

# World Journal of *Cardiology*

*World J Cardiol* 2023 January 26; 15(1): 1-44



**ORIGINAL ARTICLE****Retrospective Study**

- 1 Does the intracoronary pressure differ according to two types (diffuse or focal) of coronary spasm?  
*Teragawa H, Oshita C, Uchimura Y*

**Observational Study**

- 13 Role of fibrinogen, albumin and fibrinogen to albumin ratio in determining angiographic severity and outcomes in acute coronary syndrome  
*Makkar K, Sharma YP, Batta A, Hatwal J, Panda PK*

**Prospective Study**

- 23 Feasibility and efficacy of delayed pharmacoinvasive therapy for ST-elevation myocardial infarction  
*Sethi R, Mohan L, Vishwakarma P, Singh A, Sharma S, Bhandari M, Shukla A, Sharma A, Chaudhary G, Pradhan A, Chandra S, Narain VS, Dwivedi SK*

**SYSTEMATIC REVIEWS**

- 33 Takotsubo cardiomyopathy following envenomation: An updated review  
*Mishra AK, George AA, John KJ, Arun Kumar P, Dasari M, Afraz Pasha M, Hadley M*

**ABOUT COVER**

Editorial Board Member of *World Journal of Cardiology*, Hiroki Teragawa, MD, PhD, Head of Department, Department of Cardiovascular Medicine, JR Hiroshima Hospital, 3-1-36 Futabanosato, Higashi-Ku, Hiroshima 732-0057, Japan. [hiroki-teragawa@jrhh.or.jp](mailto:hiroki-teragawa@jrhh.or.jp)

**AIMS AND SCOPE**

The primary aim of *World Journal of Cardiology (WJC, World J Cardiol)* is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJC mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

**INDEXING/ABSTRACTING**

The WJC is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 Journal Citation Indicator (JCI) for WJC as 0.35. The WJC's CiteScore for 2021 is 0.9, and Scopus CiteScore rank 2021: Cardiology and Cardiovascular Medicine is 260/336.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Hua-Ge Yu*; Production Department Director: *Xiang Li*; Editorial Office Director: *Yun-Xiao Jiao Wu*.

**NAME OF JOURNAL**

*World Journal of Cardiology*

**ISSN**

ISSN 1949-8462 (online)

**LAUNCH DATE**

December 31, 2009

**FREQUENCY**

Monthly

**EDITORS-IN-CHIEF**

Ramdas G Pai, Dimitrios Tousoulis, Marco Matteo Ciccone, Pal Pacher

**EDITORIAL BOARD MEMBERS**

<https://www.wjnet.com/1949-8462/editorialboard.htm>

**PUBLICATION DATE**

January 26, 2023

**COPYRIGHT**

© 2023 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Takotsubo cardiomyopathy following envenomation: An updated review

Ajay K Mishra, Anu A George, Kevin John John, Pramukh Arun Kumar, Mahati Dasari, Mohammed Afraz Pasha, Michelle Hadley

**Specialty type:** Cardiac and cardiovascular systems

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): B  
Grade C (Good): C  
Grade D (Fair): D  
Grade E (Poor): 0

**P-Reviewer:** Teragawa H, Japan;  
Wang Y, China

**Received:** September 11, 2022

**Peer-review started:** September 11, 2022

**First decision:** November 2, 2022

**Revised:** November 15, 2022

**Accepted:** November 15, 2022

**Article in press:** November 15, 2022

**Published online:** January 26, 2023



**Ajay K Mishra, Michelle Hadley**, Division of Cardiology, Saint Vincent Hospital, Worcester, MA 01608, United States

**Anu A George, Pramukh Arun Kumar, Mahati Dasari**, Department of Medicine, Saint Vincent Hospital, Worcester, MA 01608, United States

**Kevin John John**, Department of Medicine, Tufts Medical Center, Boston, MA 02111, United States

**Mohammed Afraz Pasha**, Department of Medicine, North Alabama Medical Center, Florence, AL 35630, United States

**Corresponding author:** Ajay K Mishra, MBBS, MD, Academic Fellow, Division of Cardiology, Saint Vincent Hospital, No. 123 Summer Street, Worcester, MA 01608, United States. [ajay.mishra@stvincenthospital.com](mailto:ajay.mishra@stvincenthospital.com)

### Abstract

#### BACKGROUND

Takotsubo cardiomyopathy (TTC) can be diagnosed in patients presenting with clinical features of acute coronary syndrome (ACS) by using Mayo clinic criteria. Multiple precipitators have been attributed to causing TTC. Rarely it has been reported to occur following an acute envenomation.

#### AIM

This review describes the various patterns, mechanisms, and outcomes of envenomation induced TTC.

#### METHODS

In this review, we included all studies on "TTC" and "envenomation" published in the various databases before June 2022. To be included in the review articles had to have a distinct diagnosis of TTC and an envenomation

#### RESULTS

A total of 20 patients with envenomation induced TTC were identified. Most episodes of envenomation induced TTC were reported following a bee sting, scorpion sting, and snake envenomation. Fear and anxiety related to the sting, direct catecholamine toxicity and administration of exogenous beta-adrenergic agents have been commonly postulated to precipitate TTC in these patients. 95%

of these patients presented with a clinical picture of ACS. Most of these patients also fulfill at least 3 out of 4 criteria of Mayo clinic criteria for TTC. Echocardiographic evidence of Apical TTC was noted in 72% of patients. 94% of these patients had clinical improvement following optimal management and 35% of these patients were treated with guideline directed medications for heart failure.

### CONCLUSION

Envenomation following multiple insect stings and reptile bites can precipitate TTC. Most reported envenomation related TTC has been due to bee stings and scorpion bites. Common mechanisms causing TTC were fear, anxiety, and stress of envenomation. Most of these patients present with clinical presentation of ACS, ST elevation, and elevated troponin. The most common type of TTC in these patients is Apical, which improved following medical management.

**Key Words:** Takotsubo cardiomyopathy; Envenomation; Mechanism; Outcome

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Multiple envenomations following insect stings and reptile bites can cause Takotsubo cardiomyopathy. Bee stings, wasp stings, scorpion stings, snake bites, spider bites, and jellyfish stings are the commonly reported precipitators of this cardiomyopathy. Multiple mechanisms have been postulated to cause this of which fear, anxiety, and stress of envenomation are the predominant ones. Patients usually present with clinical presentation of acute coronary syndrome, ST elevation, and elevated troponin. Echocardiography commonly shows an apical pattern of cardiomyopathy. This cardiomyopathy improves with medical management.

**Citation:** Mishra AK, George AA, John KJ, Arun Kumar P, Dasari M, Afraz Pasha M, Hadley M. Takotsubo cardiomyopathy following envenomation: An updated review. *World J Cardiol* 2023; 15(1): 33-44

**URL:** <https://www.wjgnet.com/1949-8462/full/v15/i1/33.htm>

**DOI:** <https://dx.doi.org/10.4330/wjc.v15.i1.33>

## INTRODUCTION

Takotsubo cardiomyopathy (TTC), aka stress cardiomyopathy, is a reversible left ventricular dysfunction syndrome precipitated by multiple emotional and environmental triggers[1]. Patient with TTC presents with the clinical picture of an acute coronary syndrome (ACS) including chest pain, abnormal cardiac enzymes, and electrocardiography (EKG) following a distinct trigger or acute stress [2]. It is most commonly reported in postmenopausal women worldwide. TTC has been reported in around 2% of patients presenting with an initial diagnosis of ACS[3].

