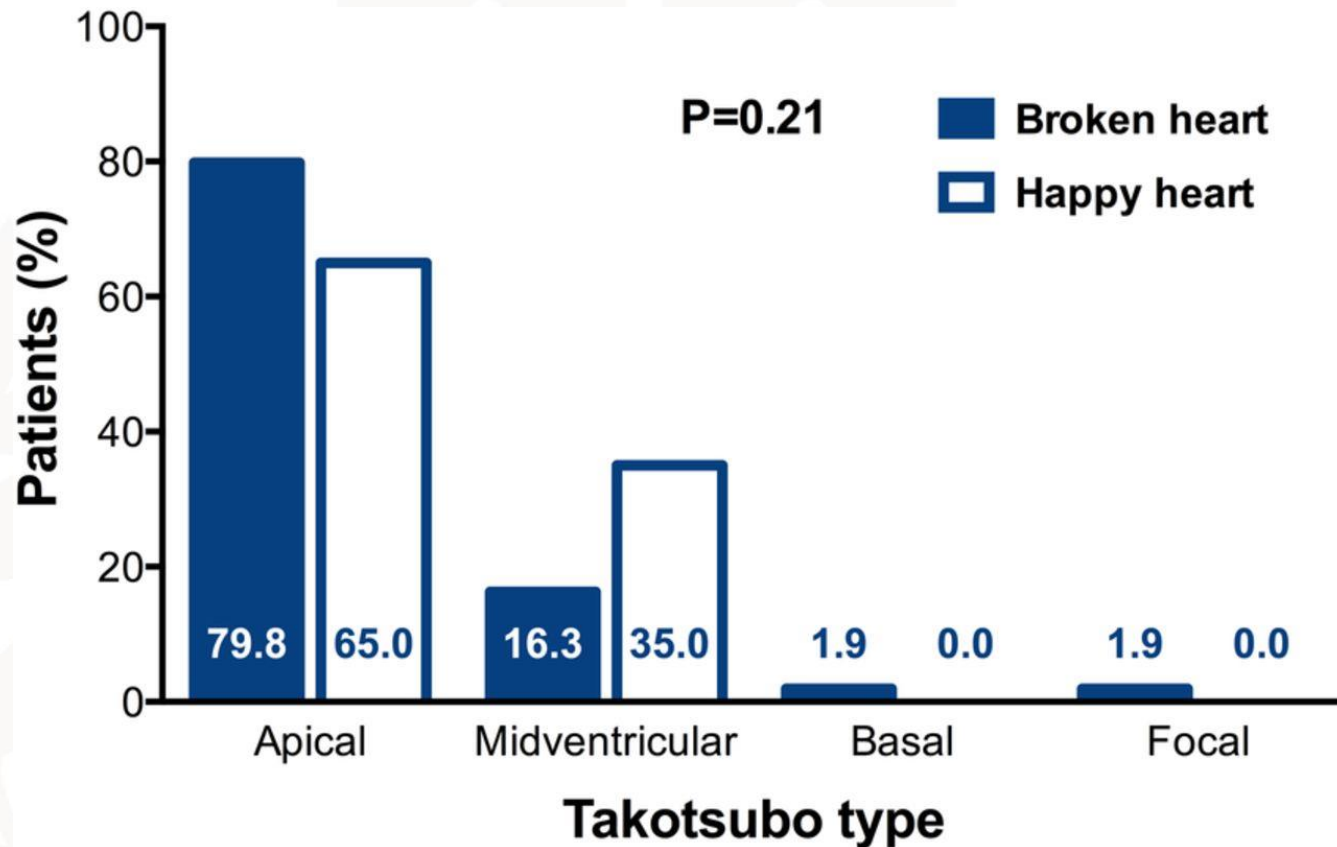
Happy heart syndrome: role of positive emotional stress in takotsubo syndrome

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 speaking 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



Happy heart syndrome: role of positive emotional stress in takotsubo syndrome



Triggers 'fisici'

- Procedure chirurgiche e cardiocirurgiche
- Cause respiratorie
- Patologie gastroenteriche
- Patologie reumatologiche
- Patologie endocrine
- Patologie ematologiche
- Patologie infettive
- Dialisi
- Patologie neurologiche
- Sostanze illecite o farmaci: cocaina, abuso di antidepressivi, β_2 stimolanti, adrenalina...
- Altri: traumi, ustioni, colpo di calore, abuso di energy drinks, puntura di medusa, ..

