Cardiovascular Revascularization Medicine xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Original article

Clinical features and outcome of epinephrine-induced takotsubo syndrome: Analysis of 33 published cases☆

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ARTICLE INFO

Article history:
Received 15 May 2016
Received in revised form 4 July 2016
Accepted 6 July 2016
Available online xxxx

Keywords:
Takotsubo
Epinephrine
Catecholamines
Broken heart syndrome

ABSTRACT

Background: Takotsubo syndrome (TS) may be triggered by innumerable physical stress factors including epinephrine administration. The aim of this study is to report on the clinical features and outcome of epinephrine-induced TS (Epi-TS) in a large cohort of published cases.
Methods: A computer assisted search of the electronic data base Pubmed was performed from 1990 to 2014. All cases deemed to have Epi-TS were retrieved and compared to the large recent report by Templin et al. (All-TS).
Results: Thirty-three cases of Epi-TS were retrieved from the literature and compared to 1750 cases of All-TS. Chest pain as a presenting symptom occurred in 45% of cases. The Epi-TS patients were on average 20.6 years younger than All-TS patients ($p < 0.0001$). The women were still predominating in Epi-TS but in a significantly lower percentage compared to ALL-TS (73% in Epi-TS vs 89.8% in All-TS, $p = 0.0054$). One third of the Epi-TS cases had basal pattern of TS compared to 2.2% of cases reported in All-TS. Epi-TS cases were characterized by high complication rates, which occurred in 57.6%. The most important risk factor for the development of TS complication was the accidental administration ($P < 0.001$) and the dose of >1 mg epinephrine ($p = 0.02$). In spite of high complication rates, the recovery was rapid with no in-hospital mortality.
Conclusion: Epi-TS is characterized by a dramatic rapid onset of symptoms after epinephrine administration. Almost half of the cases had apical sparing and one third basal pattern of TS. In spite of high complication rates, the prognosis was good with no in-hospital mortality.

1. Introduction

Takotsubo syndrome (TS) is an increasingly recognized acute cardiac disease entity. It has a clinical presentation resembling that of acute coronary syndrome (ACS) [1,2]. The disease is characterized by a transient and unique pattern of circumferential left ventricular wall motion abnormality (LVWMA). It afflicts predominantly women and often preceded by an emotional or a physical stress factor [3]. Countless physical stress factors including pheochromocytoma and epinephrine administration have been reported as a trigger factor for TS [1,4]. Hitherto, epinephrine-induced TS (Epi-TS) has been described as case reports; only one report has been published on a series of 6 Epi-TS. The purpose of this study is to present the clinical features, TS localization pattern, the complication rates and the outcome of the Epi-TS in a relatively large cohort of 33 published cases [5–30]. The implications of TS localization pattern for the pathogenesis of TS are also discussed.

2. Methods

All cases of epinephrine-induced TS or transient left ventricular dysfunction from 1990, the year where the Japanese term takotsubo was introduced, to December 2014 are critically reviewed. The cases were retrieved by searching in the pubmed using the search terms "takotsubo," "apical ballooning," "stress cardiomyopathy," and "broken heart syndrome" and linking them with the terms "epinephrine," "adrenaline," and "catecholamines". References were also checked for relevant articles including review papers. Only publications in English language (except one in French, where sufficient information could be obtained from the abstract in English and a table in the manuscript) were reviewed. In addition, adequate information could be acquired from only abstract in two further references with the use of only the available information in statistics. The following information was abstracted from the publications: the year of publications, age and gender of the patients, the indication, cause, route and the dose of epinephrine administration where available, the clinical presentation, the type of ECG changes and the cardiac biomarkers. The TS localization pattern was deemed by the description in the text or the available figures in the manuscripts. The hemodynamic complication rates after the presentation, the in-hospital mortality, the clinical course of the disease and the recovery/time where available were reviewed (Table 1). Continuous variables are presented as means ± standard deviations and categorical

☆ Disclosure: The author declares that there is no conflict of interest.

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http://dx.doi.org/10.1016/j.carrev.2016.07.005
1553-8389/

Please cite this article as: Y-Hassan S, Clinical features and outcome of epinephrine-induced takotsubo syndrome: Analysis of 33 published cases, Cardiovasc Revasc Med (2016), http://dx.doi.org/10.1016/j.carrev.2016.07.005

Table 1
Clinical features on admission, in-hospital complications and outcome in the 33 patients with epinephrine-triggered TS.