As per the Revised Mayo Clinic Criteria, TTC can be diagnosed in the presence of the following four criteria: (1) Transient left ventricular (LV) dyskinesia extending beyond a single coronary distribution, (2) Absence of acute plaque rupture or obstructive coronary artery disease, (3) New EKG abnormalities or significant troponin elevation, and (4) absence of myocarditis or pheochromocytoma[4]. Most of the time with conservative medical management recovery of LV function occurs within 21 d in up to 95% of patients[3].

While the exact mechanisms resulting in the precipitation of TTC are not fully understood, most often it has been reported following an episode of sudden physical and emotional stressors resulting in high-catecholamine states. Over the last two decades, multiple different physical stressors have been reported to precipitate TTC[3,5]. Although uncommon TTC has been reported in patients following an episode of acute envenomation[6,7]. In this narrative review, we aimed to describe the current literature on the pattern, mechanism, and outcomes of envenomation induced TTC.

## MATERIALS AND METHODS

We searched the PubMed and Medline databases for the terms “TTC” and “envenomation”. We expanded our search using the names of various agents of envenomation including “snake”, and “scorpion” and “wasp” and “bee” and “spider” and “jellyfish”. We also searched in the google scholar and Reference Citation Analysis database with similar terms. We screened the references of the initially identified manuscripts for additional manuscripts. To be included in the review articles had to have a

distinct diagnosis of TTC and envenomation. Revised Mayo Clinical Criteria was used to screen for diagnosis of TTC. Envenomation had to be confirmed based on the toxidrome specific and unique to the agent. Although evidence of the absence of coronary artery disease based on cardiac catheterization was preferred, we did include reports using an alternating modality of imaging as well. All the studies published in English, including adults with an episode of recent envenomation and subsequent diagnosis of TTC were eligible to be included in this review. In this review, we included all studies published before June 2022. All the articles were independently screened by 2 different physicians. Articles lacking clinical details, opinions, comments, and letters were excluded from this review.

## RESULTS

As shown in the strobe diagram a total of 37 articles were identified (Figure 1). Among these 18 articles were eligible to be included in the review. Six of these articles were on bee sting precipitating TTC, 3 articles each on snake envenomation and scorpion sting, and 2 articles each on wasp, spider, and jellyfish envenomation induced TTC. A total of 20 patients with envenomation induced TTC were reported from thirteen different countries around the world. Tables 1 and 2 describe the details of the presentation, pattern, management, and outcome in each of these envenomations. We have described the characteristics of each of these individual envenomation related TTC below.

On bee sting precipitating TTC the total number of articles identified from various databases was 10, among which 6 articles with complete patient details were eligible to be included in the study. A total of 6 patients were reported to have TTC following a bee sting[8-12]. All these patients fulfilled at least 3 of the 4 mayo criteria for TTC as shown in Table 2. The mean age of these patients was 57, and all of them were females. The most common pattern of TTC noted was an apical type (67%). The various mechanisms that were postulated to precipitate TTC episodes were an anaphylactic reaction, epinephrine injection, catecholamine storm, cytokine storm, and direct cardiotoxic effect of the venom. Treatment details were available in 4 out of the 6 patients. Beta-blockers (BB) were used in 3 patients; Angiotensin converting enzyme inhibitors (ACEI) were used in 2 patients. Good outcome was reported in 4 patients, but multiorgan failure and death by cardiac rupture was reported in 1 patient. Interestingly improvement in a patient with cardiogenic shock was reported following mechanical circulatory support and extracorporeal membrane oxygenation.

The total number of articles on wasp envenomation and TTC identified from various databases was 5, among which 2 articles were eligible to be included in the study. A total of 2 patients were reported to have TTC following wasp envenomation[12-15]. Both the patient's fulfilled at least 3 of the 4 mayo criteria for TTC as shown in Table 2. The mean age of the patients was 75 and one of them was male. An apical pattern of TTC was noted in both patients. The mechanisms postulated to precipitate TTC episodes were an anaphylactic reaction and epinephrine injection secondary to the effect of the venom. Treatment details were available for both patients. BB and ACEI were used in both patients. No mortality was reported, and both patients had clinical improvement.

The total number of articles identified from various databases describing spider bite and TTC was 4, among which 2 articles had patient details and were eligible to be included in the study. A total of 3 patients were reported to have TTC following spider envenomation[16,17]. All these patients fulfilled at least 2 of the 4 mayo criteria for TTC as shown in Table 2. The mean age of the patients was 37 and two of them were female. Details of the pattern of TTC were not available in 2 of the 3 patients. The various mechanisms that were postulated to precipitate TTC episodes were a direct cardiotoxic effect of the venom, catecholamine storm, epinephrine, and anti-venom injection. Treatment details were not available for most of the patients. BB and ACEI were used in one patient. All three patients had improvement following treatment.

Snake envenomation precipitating TTC related articles identified from databases were 4, among which 3 articles were eligible to be included in the study. A total of 3 patients were reported to have TTC following snake bite and subsequent envenomation[18-20]. All patients fulfilled at least 3 of the 4 mayo clinic criteria for TTC as shown in Table 2. The mean age of the patients was 60 and two of them were female. An apical type of TTC was noted in all patients with additional involvement of the mid left ventricle in two. Catecholamine surge secondary to emotional stress because of snake bite was thought to be the underlying pathology of TTC. Only one patient was treated with guideline directed therapy for LV dysfunction with BB, ACEI, and a diuretic, while others received supportive care. All the patients recovered completely.

Scorpion sting related TTC articles that were identified from databases were 6. Three articles were eligible to be included in our study. A total of four patients were reported to have TTC following scorpion bite related envenomation[6,7,21-23]. All patients fulfilled at least 3 of the 4 mayo clinic criteria for TTC as shown in Table 2. The mean age of the patients was 31 and the gender distribution was equal. Apical type of TTC was noted in 2 patients and basal type of TTC in the other two patients. Abnormal response to catecholamines mediated through microvascular dysfunction, alpha toxins acting on sodium channels in the autonomic center leading to sympathetic excitation and release of catecholamines as well as a massive outpouring of catecholamines were suggested to be the precip-

**Table 1** Baseline demographic characteristics and presenting features of study participants demographic characteristics of study participants