Cardiomiopatia Tako-Tsubo

Ruolo dello stress

Meccanismi patogenetici

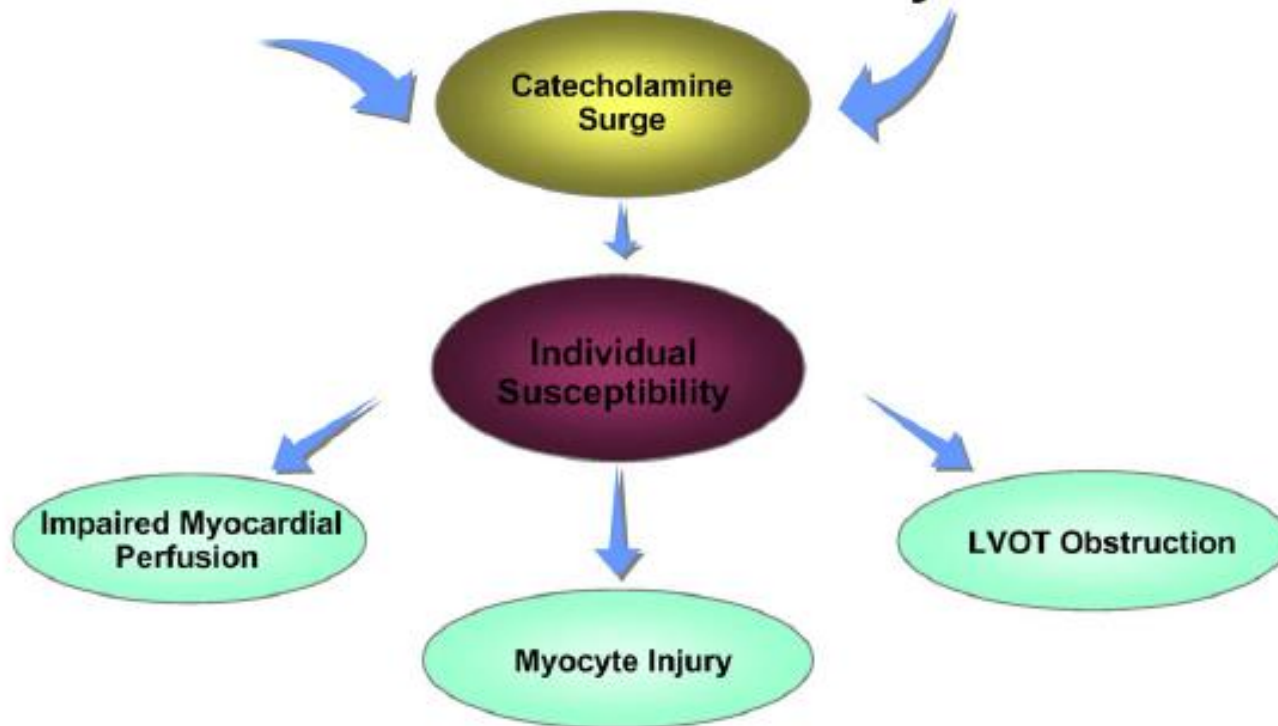
Aspetti cronobiologici

Aspetti di genere

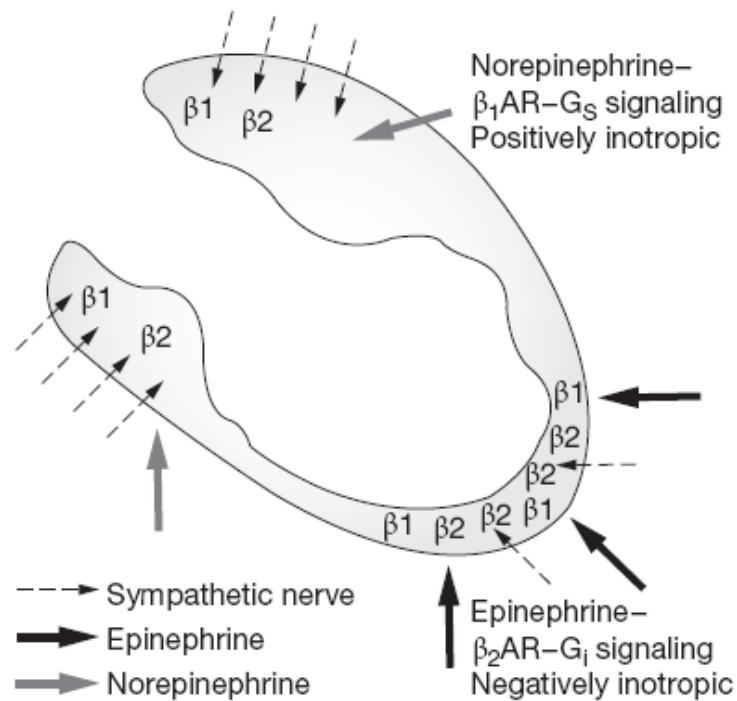
Take-home messages

Mental Stress

Physical Stress



Prasad et al, *Am Heart J* 2008



High levels of circulating E might trigger a switch in intracellular signal trafficking, from G_S protein to G_i protein signaling through the β_2 AR. This change in signaling is negatively inotropic, and the effect is greatest at the apical myocardium, in which the density of β -adrenoceptors is highest.

Figure 3 Schematic representation of the regional differences in response to high catecholamine levels, explaining stress cardiomyopathy.

Lyon et al, *Nat Clin Pract Cardiovasc Med* 2009

Cardiomiopatia Tako-Tsubo

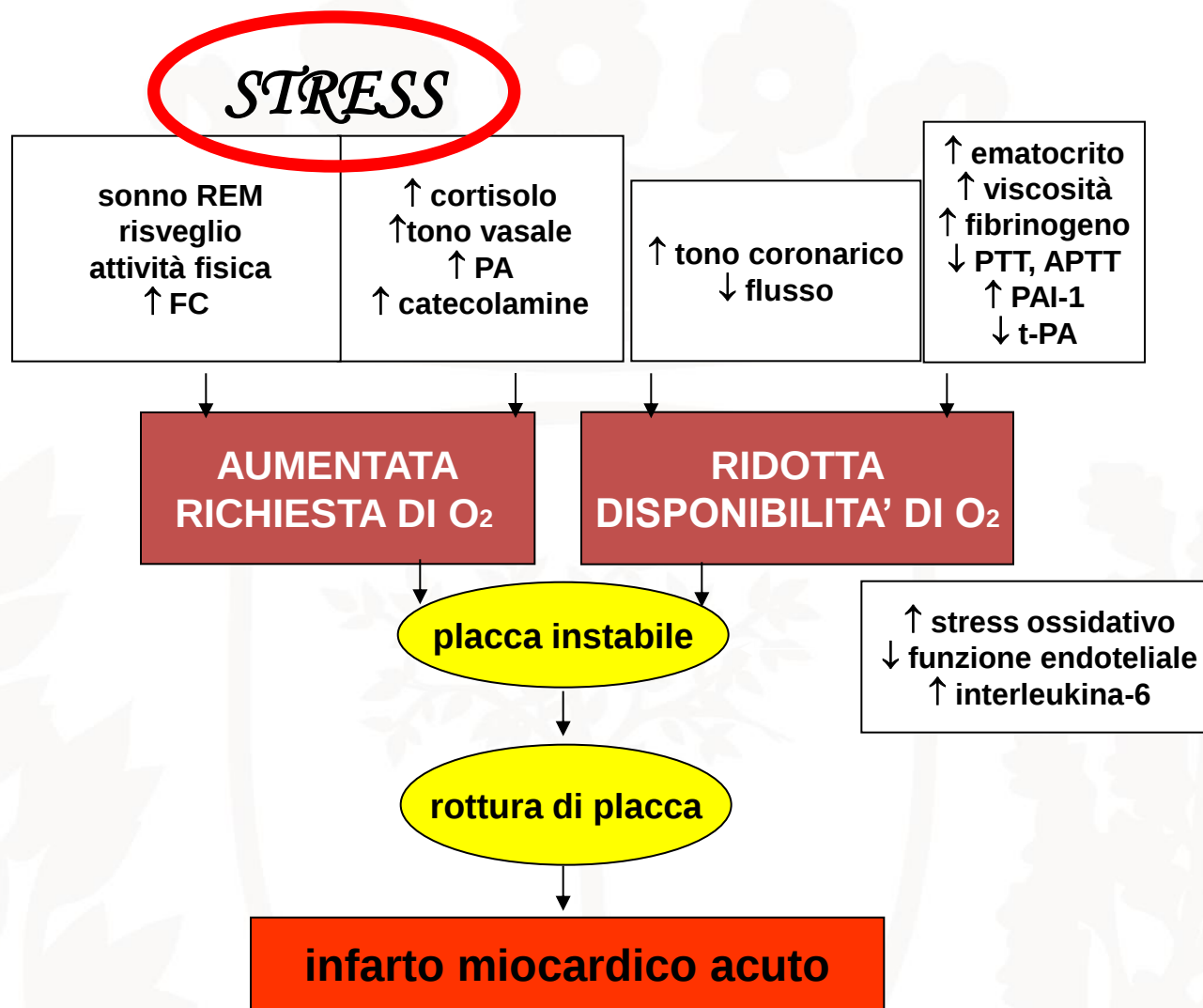
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Meccanismi patogenetici

