

Left Ventricular Apical Ballooning, Catecholamine Toxicity, and Cardiomyopathy

Alfonso Lagi

Department of Internal Medicine, Villa Donatello Hospital, Florence, Italy

ABSTRACT

Case reports and clinical experiences have implicated catecholamine. Excess likely contributes to the pathophysiologic process as a cause of cardiac dysfunction, impaired hemodynamic function, and poor outcomes. Cardiac dysfunction has also been described in many other diseases; there is likely a common underlying pathophysiology. In this review, we will examine the pathophysiology of cardiac dysfunction after catecholamine surge and discuss the evidence surrounding cardiac dysfunction.

Key words: Autonomic nervous system, cardiomyopathies, catecholamine, coronary circulation, heart diseases, ischemic heart disease, Takotsubo cardiomyopathy

Life needs of catecholamine and they are essential for survival on stress but which in turn may be cause of disease. The aim of this mini-review is to focus on and to distinguish catecholamine cardiotoxicity from catecholamine cardiomyopathy.

Both are the effect of catecholamine surge, the first with target on left ventricular myocardial dyssynergia and the second on myocardial muscle. Both coexist and work in synchrony in the same patient.

The first example is the reported Takotsubo cardiomyopathy (TC) which is a paradigm of catecholamine toxicity. It is a regional myocardial disease characterized by apical ballooning.^[1] Imaging, and especially cardiac ultrasonography, has made it possible to identify contraction asynchronies of different segments of the left ventricle under acute stress conditions. The phenomenon occurs mainly but not exclusively^[2,3] at the tip (apical ballooning) and the distal third of the left ventricle.

The cardiomyopathy, which owes its name to the known Japanese fishing vessel, has also been called “broken heart syndrome” to underline that the two segments of the left ventricle have different contractility, to indicate its possible reversibility and finally to imply that aside from its first

description (above-mentioned TC), also different diseases have the same morphological and functional framework.

A cases review with patients admitted with chest pain and TC; diagnosis was done on the basis of findings of apical ballooning and normal coronary arteries only in 7.5% of patients. Among those patients with TC, catecholamine-associated triggers were emotional trauma (in 72.5%), surgical stress (in 12.5%), adrenergic intoxication (in 7.5%), and catecholamine-producing cancer (in 7.5%). In this series, the patients affected from a functional disease, the apical ballooning, 20% presented in cardiogenic shock and were life-threatening.^[4] The others had different diseases associated with apical ballooning.

In the case, we prefer to identify the framework not as Takotsubo but as apical ballooning by referring to imaging.

The apical ballooning syndrome may be transient, permanent, or recurrent^[5] and associated or not with coronary arteries disease. The syndrome characterizes many diseases as TC, acute myocarditis, coronary vasospasm, cocaine-induced coronary vasoconstriction, and thrombosis with endogenous fibrinolysis before angiography^[1] and brain diseases as aneurysmal subarachnoid hemorrhage and emotional stress.^[6]

Address for correspondence:

Alfonso Lagi, Via G Mameli 44 – 50131, Florence, Italy. Phone: 0039 3386316900. E-mail: alfonso.lagi1@tin.it

© 2018 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

All reflect a similar pathophysiology that is caused by catecholamine-induced ventricular dysfunction. Furthermore, recurrent apical ballooning syndrome has been associated with a transient hypertensive response during exercise^[7] or with catecholaminergic storm of pheochromocytoma,^[8,9] which suggests a hypersympathetic mechanism.

Apical ballooning can be fatal^[8,10] or associate with favorable prognosis and may with different clinical pattern as chest pain, ECG changes, increase of troponin, heart failure, pulmonary edema, or cardiogenic shock depending on the different diseases that cause it but it is always due to an action of catecholamine that causes myocardial dyssynergia.

The hypothetic explanation of the pathophysiology of the apical ballooning is complex and is related to catecholamine cardiotoxicity. In these cases, probably, the plasma levels of catecholamine among patients with ballooning are very high, more than the values among myocardial infarction patients.^[11] The release of catecholamine affecting the hearth came from sympathetic cardiac terminals and from adrenal glands in reference of the specific stress.

Overactivation of the sympathoadrenergic system is an essential mechanism for survival under conditions of acute circulatory failure providing short-term adaptation to the stressful conditions of critical illnesses. The administration of exogenous catecholamine is short-term benefits and mandatory to support the failing circulation in acutely ill patients with reduced cardiac output and/or hypotension. The prolonged exposure to elevated levels of catecholamine may, by contrast, become maladaptive and can result in significant adverse effects,^[12] cause the stunned myocardium and possibly increased mortality.^[13]

Hence, we have a progressive transition from a functional disease (stunned myocardium), due to catecholamine toxicity, potentially lethal but also reversible, through catecholamine cardiomyopathy which is a structural, irreversible cardiomyopathy. The prolonged adrenergic stress is detrimental to the cardiovascular system by initiating a series of adverse effects triggering significant cardiotoxicity, whose pathophysiological mechanisms are complex and only partially elucidated. They include various degrees of cardiomyocyte necrosis and apoptosis, myocardial infiltration with poly-morphonuclear and mononuclear leukocytes, interstitial edema, subendocardial and subepicardial hemorrhages, and the progressive development of distinct foci of fibrosis over time.^[14]

The mechanisms responsible for the cardiac damage of adrenergic agents remain only partly defined: They interest hemodynamic changes as imbalance between myocardial oxygen supply (as effect of enhanced cardiac contractility

and heart rate) and demand induced by catecholamine damage cardiomyocytes; vasoconstriction in the coronary macro- and micro-circulation reduce the supply of oxygen and high-energy phosphates; cellular mechanisms as calcium overload, consequence of beta-adrenergic receptors activation, and increase of oxidative stress. The mechanisms promote cardiomyocyte cell death, both through the apoptotic and necrotic pathways.^[15,16] The resulting classic histologic finding of contraction-band necrosis, which is characterized by focal myocytolysis, myofibrillar degeneration, and irregular cross-band formation.