Ref.	Year of publication	Country	Age	Gender	Comorbidity	Clinical presentation
<b>Bee</b>						
Mishra <i>et al</i> [8]	2016	USA	63	F	Unknown	Rash, diaphoresis, chest pain, dyspnea
Aono <i>et al</i> [9]	2019	Japan	87	F	Unknown	Multiple bee stings with multi-organ failure
Seecheran <i>et al</i> [10]	2021	Caribbean	48	F	None	Obtunded, somnolent
Winogradow <i>et al</i> [12]	2011	Germany	37	F	Unknown	Local itching, spreading hives
Winogradow <i>et al</i> [12]	2011	Germany	70	F	Unknown	Swelling of throat, chest pain
Ghanim <i>et al</i> [11]	2015	Israel	37	F	None	Rash, dyspnea, impaired consciousness
<b>Wasp</b>						
Scheiba <i>et al</i> [13]	2011	Germany	81	M	Unknown	Absent pulses, gasping, unconsciousness
Geppert <i>et al</i> [14]	2010	Germany	70	F	Unknown	Chest pain and dyspnoea
<b>Spider</b>						
Alexakis <i>et al</i> [16]	2015	Greece	64	F	Hyperthyroidism	Nausea, tremor, infraorbital edema, diffuse abdominal pain, lower extremity muscle cramps
Isbister <i>et al</i> [17]	2015	Australia	33	M	Unknown	Perioral paresthesia, widespread fasciculation, diaphoresis, hypersalivation, dyspnea
Isbister <i>et al</i> [17]	2015	Australia	13	F	Unknown	Localized intense pain, urinary incontinence, profuse sweating, and vomiting
<b>Snake</b>						
Van Rensburg <i>et al</i> [18]	2015	South Africa	58	M	None	Bilateral ptosis
Murase <i>et al</i> [19]	2012	Japan	56	F	Unknown	Swelling of left foot
Delumgahawaththa <i>et al</i> [40]	2021	Sri Lanka	66	F	Hypertension, hyperlipidemia	Central chest pain
<b>Scorpion</b>						
Abroug <i>et al</i> [29]	2018	Tunisia	36	F	Unknown	Pulmonary edema, shock
Abroug <i>et al</i> [29]	2017	Tunisia	45	F	Unknown	Altered level of consciousness, respiratory failure, shock
Miranda <i>et al</i> [23]	2015	Brazil	7	M	Unknown	Localized pain, vomiting, profuse sweating, dyspnea
Jain <i>et al</i> [27]	2006	India	35	M	Unknown	Mild local pain, irritation
<b>Jellyfish</b>						
Bianchi <i>et al</i> [24]	2011	Italy	53	F	Unknown	Chest pain, fatigue, localized intense itch
Tiong <i>et al</i> [25]	2009	Australia	26	M	Unknown	Localized pain, restlessness, agitation, palpitations

USA: United States of America, M: Male, F: Female.

itators of TTC. Among the four patients, the first patient was treated with continuous positive airway pressure and dobutamine infusion, the second patient with intravenous furosemide, and the third patient with systemic steroids along with inotropic drugs. Except for the utilization of diuretics, these 3 patients were not treated with guideline directed therapy for LV dysfunction. However, complete recovery was reported in all patients within seven days.

Regarding Jelly Fish envenomation precipitating TTC, three articles were identified from databases. Two articles with one patient each had TTC following a jellyfish envenomation[24,25]. These patients fulfilled at least 3 of the 4 mayo clinic criteria for TTC as shown in Table 2. The mean age of the patients was 40 and one of them was male. Mid ventricular ballooning was noticed in both patients, with one patient showing apical involvement as well. Precipitators of TTC in these patients were thought to be secondary to stress, venom, and excess endogenous catecholamine release. These 2 patients were not treated with any medications for guideline directed therapy for LV dysfunction. Both patients were treated symptomatically and completely recovered within a week.

Table 2 Details of diagnosis, treatment, and outcome in study participants

Ref.	Agent	Mayo criteria	Type	Mechanism	Rx	Outcome
Mishra <i>et al</i> [8]	Bee	Apical hypokinesia, LVEF – 40 to 45%; Absence of CAD; ST elevation, T wave inversion Troponin elevation	Apical	-Cytotoxic storm; - Direct cardiotoxic effects of bee venom; - Anaphylactic reaction	-ACEI; -BB	Improved
Aono <i>et al</i> [9]	Bees (Multiple)	Apical hypokinesia; Absence of CAD; ST elevation in I, II, aVL, aVf, V2 to V6 and raised Troponin	Apical			-Multi organ failure; - Death by cardiac rupture
Seecheran <i>et al</i> [10]	African Bee	Apical hypokinesia; Absence of CAD; ST elevation in V1, V2, V3, raised Troponin	Apical	-Cytokine storm; - Anaphylaxis	-ARNI; - Eplerenone; - Bisoprolol; - Dapagliflozin	Improved
Winogradow <i>et al</i> [12]	Bee	Anterior, lateral, and Posterior hypokinesia; Absence of CAD; ST elevation in VI and raised Troponin	Reverse	-	-BB; -ACEI; - Aldosterone agonist	-
Winogradow <i>et al</i> [12]	Bee	Apical wall hypokinesia; Absence CAD; VFIB	Apical	-Hypersensitivity; - Epinephrine Injection	-	-
Ghanim <i>et al</i> [11]	Bees	Basal and Mid hypokinesia; Absence of CAD; ST elevation in lateral leads and depression in anterior and inferior leads and raised Troponin	Reverse	-Catecholamine storm; -Epinephrine injection	-IABP; - VAECMO; - Adrenaline; - Norepinephrine and Dopamine	Improved
Scheiba <i>et al</i> [13]	Wasp	Apical and anteroseptal hypokinesia, LVEF – 45%; Absence of CAD; ST elevation in I, aVL, V2-V4 and Troponin elevation	Apical	-Hypersensitivity; - Epinephrine Injection	-BB; -ACEI; - Aspirin	Improved
Geppert <i>et al</i> [14]	Wasp	Apical (anterior and inferior) and anteroseptal hypokinesia (46%); Absence of CAD; ST segment elevations in the leads, V1–V3, T-negatives in leads I, aVL and V2 –V4 and raised Troponin	Apical	-Epinephrine injection	-Bisoprolol; - Ramipril; - Aspirin	Improved
Alexakis <i>et al</i> [16]	Black widow spider	Hypokinesia of the basal and middle segments of the LV wall with apical sparing, LVEF – 36%; CAG not done; T wave flattening in aVL, and Troponin elevation	Reverse	-Alpha-ladrotroxin mediated catecholamine storm; -Cytokine storm	- BB; -ACEI; - Aspirin; - Clopidogrel	Improved
Isbister <i>et al</i> [17]	Funnel web spider	Diffuse global hypokinesia with LVEF of 20%; CAG not done; Diffuse ST changes and troponin elevation	-	-Toxin; -Antivenom; -Catecholamine storm		Improved
Isbister <i>et al</i> [17]	Funnel web spider	Reduced EF- 45%; CAG not done; ST depression in the inferior and anterior leads and elevated troponin	-	-Toxin; -Antivenom; -Adrenaline		Improved
Van Rensburg <i>et al</i> [18]	Cape Cobra	Mid and apical LV segment hypo or akinetic, LVEF: 27%, Absent CAD; New ST elevation across anterolateral leads, subsequent EKG showing T wave inversions in anterolateral leads, raised troponin	Mid ventricular and apical; (Apical ballooning)	-Catecholamine storm; -Cytokine storm; - Catecholamine; release associated with Intensive Care Unit medication	Supportive care; Anti-snake venom administered for snake bite	Recovery of RWMA within a week (ECHO)
Murase <i>et al</i> [19]	<i>Gloydius blomhoffii</i> Snake ( <i>Mamushi</i> )	Abnormal LV systolic function, apical akinesis, hyperdynamic basal segment of LV; No stenotic lesions noted on the CT scan; EKG changes T inversions in 1, a	Apical	-Unknown	Supportive management; No Anti snake venom	Complete recovery (ECHO); (4 d)