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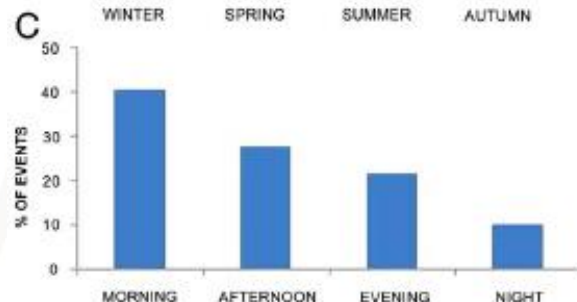
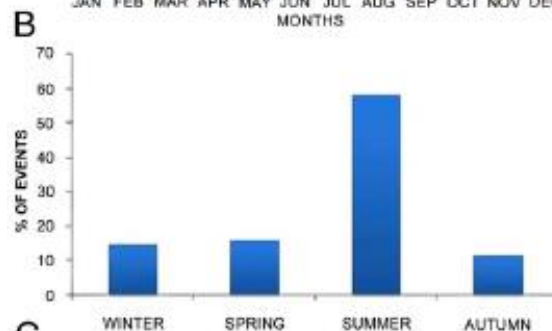
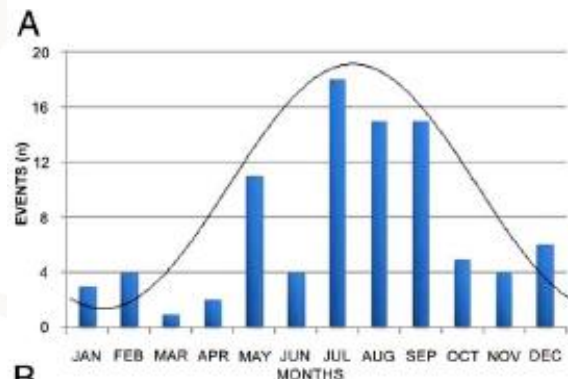


Manfredini et al, Encyclopedia Stress, Elsevier 2007

Chronobiological Patterns of Onset of Tako-Tsubo Cardiomyopathy

A Multicenter Italian Study

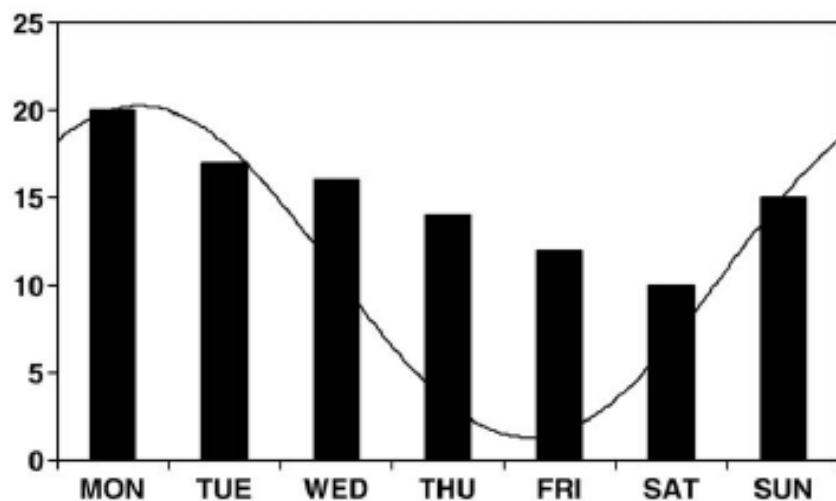
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Roberto Manfredini, MD



Citro et al, *J Am Coll Cardiol* 2009

Monday preference in onset of takotsubo cardiomyopathy[☆]

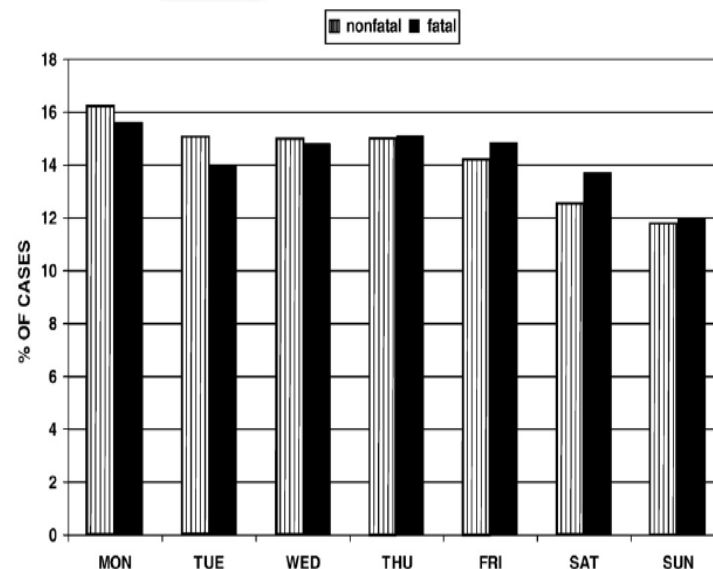
Roberto Manfredini MD^{*,a}, Rodolfo Citro MD^b, Mario Previtali MD^c, Olga Vriz MD^d, Quirino Ciampi MD^e, Marco Pascotto MD^f, Ercole Tagliamonte MD^g, Gennaro Provenza MD^b, Fabio Manfredini MD^h, Eduardo Bossone MD, PhDⁱ for the Takotsubo Italian Network investigators



Manfredini et al, *Am J Emerg Med* 2010

Seasonal and weekly patterns of hospital admissions for nonfatal and fatal myocardial infarction[☆]

Roberto Manfredini MD^{a,b,*}, Fabio Manfredini MD^c, Benedetta Boari MD^d, Elisabetta Bergami MD^d, Elisa Mari MD^d, Susanna Gamberini MD^b, Raffaella Salmi MD^d, Massimo Gallerani MD^d



Manfredini et al, *Am J Emerg Med* 2009

Breaking Heart

Chronobiologic Insights into Takotsubo Cardiomyopathy

Roberto Manfredini, MD^{a,*}, Raffaella Salmi, MD^b,
Fabio Fabbian, MD^c, Fabio Manfredini, MD^d,
Massimo Gallerani, MD^e, Eduardo Bossone, MD^{f,g}