Authors	Year	Age	Gender	Events for which Epin administered	Reasons for Epin administration	Presenting symptoms or manifestation	TS localization	Complications	Recovery/Time where available
Fyfe et al. [5]	1991	30	Female	Cone biopsy of the cervix	Accidental	VES, VT	Global, Biventricular	Pulmonary edema and cardiogenic shock	Yes/10 days
Sato et al. [6]	2000	39	Female	Surgery	Therapeutic	ES and increase in BP and HR	Global, biventricular	No	Yes/1 week
Budhwani et al. [7] (abstract)	2004	35	Female	Cervix uteri injected	Accidental	Hemodynamic compromise	Severe LVD	Severe hemodynamic compromise	Yes
Kim et al. [8]	2008	47	Male	Nasal operation	Therapeutic	Hypotension and tachycardia	Basal	No	Yes/2 days
Wong et al. [9]	2008	56	Female	Hypotension	Therapeutic	Chest pain	Apical	No	Yes
Zubrinich et al. [10]	2008	76	Female	Angioedema	Therapeutic	Chest pain	Apical	No	Yes/6 week
Lainez et al. [11]	2009	61	Female	Suspected severe anaphylactic reaction	Therapeutic	LBBB in ECG	Apical	No	Yes
Abraham et al. [12]	2009	30	Female	Suicide	Suicide	Chest pain	Apical	Heart failure	Yes
Abraham et al. [12]	2009	24	Female	Liposuction	Inadvertent	Chest pain	Apical	Heartfailure	Yes
Abraham et al. [12]	2009	48	Female	Face lift	Inadvertent	Chest pain	Basal	Heart failure	Yes
Abraham et al. [12]	2009	44	Female	Keloid scar	Inadvertent	Chest pain	Basal	Heart failure	Yes
Abraham et al. [12]	2009	20	Male	Colonoscopy	Inadvertent	Chest pain	Basal	Heart failure	Yes
Abraham et aal [12]	2009	54	Female	Vasovagal syncope	Incorrectly	Chest pain	Basal	No	Yes
Manivannan et al. [13]	2009	41	Female	Bee sting	Therapeutic, high dose	Chest pain	Mid-ventricular	No	Yes
Volz et al. [14]	2009	27	Male	Self injection	Self injection	Circulatory failure	Mid-ventricular	Heart failure and cardiogenic shock	Yes/7 days
Litvinov et al. [15]	2009	24	Female	Tomato anaphylaxis	Inadvertent	Chest pain	Basal	Heart failure and cardiogenic shock	Yes/7 days
Osuorji et al. [16]	2009	46	Female	Status asthmaticus	Therapeutic	ECG changes	Apical	N/A	Yes/3 days
von Knobelsdorff-Brenkenhoff et al. [17]	2010	31	Female	Endoscopic sinus surgery	Therapeutic	Non sustained VT	Mid-ventricular	No	Yes/7 days
von Knobelsdorff-Brenkenhoff et al. [17]	2010	59	Male	Surgery	Therapeutic	SVES	Mid-ventricular	No	Yes/17 day
Morel et al. [18]	2010	16	Male	Anaphylactic reaction	Therapeutic and then repeated accidental	Rapid hemodynamic deterioration	Basal	No	Yes
Härle et al [19]	2011	39	Female	Diagnostic purposes	Accidental	Chest pain and dyspnea	Mid-ventricular	Pulmonary edema	Yes/10 days
Dewachter et al. [20]	2011	65	Female	General anesthesia	Therapeutic	Hypotension and tachycardia	Apical	Pulmonary edema and shock	Yes/10 days
Magri et al. [21]	2011	26	Female	Allergic reaction	Therapeutic	Chest pain or discomfort	Basal	No	Yes/2 weeks
Scheiba et al. [22]	2011	81	Male	Hymenoptera sting	Therapeutic	Shock and unconsciousness	Apical	Unconsciousness, pulseless, cardiogenic shock, ventricular fibrillation which is defibrillated	Yes
Winogradow et al. [23]	2011	37	Female	Bee sting	Therapeutic	Shortness of breath	Apical	Pulmonary edema and shock	Yes
Winogradow et al. [23]	2011	70	Female	Wasp sting	Therapeutic	Chest pain	Apical	No	Yes
Patankar et al. [24]	2012	44	Female	Angioedema	Incorrect dose	Hypotension and tachycardia	Apical	Shock and pulmonary edema	Yes
Kajander et al. [25]	2013	49	Female	Anaphylactic reaction	Therapeutic	Chest pain	Basal	Heart failure, shock and unconsciousness	Yes/1 week
Copetti et al. [26]	2013	77	Male	Cardiac arrest	Therapeutic	After resuscitation, the disease observed	Apical	cardiac arrest on admission, the disease recovered after 30 min)	Yes/30 min
Khoueiry et al. [27]	2013	44	Female	Contrast allergy	Therapeutic	Chest pain	Basal	Pulmonary edema	Yes
Esnault et al. [28] (French, abstract)	2014	49	Female	Operation	Inadvertent	N/A	Reverse (Basal)	Cardiogenic shock	Yes/4 days
Ituk et al. [29]	2014	54	Male	Retrobulbar block	Therapeutic	Increase in BP and HR	Apical	Pulmonar edema and cardiogenic shock	Yes/1 day
Sundboll et al. [30] (abstract)	2014	67	Male	Surgery	Therapeutic	Increase in BP and HR	Apical	N/A	Yes/5 days

BP, blood pressure; ECG, electrocardiogram; Epin, epinephrine; ES, extrasystole; HR, heart rate; LBBB, left bundle branch block; LVD, left ventricular dysfunction; N/A, not available; TS, takotsubo syndrome; SVES, supraventricular extrasystole; TS, takotsubo syndrome; VES, ventricular extraslag; VT, ventricular tachycardia.