		VL, V1-6, raised troponin				
Delumgahawaththa <i>et al</i> [40]	<i>Unidentified (Possibly Russel Viper)</i>	Hypokinetic mid and apex of LV segments, with ballooning, LVEF: 35%; Absence of CAD; EKG changes with ST elevation in 1 and a VL, T wave inversion II, III, a VF, V 2-6, Troponin elevation	Mid LV and Apical LV	-Catecholamine storm; -Direct myocardial toxicity; -Microvascular spasm	ACEI, BB, Diuretic, single antiplatelet, statin; Anti-snake venom	Partial recovery in 1 mo and complete in 5 mo (ECHO)
Abroug <i>et al</i> [29]	<i>Androctonus australis</i>	Patient 1: Basal ballooning of left and right ventricles; CAG not done; Troponin elevation; ST depression in four precordial leads; No other causes to explain the cardiac dysfunction. Patient 2: Impaired systolic function on echocardiogram. Basal ballooning on cardiac MRI in 24 hours; CAG not done; Troponin and ProBNP elevation; No other causes to explain the cardiac dysfunction	Basal ballooning in both patients	-Catecholamine storm; - Microvascular dysfunction	-CPAP, Dobutamine infusion; -No management mentioned	Patient 1: Discharged in 5 d, MRI in one month was normal. Patient 2: Discharged in 4 d with normal LV function on repeat echocardiography examination before discharge
Miranda <i>et al</i> [23]	<i>Tityus serrulatus</i>	Apical ballooning with hypokinesia; CAG not done; ST segment elevation in V1-V3, DI and aVL; No other causes to explain the cardiac dysfunction	Apical	-Alpha toxins act on voltage-gated sodium channels causing catecholamine storm; -Cytokine storm	-IV furosemide	Day 6 - asymptomatic, discharged; Cardiac MRI in 7 mo showed complete recovery of wall motion in apical region
Jain <i>et al</i> [27]	<i>Mesobuthus tamulus</i>	Apical, apicolateral hypokinesia; CAG not done; ST segment elevation in V1-V3 and T wave inversion; Absence of other causes of cardiac dysfunction	Apical	-Catecholamine storm; - Microvascular dysfunction	-Systemic steroids, inotropic drugs;	-Improved LVEF in 7 d; -Cerebellar infarction with clinical signs
Bianchi <i>et al</i> [24]	<i>Pelagia noctiluca</i> - A common Mediterranean jellyfish	Apical akinesis with severe left ventricular dysfunction; Absence of CAG; Acute myocardial infarction including persistent ST elevation despite thrombolysis performed for symptom relief and raised Troponin	Apical and mid-ventricular	-Direct toxicity; - Catecholamine storm; -Cytokine storm	-Symptomatic management	Improved. Completely symptom free, improved LVEF in 7 d
Tiong <i>et al</i> [25]	<i>Carukia barnesi</i> - A cubozoan/box jellyfish found in Australia	Mid-ventricular stress cardiomyopathy with apical sparing; No CAG; Persistent hyperacute T waves, rise in troponin	Mid-ventricular ballooning with apical sparing	-Sympathetic overdrive; - Catecholamine storm	-Supportive with high flow oxygen, morphine; - Magnesium sulfate IV	- Improved, discharged in 3 d

aVL: Augmented unipolar lead L; aVF: Augmented unipolar lead F; LV: Left Ventricle; LVEF: Left ventricular ejection fraction; ACEI: Angiotensin converting enzyme inhibitor; BB: Beta blocker; CAD: Coronary artery disease; CAG: Coronary angiogram; ARNI: Angiotensin receptor-neprilysin inhibitor; VFIB: Ventricular fibrillation; ECHO: Echocardiography; EKG: Electrocardiogram; IV: intravenous; RWMA: Regional wall motion abnormality; CT: Computed tomography; MRI: Magnetic resonance imaging; CPAP: Continuous positive airway pressure; Pro BNP: Pro brain natriuretic peptide; IABP: Intra-aortic balloon pump; VAECMO: Veno-arterial extra corporeal membrane oxygenation.

## DISCUSSION

TTC, aka stress induced cardiomyopathy, transient apical ballooning syndrome, and broken heart syndrome is a reversible cardiomyopathy that is increasingly being diagnosed in patients presenting with ACS following a triggering event, precipitator. Multiple emotional, environmental, physical, and iatrogenic triggers have consistently been reported to precipitate such events[1-3,5,26]. While multiple stressors have been known to predispose TTC, in this review article, we highlight the multiple reported cases of TTC following envenomation which has not been reviewed before. In this descriptive review, we also discuss the various mechanisms of envenomation that have been postulated to precipitate TTC in the medical literature. Envenomation and stings have various cardiac complications including vasovagal episodes, myocarditis, ACS, and TTC. In this review, we have specifically focused on their implications in the presence of TTC. As mentioned in **Figure 2** multiple mechanisms have been postulated to result in sympathetic activation which ultimately precipitates the transient LV

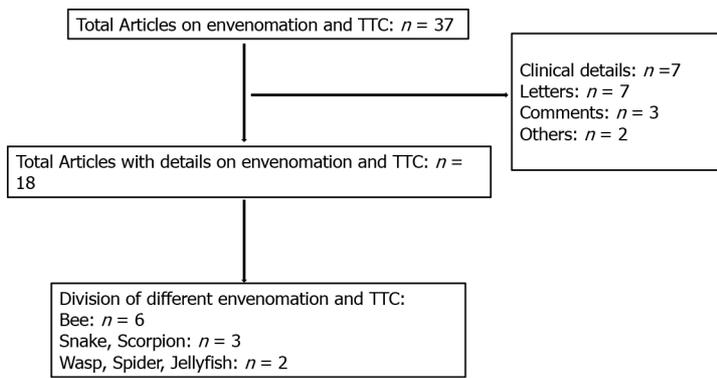


Figure 1 Strobe diagram showing the flow of the articles. TTC: Takotsubo cardiomyopathy.

Agent	Fear/Anxiety	Cytokine storm	Direct Injury	Anaphylaxis/Hypersensitivity	Epinephrine
Bee	+	+	+	+	+
Wasp	+	-	-	+	+
Spider	+	+	+	-	+
Snake	+	-	+	-	+
Scorpion	+	+	+	-	+
Jelly fish	+	-	+	-	-

DOI: 10.4330/wjc.v15.i1.33 Copyright ©The Author(s) 2023.

Figure 2 Various mechanisms precipitating takotsubo cardiomyopathy following envenomation.

dysfunction. Excessive sympathetic stimulation in these patients could be initiated by stress and subsequently worsen in the presence of another mechanism. Five distinct mechanisms have been consistently reported across the literature.