Clinics Review Articles

HEART FAILURE CLINICS

Takotsubo (Stress) Cardiomyopathy

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APRIL 2013

Cardiomiopatia Tako-Tsubo

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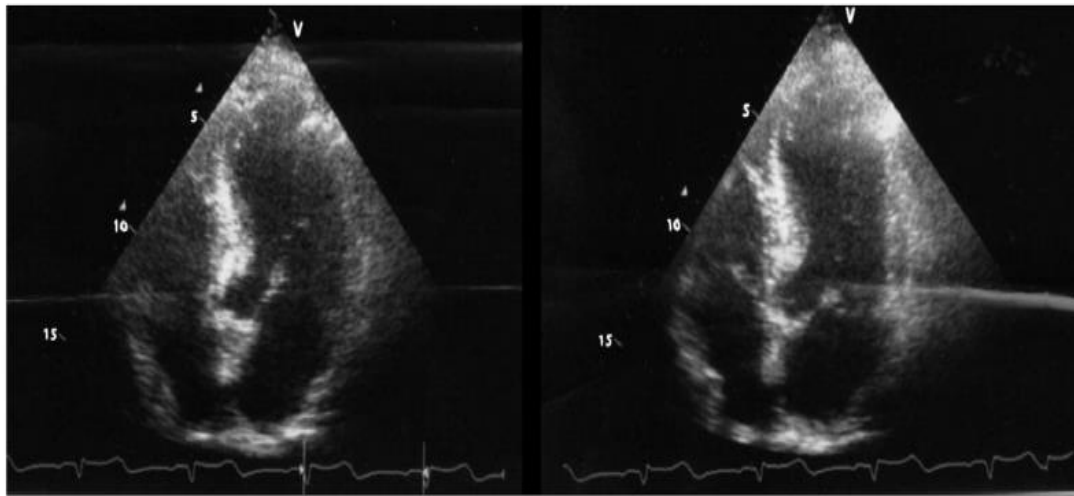
Aspetti di genere

Take-home messages

Non solo donne.....

Les liaisons dangereuses: Tako-Tsubo syndrome after an adulterous intercourse in an elderly male

81-year-old man, smoker, no CV risk factors, referred for chest pain 12 hours after an adulterous intercourse with a young woman. Complete recovery in 6 days, asymptomatic at 6-month follow-up.



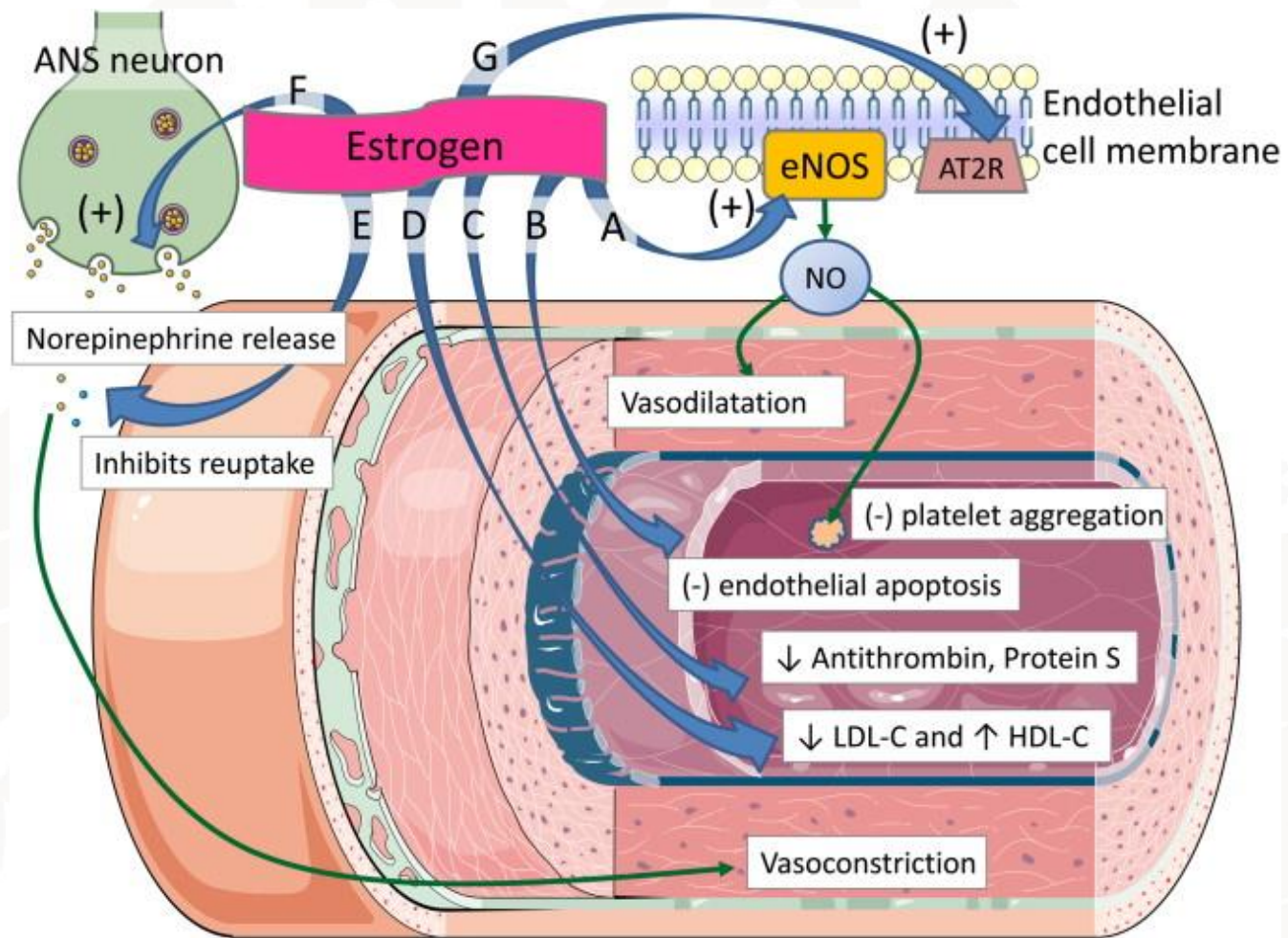
Brunetti et al, Int J Cardiol 2011

Oppure proprio donne.....

Bacco, tabacco e Venere

Andrea Coradi





Chou & Saw, *Can J Cardiol* 2014

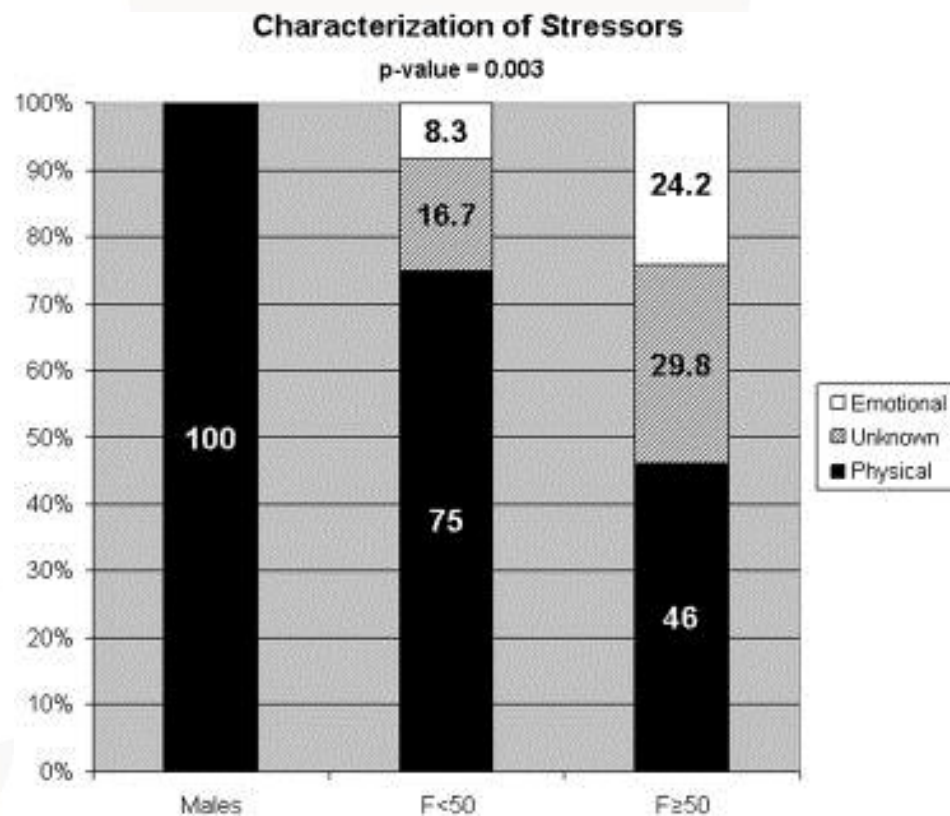
Esistono differenze di genere?