More factors play together in catecholamine cardiomyopathy: Differential regional coronary vasoconstriction, as effect of alpha receptor stimulation, causes the apical cardio depression with an apical-basal gradient; increase of ventricular pressure and aortic afterload cause significant left ventricular outflow tract obstruction which, associated with acute left ventricular systolic dysfunction, poses a major therapeutic challenge.^[16,17] In other words, negative inotropy and increased afterload for left ventricular outflow tract obstruction are life-threatening and causes of hemodynamic distress, associated with hypotension and cardiogenic shock.

The prevalence of one factor over the another and the pathological anatomy of the coronary arteries probably makes the difference between the catecholamine cardiotoxicity and cardiomyopathy.

REFERENCES

1. Sato H, Tateishi H, Uchida T, Dote K, Ishihara M. Tako-tsubo-like Left Ventricular Dysfunction due to Multivessel Coronary Spasm. In: Kodama K, Haze K, Hon M, editors. *Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure*. Tokyo: Kagakuhyoronsha; 1990. p. 56-64.
2. Di Palma G, Daniele GP, Antonini-Canterin F, Piazza R, Nicolosi GL. Cardiogenic shock with basal transient left ventricular ballooning (Takotsubo-like cardiomyopathy) as first presentation of pheochromocytoma. *J Cardiovasc Med (Hagerstown)* 2010;11:507-10.
3. Kim S, Yu A, Filippone LA, Kolansky DM, Raina A. Inverted-takotsubo pattern cardiomyopathy secondary to pheochromocytoma: A clinical case and literature review. *Clin Cardiol* 2010;33:200-5.
4. Coupez E, Eschalier R, Pereira B, Pierrard R, Souteyrand G, Clerfond G, *et al*. A single pathophysiological pathway in takotsubo cardiomyopathy: Catecholaminergic stress. *Arch Cardiovasc Dis* 2014;107:245-52.
5. Rossi AP, Bing-You RG, Thomas LR. Recurrent takotsubo cardiomyopathy associated with pheochromocytoma. *Endocr Pract* 2009;15:560-2.
6. Krishnamoorthy V, Mackensen GB, Gibbons EF, Vavilala MS. Cardiac dysfunction after neurologic injury: What do we know and where are we going? *Chest* 2016;149:1325-31.
7. Dhoble A, Abdelmoneim SS, Bernier M, Oh JK, Mulvagh SL.

- Transient left ventricular apical ballooning and exercise induced hypertension during treadmill exercise testing: Is there a common hypersympathetic mechanism? *Cardiovasc Ultrasound* 2008;6:37.
8. Loscalzo J, Roy N, Shah RV, Tsai JN, Cahalane AM, Steiner J, *et al.* Case 8-2018: A 55-year-old woman with shock and labile blood pressure. *N Engl J Med* 2018;378:1043-53.
 9. Kobayashi Y, Hirohata A. Pheochromocytoma found in takotsubo cardiomyopathy patients. *J Invasive Cardiol* 2014;26:E76-7.
 10. Del Buono MG, O'Quinn MP, Garcia P, Gerszten E, Roberts C, Moeller FG, *et al.* Cardiac arrest due to ventricular fibrillation in a 23-year-old woman with broken heart syndrome. *Cardiovasc Pathol* 2017;30:78-81.
 11. Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, *et al.* Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;352:539-48.
 12. Dunser MW, Hasibeder WR. Sympathetic overstimulation during critical illness: Adverse effects of adrenergic stress. *J Intensive Care Med* 2009;24:293-316.
 13. Schmittinger CA, Torgersen C, Luckner G, Schroder DC, Lorenz I, Dunser MW. Adverse cardiac events during catechol-amine vasopressor therapy: A prospective observational study. *Intensive Care Med* 2012;38:950-8.
 14. Costa VM, Carvalho F, Bastos ML, Carvalho RA, Carvalho M, Remião F, *et al.* Contribution of catecholamine reactive intermediates and oxidative stress to the pathologic features of heart diseases. *Curr Med Chem* 2011;18:2272-314.
 15. Liaudet L, Calderari B, Pacher P. Pathophysiological mechanisms of catecholamine and cocaine-mediated cardiotoxicity. *Heart Fail Rev* 2014;19:815-24.
 16. El Mahmoud R, Mansencal N, Pillière R, Leyer F, Abbou N, Michaud P, *et al.* Prevalence and characteristics of left ventricular outflow tract obstruction in tako-tsubo syndrome. *Am Heart J* 2008;156:543-8.
 17. Shah BN, Curzen NP. Dynamic left ventricular outflow tract obstruction and acute heart failure in tako-tsubo cardiomyopathy. *J Am Coll Cardiol* 2011;58:1195-6.

How to cite this article: Lagi A, Left Ventricular Apical Ballooning, Catecholamine Toxicity, and Cardiomyopathy. *J Clin Cardiol Diagn* 2018;1(1):1-3.