**Fear, Anxiety, emotional stress**

The sudden and accidental exposure to a sting or a bite that is perceived as threatening can result in peak stress. Acute emotional stress is known to increase regional cerebral blood flow in the hippocampus, brainstem, and basal ganglia and increase brain activation along with an increasing concentration of epinephrine and norepinephrine in the brain simultaneously. After an episode of acute stress, the interaction of the neocortex, limbic system, reticular activating system, brain stem, and spinal cord results in the interpretation of the stimulus as a threat. Subsequently, activation of the brainstem results in a neural stress response which results in the secretion of norepinephrine from locus coeruleus in the brain which then stimulates the hypothalamic-pituitary-adrenal axis. The sympathetic pathway through the posterior hypothalamus descends to the spinal cord and facilitates the release of norepinephrine. This increased catecholamine secretion from sympathetic nerve endings and secretion of epinephrine and norepinephrine from chromaffin cells in the adrenal medulla can subsequently affect the cardiac adrenergic receptors. Which subsequently contributes to the classical presentation of TTC. As shown in Figure 2, emotional stress was the precipitator of TTC across all the bites[18,27-29].

**Cytokine storm**

During an animal bite or an envenomation, venom is injected with the help of stinging apparatus into the dermal-epidermal junction, subcutaneous tissues, vessels, or muscle fibers. Venoms are chemically a diverse mixture of proteins, amines, and salts produced for predation or protection and can result in significant injury on injection to humans as well. Following the bite metalloproteinase, and L-Amino acid oxidase present in these venoms result in local dermal proteolysis, tissue destruction, and apoptosis, subsequently providing access to toxins to circulation, and target organ. Once within circulation, these toxins can alter the structure and function of endothelial cells. These agents are not only highly proinflammatory resulting in the secretion of excessive inflammatory markers they also precipitate dysregulation of neutrophils, mononuclear phagocytic system, and granulocytes thus

accelerating inflammation and cell damage. Dysregulation and excessive stimulation of these cytokines, and pro inflammatory mediators result in cytokine storm causing multiorgan dysfunction. Multiple infections [including Novel coronavirus disease 19 (COVID-19)], toxins, cancers, and diseases are known to cause TTC due to cytokine storms precipitated by endothelial dysfunction[18,30,31].

### **Direct catecholamine injury/toxicity**

Emotional stress like pheochromocytoma is associated with an excessive outburst of catecholamine. In patients with TTC, catecholamine levels can be extremely high as compared to other cardiac diseases. Similarly, patients with TTC have been shown to have higher ventricular catecholamine sensitivity. Alpha ladtotoxin in spider venom and alpha toxin in scorpion venom has been reported to precipitate catecholamine storm. Subsequently, excessive norepinephrine released from cardiac sympathetic nerve terminals can result in a reduction of cardiac myocyte viability. Transient elevations of catecholamines in TTC result in localized focal mononuclear inflammatory cells, fibrosis, and contractions bands in cardiac myocytes. This is evident with elevated cardiac enzymes and localized areas of edema, without late enhancement in magnetic resonance imaging. Direct catecholamine injury was also commonly reported to be the precipitate TTC following all the envenomations[28,31-33].

### **Anaphylaxis/ Hypersensitivity**

Anaphylaxis secondary to bites and envenomation is immunoglobulin E (IgE) mediated. In patients with prior sensitization, systemic reactions can occur in up to 9% of patients. Major allergens like Antigen 5, phospholipase A1, phospholipase A2, hyaluronidase, and acid phosphatase can precipitate classic Ig E mediated anaphylactic response. Subsequently, mast cells and basophils degranulate releasing proinflammatory markers including histamine and proteases. Which results in the activation, influx, and migration of neutrophils and lymphocytes and the secretion of chemokines and cytokines. Anaphylaxis induced myocardial injury can be diverse. In a study including 300 patients with anaphylaxis myocardial injury was reported in 7.3% of patients. The etiologies of myocardial injury were anaphylactic cardiomyopathy, TTC, and Kounis syndrome. The causes of excessive catecholamine release precipitating TTC in anaphylaxis are multifactorial. Histamine can stimulate the adrenal medulla directly to produce catecholamine, compensatory catecholamine release due to activation of the renin-angiotensin-aldosterone axis, and external administration of adrenaline for anaphylaxis and norepinephrine for persistent shock. This form of TTC was only reported following bee and wasp stings [3,28,31,33].

### **Exogenous Beta-adrenergic receptor stimulation**

In normal patients beta1-adrenergic receptor (B1AR) and B2AR receptors density are highest in the apex, thus making it susceptible to exposure to higher levels of catecholamine. Following exposure to suprathereapeutic doses of catecholamine signal trafficking of catecholamine receptors occurs, which is a form of protective response of cardiac myocytes to stress. This switching of Gs to Gi coupling of B2AR receptors results in reduced inotropy and apoptosis of cardiac myocytes. This suprathereapeutic level of catecholamine surge is classical of pheochromocytoma thus requiring evaluation of the same and has been incorporated into the Mayo clinic criteria for diagnosis of TTC. Exogenous catecholamines have been consistently reported to precipitate TTC. TTC has been reported following the administration of epinephrine to patients subcutaneously, intravenously, and through inhalation. Iatrogenic large volume adrenaline injection has also been reported to precipitate TTC. As shown in Image 2 exogenous catecholamine injection was the second most reported mechanism of TTC after emotional stress in these patients[11-13,28,31,34-37].

Multiple other mechanisms including microvascular dysfunction and spasm, abnormal myocardial metabolism and intracellular lipid accumulation, myocardial inflammation, estrogen excess, and endothelial dysfunction have been postulated[28,31,38]. In patients with envenomation induced TTC, multiple mechanisms can initiate and precipitate cardiac dysfunction.

### **Clinical Profile**

In this narrative review, we summarized the clinical features following envenomation induced TTC. Most insect stings and reptile bites are accidental. Following these bites and stings, clinical manifestations can vary from an asymptomatic state and mild local reactions to severe multiorgan dysfunction based on the dose and the characteristics of the venom. TTC can occur irrespective of prior cardiac comorbidities and in absence of traditional cardiac risk factors. To summarize the clinical features of these envenomations with TTC we combined the episodes of TTC following all the envenomation. To date envenomation resulting in TTC has been described in the above-mentioned animals. Almost all these patients presented with a clinical picture of ACS (95%) and had EKG changes and elevated troponin (100% each). Sixty percent of these patients had ST segment elevation ( $n = 12$ ), and 15% of them had ST depression and T wave inversion simultaneously ( $n = 3$ ). Among patients with echocardiographic evidence of TTC ( $n = 18$ ), Apical TTC was found in 72% of patients ( $n = 13$ ), reverse TTC in 28% ( $n = 5$ ), and midventricular TTC was reported in 17% ( $n = 3$ ) of patients. Details of Coronary angiogram (CAG) were mentioned in 85% of patients ( $n = 17$ ) and all the CAG were negative for any acute

obstructive disease.

Conservative medical management was initially done on all the patients. Management was mostly physician directed and clinical feature driven. Medications for heart failure management were given to 35% ( $n = 7$ ) of patients. These 7 patients were treated with ACEI, and BB together. Inotropic agents were used in 15% ( $n = 3$ ) and aldosterone agonist was used in 10% ( $n = 2$ ) of patients. Details of clinical outcomes were available for 18 patients among whom 17 (94%) had clinical improvement. Improvement in LV ejection fraction (LVEF) and regional wall motion abnormality was reported in all patients with clinical improvement. Death occurred in one patient following multi organ dysfunction and cardiac rupture after multiple bee stings. As *per* the author's knowledge, this is the first review summarizing the various mechanisms, clinical features, management, and outcome following envenomation's precipitating TTC[34,35,39].