Gli uomini hanno più spesso uno stress fisico, le donne uno emotivo



Distinctive Clinical Characteristics According to Age and Gender in Apical Ballooning Syndrome (Takotsubo/Stress Cardiomyopathy): An Analysis Focusing on Men and Young Women

SANDEEP M. PATEL, MD,¹ RAMESH G. CHOKKA, MD,² KAVITA PRASAD, MD,³ AND ABHIRAM PRASAD, MD, FRCP, FACC²



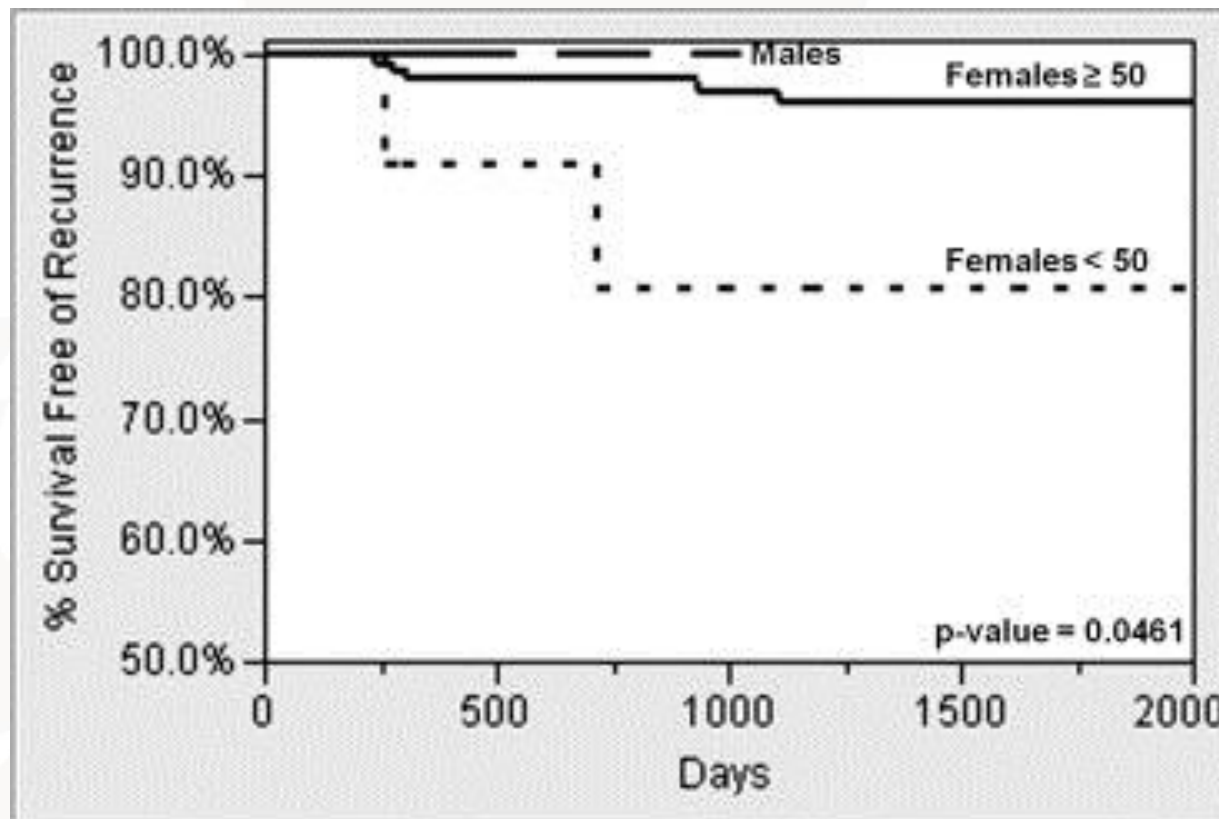
Patel et al, *J Cardiac Fail* 2013

Distinctive Clinical Characteristics According to Age and Gender in Apical Ballooning Syndrome (Takotsubo/Stress Cardiomyopathy): An Analysis Focusing on Men and Young Women

SANDEEP M. PATEL, MD,¹ RAMESH G. CHOKKA, MD,² KAVITA PRASAD, MD,³ AND ABHIRAM PRASAD, MD, FRCP, FACC²

N=224
M=12 (RR 0%)
F<50=12 (RR 16%)
F>50=200 (RR 3%)

RR recurrence rate



Patel et al, *J Cardiac Fail* 2013

Gender Differences in Patients with Takotsubo Cardiomyopathy: Multi-Center Registry from Tokyo CCU Network

Tsutomu Murakami, Tsutomu Yoshikawa*, Yuichiro Maekawa, Tetsuro Ueda, Toshiaki Isogai, Konomi Sakata, Ken Nagao, Takeshi Yamamoto, Morimasa Takayama

The Tokyo CCU Network Scientific Committee, Tokyo, Japan

	All patients (n = 368)	Male (n = 84)	Female (n = 284)	P value
Age (years) [range]	76 [67–82]	72 [64–81]	76 [68–83]	0.040
Hospitalization within 24 hours	86.7%	92.9%	84.9%	0.058
Symptom				
Chest pain	48.6%	39.3%	51.4%	0.051
Dyspnea	33.4%	35.7%	32.8%	0.613
Preceding stress				
No stress	36.1%	31.0%	37.7%	0.260
Physical stress ^a	35.6%	50.0%	31.3%	0.002
Emotional stress	28.3%	19.0%	31.0%	0.039
Vital signs				
Systolic blood pressure (mm Hg) [range]	133 [111–160]	131 [110–164]	134 [112–160]	0.690
Diastolic blood pressure (mm Hg) [range]	79 [66–91]	80 [64–92]	79 [67–91]	0.719
Heart rate (bpm) [range]	87 [75–108]	88 [72–114]	87 [75–104]	0.921
Arterial oxygen saturation (%) [range]	98 [95–99]	98 [94–99]	98 [95–99]	0.857

^a Physical stress included acute respiratory failure, central nervous system disorders, infection, post-surgery, trauma, etc.