This review has a few limitations. All patients with TTC secondary to envenomation were included from case studies spanning more than a decade. Most studies did not rule out pheochromocytoma. Most of these patients did not have baseline echocardiography before admission. Studies also lacked details of CAG at presentation and echocardiographic details during follow up. Even though multiple mechanisms of TTC were considered, case studies did not report levels of inflammatory markers, catecholamine levels, IgE levels, Eosinophil counts, or advanced cardiac imaging. Most of these reports did not mention the different components of the venom which were instrumental in the precipitation of TTC[39,40]. Classification of the severity of these toxidromes, varied treatment protocols and non-availability of recurrence, functional status at discharge, and long term follow up data continue to be a challenge[3,4,26,33,33,39-41]. However, this review has the strength of describing the patterns and mechanisms of envenomation related TTC and their outcome. We also recommend that future case studies should focus on using a uniform diagnostic criterion for diagnosing and reporting TTC from episodes of stings or envenomation. Future studies should identify specific components in the venom precipitating catecholamine storm, microvascular injury, and myocardial damage[42-44]. Uniform echocardiography at diagnosis and follow up should be done consistently. All available details including imaging modalities and pattern of cardiac involvement should be consistently reported[45]. Given the rarity of these events, randomized trials on these specific etiologies might be difficult, interim optimal medical management during the envenomation and goal directed therapy for heart failure should be considered in patients who have evidence of LV dysfunction with low ejection fraction, unless complete recovery of clinical symptoms, signs, and LVEF is documented at the time of discharge from hospital. Guideline directed heart failure medications including BB and ACEI can be administered and consistent reporting of these subgroups of patients should be encouraged.

## CONCLUSION

In conclusion, multiple insect stings and reptile bites related envenomation can precipitate TTC. Most envenomation related TTC has been due to bee stings and scorpion bites. Fear and anxiety related to the sting, direct catecholamine toxicity, and administration of exogenous beta-adrenergic agents have been commonly postulated to precipitate TTC in these patients. Most of these patients present with clinical presentation of ACS, ST elevation, and elevated troponin. Most of these patients also fulfill at least 3 out of 4 criteria of Mayo clinic criteria for TTC. The most common type of TTC in these patients is Apical, which improves following medical management. One third of these patients were treated with ACEI and BB with reported improvement in outcome.

## ARTICLE HIGHLIGHTS

### **Research background**

Multiple different physical, emotional and iatrogenic stressors have been known to precipitate stress induced cardiomyopathy also called takotsubo cardiomyopathy (TTC).

### **Research motivation**

Rarely TTC has been reported in patients following an episode of acute envenomation secondary to insect stings and reptile bites.

### **Research objectives**

This review aimed to narrate the current literature on the patterns, mechanisms, and outcomes of envenomation induced TTC.

### **Research methods**

This review included all studies on "TTC" and "envenomation" published in PubMed, Google Scholar,

and Reference Citation Analysis databases before June 2022. Articles had to have a distinct diagnosis of TTC with Revised Mayo Clinical Criteria and documented envenomation.

### Research results

Envenomation related TTC was reported from all over the world. The reports of envenomation induced TTC were reported mostly following a bee sting, scorpion sting, and snake envenomation. Fear and anxiety related to the sting, direct catecholamine toxicity, and administration of exogenous beta-adrenergic agents were postulated to precipitate TTC in these patients. Most patients presented with a clinical picture of acute coronary syndrome (ACS), ST elevation, and elevated troponin. Echocardiographic evidence of Apical TTC was noted in most of the patients. Almost all of these patients had clinical improvement following optimal management.

### Research conclusions

Envenomation following multiple insect stings and reptile bites can precipitate TTC. Most reported envenomation related TTC has been due to bee and scorpion stings. Common mechanisms causing TTC following envenomation are fear, anxiety, and stress. Most of these patients present with clinical presentation of ACS. The most common type of TTC in these patients is Apical, which improved following medical management.

### Research perspectives

Multiple envenomations following insect stings and reptile bites can cause TTC. Worldwide bee stings, wasp stings, scorpion stings, snake bites, spider bites, and jellyfish stings are the commonly reported precipitators of this cardiomyopathy. Multiple mechanisms have been postulated to cause this of which fear, anxiety, and stress of envenomation are the predominant ones. Patients usually present with a clinical presentation of ACS. Echocardiography commonly shows an apical pattern of cardiomyopathy. This cardiomyopathy improves with medical management.

---

## FOOTNOTES

**Author contributions:** Mishra AK, George AA, Hadley M planned and formulated the study; George AA, John KJ, ArunKumar P, Dasari M, Pasha MA collected and analyzed the data; Mishra AK, George AA completed the manuscript; Mishra AK, Hadley M reviewed the manuscript and Hadley M approved the manuscript; All authors reviewed and agreed with the final content of the article.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**PRISMA 2009 Checklist statement:** All the authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** United States

**ORCID number:** Ajay K Mishra [0000-0003-4862-5053](https://orcid.org/0000-0003-4862-5053); Anu A George [0000-0002-6769-732X](https://orcid.org/0000-0002-6769-732X); Kevin John John [0000-0003-3382-0294](https://orcid.org/0000-0003-3382-0294); Pramukh Arun Kumar [0000-0003-3497-1334](https://orcid.org/0000-0003-3497-1334); Mahati Dasari [0000-0003-0578-8944](https://orcid.org/0000-0003-0578-8944); Mohammed Afraz Pasha [0000-0001-6629-6690](https://orcid.org/0000-0001-6629-6690).

**S-Editor:** Liu GL

**L-Editor:** A

**P-Editor:** Liu GL

---

## REFERENCES

- 1 **Prasad A**, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *Am Heart J* 2008; **155**: 408-417 [PMID: [18294473](https://pubmed.ncbi.nlm.nih.gov/18294473/) DOI: [10.1016/j.ahj.2007.11.008](https://doi.org/10.1016/j.ahj.2007.11.008)]
- 2 **John K**, Lal A, Mishra A. A review of the presentation and outcome of takotsubo cardiomyopathy in COVID-19. *Monaldi Arch Chest Dis* 2021; **91** [PMID: [33759445](https://pubmed.ncbi.nlm.nih.gov/33759445/) DOI: [10.4081/monaldi.2021.1710](https://doi.org/10.4081/monaldi.2021.1710)]
- 3 **Murakami T**, Komiyama T, Kobayashi H, Ikari Y. Gender Differences in Takotsubo Syndrome. *Biology (Basel)* 2022; **11** [PMID: [35625378](https://pubmed.ncbi.nlm.nih.gov/35625378/) DOI: [10.3390/biology11050653](https://doi.org/10.3390/biology11050653)]

- 4 **Sahu KK**, Mishra AK, Lal A. Newer Insights Into Takotsubo Cardiomyopathy. *Am J Med* 2020; **133**: e318 [PMID: 31982085 DOI: [10.1016/j.amjmed.2019.11.008](https://doi.org/10.1016/j.amjmed.2019.11.008)]
- 5 **George AA**, John KJ, Selvaraj V, Mishra AK. Endocrinological abnormalities and Takotsubo cardiomyopathy. *Monaldi Arch Chest Dis* 2021; **91** [PMID: 33840185 DOI: [10.4081/monaldi.2021.1859](https://doi.org/10.4081/monaldi.2021.1859)]
- 6 **Akashi YJ**, Goldstein DS, Barbaro G, Ueyama T. Takotsubo cardiomyopathy: a new form of acute, reversible heart failure. *Circulation* 2008; **118**: 2754-2762 [PMID: 19106400 DOI: [10.1161/CIRCULATIONAHA.108.767012](https://doi.org/10.1161/CIRCULATIONAHA.108.767012)]
- 7 **Ben Jemaa A**, Bahloul M, Kallel H, Turki O, Dlala M, Bouaziz M. [Inverted Takotsubo Syndrome due to Severe Scorpion Envenomation: Report of one Case]. *Med Trop Sante Int* 2021; **1** [PMID: 35586636 DOI: [10.48327/PWX0-M245](https://doi.org/10.48327/PWX0-M245)]
- 8 **Mishra S**, Mishra A, Mishra JP. Bee sting: A rare cause of Takotsubo Cardiomyopathy. *Int J Cardiol* 2016; **223**: 787-789 [PMID: 27573610 DOI: [10.1016/j.ijcard.2016.08.312](https://doi.org/10.1016/j.ijcard.2016.08.312)]
- 9 **Aono J**, Saito M, Inaba S, Kurata A, Uetani T, Annen S, Higashi H, Higaki J, Ikeda S. Multiple Bee Sting-Induced Life-Threatening Takotsubo Cardiomyopathy. *Circ J* 2019; **83**: 489 [PMID: 30158343 DOI: [10.1253/circj.CJ-18-0047](https://doi.org/10.1253/circj.CJ-18-0047)]
- 10 **Seecheran RV**, Ramdin R, Singh S, Seecheran V, Persad S, Peram L, Raza SS, Seecheran NA. Africanized Honey Bee Sting-Induced Stress-Related Cardiomyopathy: A Bee or Octopus Trap. *Cureus* 2021; **13**: e16681 [PMID: 34466318 DOI: [10.7759/cureus.16681](https://doi.org/10.7759/cureus.16681)]
- 11 **Ghanim D**, Adler Z, Qarawani D, Kusniec F, Amir O, Carasso S. Takotsubo cardiomyopathy caused by epinephrine-treated bee sting anaphylaxis: a case report. *J Med Case Rep* 2015; **9**: 247 [PMID: 26518383 DOI: [10.1186/s13256-015-0722-5](https://doi.org/10.1186/s13256-015-0722-5)]
- 12 **Winogradow J**, Geppert G, Reinhard W, Resch M, Radke PW, Hengstenberg C. Tako-tsubo cardiomyopathy after administration of intravenous epinephrine during an anaphylactic reaction. *Int J Cardiol* 2011; **147**: 309-311 [PMID: 21247644 DOI: [10.1016/j.ijcard.2010.12.063](https://doi.org/10.1016/j.ijcard.2010.12.063)]
- 13 **Scheiba N**, Viedt-Suelmann C, Schäkel K. Tako-tsubo cardiomyopathy after a hymenoptera sting and treatment with catecholamines. *Acta Derm Venereol* 2011; **91**: 593-594 [PMID: 21547339 DOI: [10.2340/00015555-1119](https://doi.org/10.2340/00015555-1119)]
- 14 **Geppert G**, Radke PW, Kurowski V, Hunold P, Schunkert H. [Wasp sting, adrenaline injection and acute thoracic pain: an unusual case of stress-induced (tako-tsubo) cardiomyopathy]. *Med Klin (Munich)* 2010; **105**: 246-248 [PMID: 20455042 DOI: [10.1007/s00063-010-1032-8](https://doi.org/10.1007/s00063-010-1032-8)]
- 15 **Hausen S**, Treusch A, Hermes C, Bookstegers P. [Wasp-sting-induced pheochromozytoma crisis with stress-related cardiomyopathy (Takotsubo)]. *Med Klin Intensivmed Notfmed* 2014; **109**: 621-624 [PMID: 25369903 DOI: [10.1007/s00063-014-0440-6](https://doi.org/10.1007/s00063-014-0440-6)]
- 16 **Alexakis LC**, Arapi S, Stefanou I, Gargalianos P, Astriti M. Transient reverse takotsubo cardiomyopathy following a spider bite in Greece: a case report. *Medicine (Baltimore)* 2015; **94**: e457 [PMID: 25654384 DOI: [10.1097/MD.0000000000000457](https://doi.org/10.1097/MD.0000000000000457)]
- 17 **Isbister GK**, Sellors KV, Beckmann U, Chiew AL, Downes MA, Berling I. Catecholamine-induced cardiomyopathy resulting from life-threatening funnel-web spider envenoming. *Med J Aust* 2015; **203**: 302-304 [PMID: 26424069 DOI: [10.5694/mja15.00279](https://doi.org/10.5694/mja15.00279)]
- 18 **Van Rensburg A**, Kyriakakis C. A tale of a cobra and an octopus: Takotsubo cardiomyopathy following a snake bite. *Am J Med* 2015; **128**: e5-e6 [PMID: 25460533 DOI: [10.1016/j.amjmed.2014.10.045](https://doi.org/10.1016/j.amjmed.2014.10.045)]
- 19 **Murase K**, Takagi K. Takotsubo cardiomyopathy in a snake bite victim: a case report. *Pan Afr Med J* 2012; **13**: 51 [PMID: 23330042]
- 20 **Mishra AK**, Dai Q, Sahu KK, ElMeligy A. Atypical Takotsubo Cardiomyopathy in COVID-19. *Am J Med Sci* 2021; **362**: e41-e42 [PMID: 34446260 DOI: [10.1016/j.amjms.2021.01.024](https://doi.org/10.1016/j.amjms.2021.01.024)]
- 21 **Miranda CH**, Braggion-Santos MF, Schmidt A, Pazin Filho A, Cupo P. Evolution of the electrocardiogram QRS complexes voltage in scorpion envenomation-induced Takotsubo syndrome. *Am J Emerg Med* 2015; **33**: 837-838 [PMID: 25842284 DOI: [10.1016/j.ajem.2015.02.039](https://doi.org/10.1016/j.ajem.2015.02.039)]
- 22 **Madias JE**. Voltage attenuation of the electrocardiogram QRS complexes in a patient with "scorpion envenomation"-induced Takotsubo syndrome. *Am J Emerg Med* 2015; **33**: 838 [PMID: 25766301 DOI: [10.1016/j.ajem.2015.02.040](https://doi.org/10.1016/j.ajem.2015.02.040)]
- 23 **Miranda CH**, Braggion-Santos MF, Schmidt A, Pazin-Filho A, Cupo P. The first description of cardiac magnetic resonance findings in a severe scorpion envenomation: Is it a stress-induced (Takotsubo) cardiomyopathy like? *Am J Emerg Med* 2015; **33**: 862.e5-862.e7 [PMID: 25601163 DOI: [10.1016/j.ajem.2014.12.044](https://doi.org/10.1016/j.ajem.2014.12.044)]
- 24 **Bianchi R**, Torella D, Spaccarotella C, Mongiardo A, Indolfi C. Mediterranean jellyfish sting-induced Tako-Tsubo cardiomyopathy. *Eur Heart J* 2011; **32**: 18 [PMID: 20876068 DOI: [10.1093/eurheartj/ehq349](https://doi.org/10.1093/eurheartj/ehq349)]
- 25 **Tiong K**. Irukandji syndrome, catecholamines, and mid-ventricular stress cardiomyopathy. *Eur J Echocardiogr* 2009; **10**: 334-336 [PMID: 18801721 DOI: [10.1093/ejehocardi/jen246](https://doi.org/10.1093/ejehocardi/jen246)]
- 26 **John Binu A**, Kumar Mishra A, Gunasekaran K, Iyadurai R. Cardiovascular manifestations and patient outcomes following snake envenomation: a pilot study. *Trop Doct* 2019; **49**: 10-13 [PMID: 30486743 DOI: [10.1177/0049475518814019](https://doi.org/10.1177/0049475518814019)]
- 27 **Jain MK**, Indurkar M, Kastwar V, Malviya S. Myocarditis and multiple cerebral and cerebellar infarction following scorpion sting. *J Assoc Physicians India* 2006; **54**: 491-492 [PMID: 16909701]
- 28 **Pelliccia F**, Kaski JC, Crea F, Camici PG. Pathophysiology of Takotsubo Syndrome. *Circulation* 2017; **135**: 2426-2441 [PMID: 28606950 DOI: [10.1161/CIRCULATIONAHA.116.027121](https://doi.org/10.1161/CIRCULATIONAHA.116.027121)]
- 29 **Abroug F**, Ouanes I, Maatouk M, Golli M, Ouanes-Besbes L. Inverted Takotsubo syndrome in *Androctonus australis* scorpion envenomation. *Clin Toxicol (Phila)* 2018; **56**: 381-383 [PMID: 28905655 DOI: [10.1080/15563650.2017.1377221](https://doi.org/10.1080/15563650.2017.1377221)]
- 30 **George AA**, Mishra AK, Sargent J. Letter to the Editor Regarding "Pipeline Embolization in Patients with Posterior Circulation Subarachnoid Hemorrhages: Is Takotsubo Cardiomyopathy a Limiting Factor? *World Neurosurg* 2020; **144**: 303-304 [PMID: 33227853 DOI: [10.1016/j.wneu.2020.08.110](https://doi.org/10.1016/j.wneu.2020.08.110)]
- 31 **Lyon AR**, Citro R, Schneider B, Morel O, Ghadri JR, Templin C, Omerovic E. Pathophysiology of Takotsubo Syndrome: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2021; **77**: 902-921 [PMID: 33602474 DOI: [10.1016/j.jacc.2020.10.060](https://doi.org/10.1016/j.jacc.2020.10.060)]
- 32 **de Pender AM**, Winkel KD, Ligthelm RJ. A probable case of Irukandji syndrome in Thailand. *J Travel Med* 2006; **13**: 240-243 [PMID: 16884407 DOI: [10.1111/j.1708-8305.2006.00041.x](https://doi.org/10.1111/j.1708-8305.2006.00041.x)]
- 33 **Ryan RYM**, Seymour J, Loukas A, Lopez JA, Ikonomopoulou MP, Miles JJ. Immunological Responses to Envenomation.