doi:10.1371/journal.pone.0136655.t001

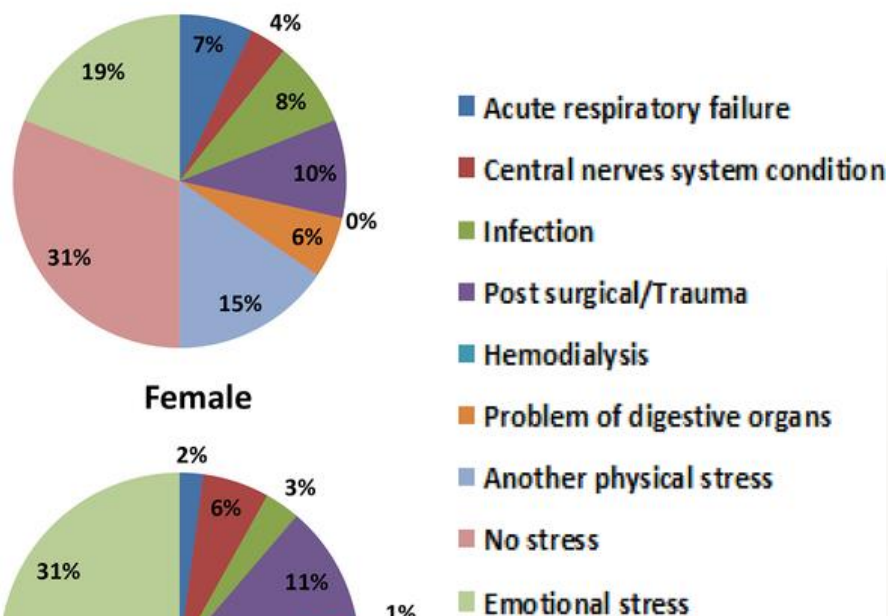
Murakami et al, *PLoS ONE* 2015

Gender Differences in Patients with Takotsubo Cardiomyopathy: Multi-Center Registry from Tokyo CCU Network

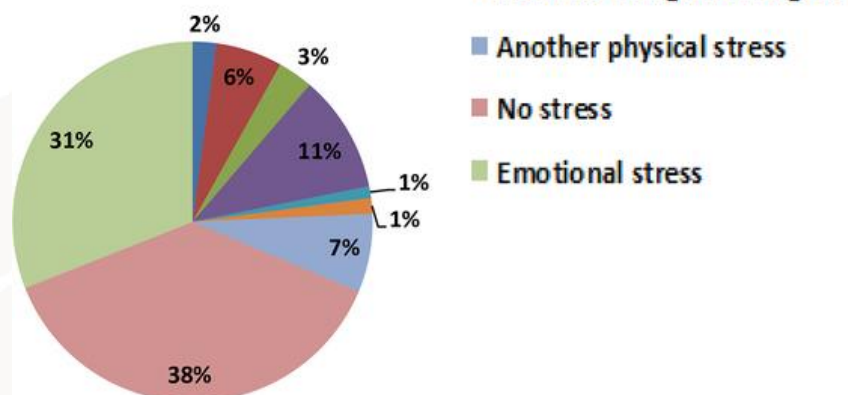
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The Tokyo CCU Network Scientific Committee, Tokyo, Japan

Male



Female



Murakami et al, *PLoS ONE* 2015

Gender Differences in Patients with Takotsubo Cardiomyopathy: Multi-Center Registry from Tokyo CCU Network

Tsutomu Murakami, Tsutomu Yoshikawa*, Yuichiro Maekawa, Tetsuro Ueda, Toshiaki Isogai, Konomi Sakata, Ken Nagao, Takeshi Yamamoto, Morimasa Takayama

The Tokyo CCU Network Scientific Committee, Tokyo, Japan

	Odds ratio	95% Confidence	P value
Male gender	4.32	1.41–13.6	0.011
Chronic kidney disease present	1.46	0.48–4.84	0.511
High age	1.12	0.36–3.47	0.839
High White blood cell count	4.38	1.38–16.9	0.011
High C-reactive protein level	1.42	0.45–4.70	0.548
High brain natriuretic peptide level	2.61	0.78–9.48	0.119
Low left ventricular ejection fraction	2.09	0.68–7.08	0.198
Physical stress present	0.92	0.28–2.79	0.878

doi:10.1371/journal.pone.0136655.t004

Stepwise multiple logistic regression analysis.

Murakami et al, *PLoS ONE* 2015

Gender differences in the manifestation of tako-tsubo cardiomyopathy

Birke Schneider ^{a,*}, Anastasios Athanasiadis ^b, Claudia Stöllberger ^c, Wolfgang Pistner ^d, Johannes Schwab ^e, Uta Gottwald ^f, Ralph Schoeller ^g, Birgit Gerecke ^h, Ellen Hoffmann ⁱ, Christian Wegner ^j, Udo Sechtem ^b

Clinical characteristics of 324 female and male patients with tako-tsubo cardiomyopathy.

Characteristics	Female		Male		p Value
Patients	296	(91%)	28	(9%)	
Age (years)	68 ± 12	(27–90)	66 ± 12	(37–84)	0.31
Symptoms					
Chest pain	217	(73%)	16	(57%)	0.08
Dyspnea	45	(15%)	5	(18%)	0.78
Syncope	9	(3%)	1	(4%)	0.60
Shock/Resuscitation	2	(1%)	4	(14%)	<0.001
Other	16	(5%)	1	(4%)	1.00
None	7	(2%)	1	(4%)	0.52
Triggering event	226	(76%)	24	(86%)	0.35
Emotional stress	111	(38%)	6	(21%)	0.10
Physical stress	88	(30%)	16	(57%)	0.005
Both	27	(9%)	2	(7%)	1.00
None	70	(24%)	4	(14%)	0.93
Time from symptom onset to hospital admission					
Hours	7.6 ± 6.8	(0–23.8)	7.2 ± 7.1	(0–23.0)	0.57
Cardiac markers					
CK median × ULN	1.17	(0.72–1.80)	1.55	(1.10–2.11)	0.05
CK-MB median × ULN	1.34	(0.85–2.20)	1.28	(0.75–1.77)	0.76
Troponin median × ULN	7.2	(2.9–17.9)	10.7	(7.6–29.0)	0.03
Angiography					
Symptom onset to angiography (days)	1	(0–2)	1	(0–2.75)	0.48
LV ejection fraction	49 ± 14	(18–81)	46 ± 15	(23–80)	0.23
Apical ballooning	189	(64%)	18	(64%)	1.00
Mid-ventricular ballooning	107	(36%)	10	(36%)	
Intraaortic balloon pump	2	(1%)	1	(4%)	0.24

Schneider et al, *Int J Cardiol* 2016

In-hospital mortality among patients with takotsubo cardiomyopathy: A study of the National Inpatient Sample 2008 to 2009