- Front Immunol* 2021; **12**: 661082 [PMID: 34040609 DOI: 10.3389/fimmu.2021.661082]
- 34 **Surineni K**, Afzal MR, Barua R, Parashara D. Epinephrine-Induced Takotsubo Cardiomyopathy. *Fed Pract* 2016; **33**: 28-30 [PMID: 30766140]
- 35 **Cha YS**, Kim H, Bang MH, Kim OH, Kim HI, Cha K, Lee KH, Hwang SO. Evaluation of myocardial injury through serum troponin I and echocardiography in anaphylaxis. *Am J Emerg Med* 2016; **34**: 140-144 [PMID: 26597331 DOI: 10.1016/j.ajem.2015.09.038]
- 36 **Spina R**, Song N, Kathir K, Muller DWM, Baron D. Takotsubo cardiomyopathy following unintentionally large subcutaneous adrenaline injection: a case report. *Eur Heart J Case Rep* 2018; **2**: yty043 [PMID: 31020123 DOI: 10.1093/ehjcr/ty043]
- 37 **Mendoza I**, Novaro GM. Repeat recurrence of takotsubo cardiomyopathy related to inhaled beta-2-adrenoceptor agonists. *World J Cardiol* 2012; **4**: 211-213 [PMID: 22761975 DOI: 10.4330/wjc.v4.i6.211]
- 38 **Li P**, Li C, Mishra AK, Cai P, Lu X, Sherif AA, Jin L, Wang B. Impact of malnutrition on in-hospital outcomes in takotsubo cardiomyopathy. *Nutrition* 2022; **93**: 111495 [PMID: 34735920 DOI: 10.1016/j.nut.2021.111495]
- 39 **Mishra A**, Binu A, Abraham G, Vanjare H, George T, Iyadurai R. Cerebrovascular Injury Following Scorpion Sting and Snake Envenomation: A Case Series. *Can J Neurol Sci* 2018; **45**: 669-674 [PMID: 30289088 DOI: 10.1017/cjn.2018.328]
- 40 **Delumgahawaththa WMS**, Roshanthan S, Sathananthan PP, Seneviratne NHG. Chest Pain Following an Unidentified Snake Bite. *Sri Lankan Journal of Cardiology* 2021; **4**: 52-57
- 41 **Sahu KK**, Mishra AK, Doshi A, Martin KB. Heartbroken twice: a case of recurrent Takotsubo cardiomyopathy. *BMJ Case Rep* 2020; **13** [PMID: 31915184 DOI: 10.1136/ber-2019-232253]
- 42 **Boyd B**, Solh T. Takotsubo cardiomyopathy: Review of broken heart syndrome. *JAAPA* 2020; **33**: 24-29 [PMID: 32039951 DOI: 10.1097/01.JAA.0000654368.35241.fc]
- 43 **George AA**, John KJ, Jha A, Mishra AK. Infections precipitating Takotsubo cardiomyopathy, an uncommon complication of a common infection. *Monaldi Arch Chest Dis* 2022 [PMID: 36226557 DOI: 10.4081/monaldi.2022.2408]
- 44 **Sunil KK**, Joseph JK, Joseph S, Varghese AM, Jose MP. Cardiac Involvement in Vasculotoxic and Neurotoxic Snakebite - A not so Uncommon Complication. *J Assoc Physicians India* 2020; **68**: 39-41 [PMID: 33187035]
- 45 **Nayar J**, John K, Philip A, George L, George A, Lal A, Mishra A. A Review of Nuclear Imaging in Takotsubo Cardiomyopathy. *Life (Basel)* 2022; **12** [PMID: 36294911 DOI: 10.3390/life12101476]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**Help Desk:** <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