Waleed Brinjikji, MD,^a Abdulrahman M. El-Sayed, DPhil,^{b,c} and Samer Salka, MD, FACC^d Dearborn, MI; and New York, NY

	Takotsubo patients	n (%), mortality	Unadjusted mortality OR (95% CI)
n	24701	1027 (4.2)	—
Age, mean ± SD	66.9 ± 30.7	—	—
Age group			
< 50 y	2689 (10.9)	105 (3.9)	Ref
50-64 y	7290 (29.5)	245 (3.4)	0.86 (0.68-1.08)
> 64 y	14722 (59.6)	677 (4.6)	1.19 (0.96-1.46)
Gender			
Female, n (%)	21994 (89.0)	799 (3.6)	Ref
Male, n (%)	2707 (11.0)	228 (8.4)	2.44 (2.09-2.84)*
Race, n (%)			
White	16680 (84.0)	668 (4.0)	Ref
Black	1178 (5.9)	49 (4.2)	1.04 (0.77-1.40)
Hispanic	1032 (5.2)	50 (4.9)	1.22 (0.91-1.64)
Asian	353 (1.8)	15 (4.2)	1.06 (0.63-1.79)
Mean ± SD CCI	1.4 ± 2.7	—	—
Chronic comorbidities			
Obesity	1494 (6.1)	29 (2.0)	0.44 (0.31-0.64)*
HTN	14434 (58.4)	428 (3.0)	0.49 (0.44-0.56)*
Hyperlipidemia	9261 (37.5)	119 (1.3)	0.21 (0.17-0.25)*
Diabetes mellitus	4661 (18.9)	157 (3.4)	0.77 (0.64-0.91)*
Smoking	3250 (13.2)	81 (2.5)	0.56 (0.44-0.70)*
Malignancy	3547 (14.4)	288 (8.1)	2.45 (2.13-2.82)*
Anxiety disorder	2204 (8.9)	22 (1.0)	0.22 (0.14-0.34)*
Mood disorder	3696 (15.0)	67 (1.8)	0.39 (0.30-0.50)*

HTN, Hypertension; Ref, reference.

*P < .001.

Brinjikji et al, *Am Heart J* 2012

In-hospital mortality among patients with takotsubo cardiomyopathy: A study of the National Inpatient Sample 2008 to 2009

Waleed Brinjikji, MD,^a Abdulrahman M. El-Sayed, DPhil,^{b,c} and Samer Salka, MD, FACC^d Dearborn, MI; and New York, NY

	OR (95% CI)	P
Age group		
<50 y	Ref	Ref
50-64 y	1.01 (0.77-1.32)	.95
>64 y	1.04 (0.82-1.35)	.73
Gender		
Female	Ref	Ref
Male	2.07 (1.71-2.49)	<.0001
Race		
White	Ref	Ref
Black	0.87 (0.63-1.17)	.35
Hispanic	0.92 (0.67-1.24)	.59
Asian	0.65 (0.36-1.09)	.10
CCI*	1.19 (1.13-1.26)	<.0001
Underlying critical illness		
No	Ref	Ref
Yes	10.87 (9.08-13.08)	<.0001



Brinjikji et al, *Am Heart J* 2012

Out-of-hospital versus in-hospital Takotsubo cardiomyopathy: Analysis of 3719 patients in the Diagnosis Procedure Combination database in Japan[☆]

Toshiaki Isogai ^{a,b}, Hideo Yasunaga ^{a,*}, Hiroki Matsui ^a, Hiroyuki Tanaka ^b, Tetsuro Ueda ^b, Hiromasa Horiguchi ^c, Kiyohide Fushimi ^d

Multivariable logistic regression model for in-hospital mortality in patients with TC.

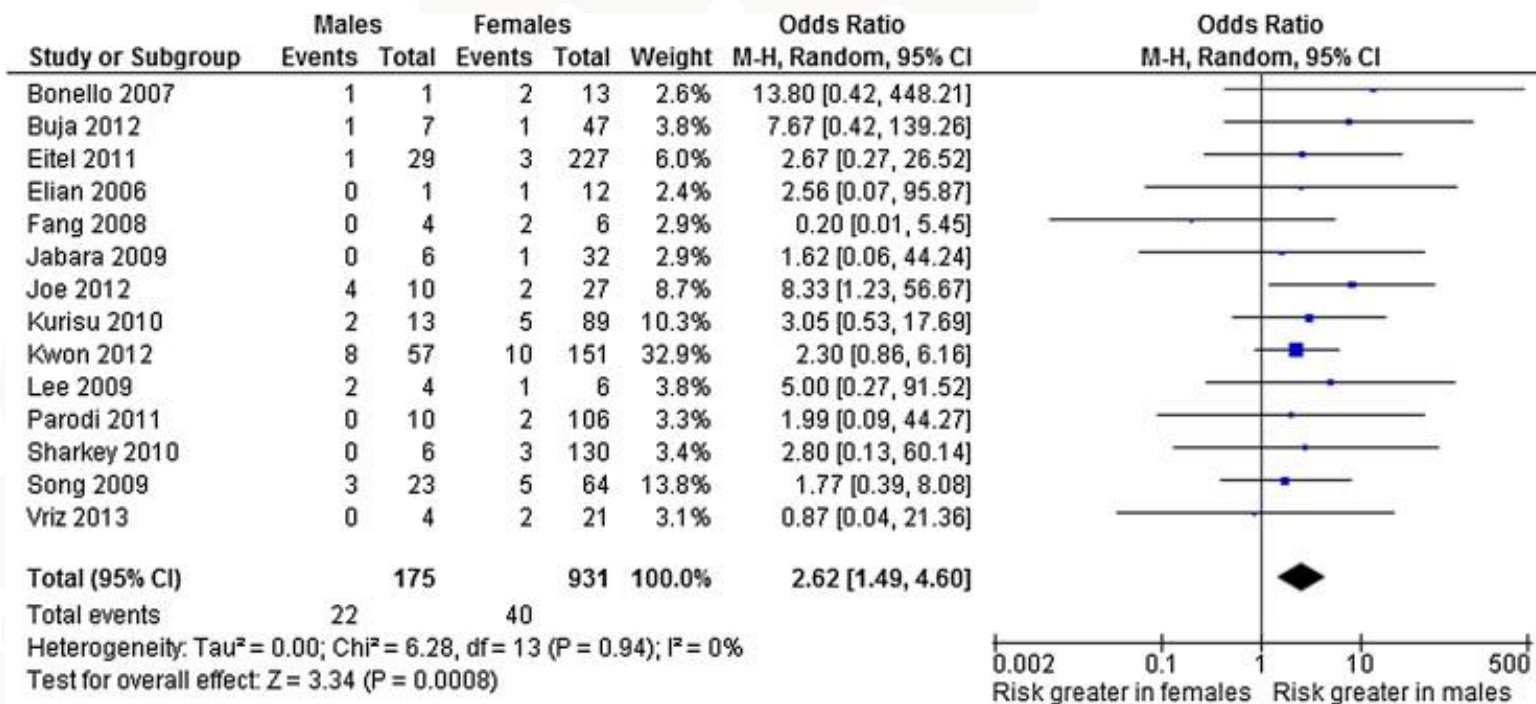
	Odds ratio	95% CI	p-Value
In-hospital TC (reference: out-of-hospital TC)	2.02	1.43 to 2.85	<0.001
Age (years), by 10-year increase	1.33	1.15 to 1.53	<0.001
Male sex (reference: female)	1.24	0.91 to 1.70	0.176
Ambulance use (reference: non-use)	1.09	0.82 to 1.47	0.550
Hospital volume (case/year)	1.03	0.98 to 1.07	0.216
Academic hospital (reference: non-academic hospital)	0.97	0.68 to 1.37	0.845
Japan Coma Scale at admission (reference: 0 [alert])			
1-3 (drowsy)	2.10	1.43 to 3.07	<0.001
Male sex (reference: female)			1.24
Chronic pulmonary disease	1.11	0.67 to 1.84	0.684
Chronic liver disease	2.69	1.33 to 5.42	0.006
Chronic renal failure	1.62	0.95 to 2.77	0.078
Peptic ulcer disease	0.99	0.53 to 1.85	0.966
Thyrotoxicosis	0.85	0.11 to 6.65	0.879
Rheumatic disease	2.92	1.46 to 5.83	0.002
Psychiatric disease	0.43	0.19 to 0.96	0.039
Sepsis	2.02	1.17 to 3.49	0.011
Pneumonia	3.07	2.15 to 4.38	<0.001
Cerebrovascular diseases	1.99	1.24 to 3.20	0.004
Acute renal failure	3.76	1.80 to 7.84	<0.001
Acute gastrointestinal diseases	2.51	1.16 to 5.41	0.019
Status asthmaticus	0.72	0.09 to 5.50	0.751
Seizure or status epilepticus	0.87	0.26 to 2.92	0.824
External injury	1.25	0.60 to 2.60	0.549
Surgical operation under general anesthesia within 7 days after admission	1.15	0.62 to 2.13	0.661

CI = confidence interval

Isogai et al, *Int J Cardiol* 2014

Meta-Analysis of Clinical Correlates of Acute Mortality in Takotsubo Cardiomyopathy

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Singh et al, *Am J Cardiol* 2014

Gender Differences and Predictors of Mortality in Takotsubo Cardiomyopathy: Analysis from the National Inpatient Sample 2009–2010 Database

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Variable	Total (n = 7,510)	Males (n = 705; 9.4%)	Females (n = 6,805; 90.6%)	p value ^a
Age, years	65.6 (64.9–66.2)	59.5 (56.6–62.3)	66.2 (65.5–66.8)	<0.001
Length of stay, days	4.9 (4.5–5.2)	5.9 (4.5–7.2)	4.8 (4.4–5.1)	0.12
Cardiometabolic risk factors				
Diabetes	1,507 (20)	112 (15.9)	1,395 (20.5)	0.19
Hypertension	4,619 (61.5)	393 (55.8)	4,226 (62.1)	0.14
Hyperlipidemia	3,304 (44)	249 (35.3)	3,055 (44.9)	0.03
Obesity	638 (8.5)	44 (6.3)	594 (8.7)	0.32
Tobacco	1,247 (16.6)	162 (22.9)	1,085 (15.9)	0.03
Prior CAD	3,525 (46.9)	335 (47.4)	3,190 (46.8)	0.89
Other risk factors				
Anxiety	753 (10)	48 (6.8)	705 (10.3)	0.17
Alcohol	244 (3.3)	64 (9.1)	180 (2.6)	<0.001
Cocaine	37 (0.5)	5 (0.8)	32 (0.5)	0.01
Amphetamine	9 (0.1)	9 (1.3)	–	<0.001
Depression	1,100 (14.7)	42 (5.9)	1,058 (15.6)	<0.01
Migraine	179 (2.4)	11 (1.5)	168 (2.5)	0.48
Seizure	95 (1.3)	20 (2.8)	75 (1.1)	0.08
Malignancy	360 (4.7)	48 (6.8)	312 (4.5)	0.23
Acute critical illness				
Sepsis	347 (4.6)	63 (9)	284 (4.2)	<0.01
Acute CVA	161 (2.2)	30 (4.2)	131 (1.9)	0.07
Respiratory failure	987 (13.1)	129 (18.2)	858 (12.6)	0.06
Acute renal failure	626 (8.33)	78 (11.1)	548 (8.1)	0.21
Complications				
Mortality	180 (2.4)	34 (4.8)	146 (2.1)	0.04
Ventricular arrhythmia	425 (5.7)	54 (7.7)	371 (5.4)	0.27
Sudden cardiac death	173 (2.3)	39 (5.6)	134 (1.9)	<0.01

Krishnamoorthy et al, *Cardiology* 2015

Takotsubo cardiomyopathy, sepsis and clinical outcome: does gender matter? ☆

Takotsubo cardiomyopathy and sepsis: in-hospital vs. out-of-hospital mortality

	Overall	Out-of-hospital	In-hospital	P
Male	3719 833 (22.4%)	3300 702 (21.3%)	419 131 (31.3%)	<.001
Female	2886 (77.6%)	2598 (78.7%)	288 (68.7%)	
Sepsis	105 (2.8%)	63 (1.9%)	42 (10.0%)	<.001
Multivariate analysis				
		Odds ratio	95% CI	P
In-hospital TC		2.02	1.43-2.85	<.001
Age (by 10-year increase)		1.33	1.15-1.53	<.001
Male sex (reference: female)		1.24	0.91-1.70	NS
Sepsis		2.02	1.17-3.49	.011

(Japan, Diagnosis Procedure Combination database 2010-2013) [19].

Takotsubo cardiomyopathy and sepsis: in-hospital mortality

			Mortality (OR, 95% CI)	P
All	24701 (100%)	Female 21994 (89.0%)		
		Male 2707 (11.0%)	2.44 (2.09-2.84)	<.05
Sepsis (all)		Female 1426 (6.5%)		
		Male 336 (12.4%)	2.04 (1.80-2.32)	<.001
Sepsis (fatal)	380 (21.6)	Female 296 (20.8%)	10.48 (8.97-12.25)	
		Male 84 (24.9)	5.12 (3.80-6.91)	<.001
Multivariate analysis				
Age			ref	
>50 y			1.01 (0.77-1.32)	NS
50-64 y			1.04 (0.82-1.35)	NS
>64 y				
Gender				
Female			ref	
Male			2.07 (1.71-2.49)	<.001
Underlying critical illness (including sepsis)				
NO			ref	
YES			10.87 (9.08-13.08)	<.001

(USA, National Inpatient Sample 2008 to 2009) [18].

Manfredini et al, *Am J Emerg Med* 2015

Cardiomiopatia Tako-Tsubo

Ruolo dello stress

Meccanismi patogenetici

Aspetti cronobiologici

Aspetti di genere

Take-home messages



**KEEP
CALM
AND
AVOID
TAKOTSUBO**