

Tako-Tsubo Syndrome: A Latent Disease

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The first description of Takotsubo syndrome (TTS), also known as broken heart syndrome, apical dyskinesia syndrome, stress-induced cardiomyopathy, apical bulge syndrome or ampullary cardiomyopathy was made in 1990 [1-4] by Dr. Hikaru Sato, who reported a left ventricular dysfunction, which acquired a silhouette similar to an old Japanese vessel used to fish octopus (tako = octopus, tsubo = vessel) [5], although it is in 2001 when it was consolidated as an independent entity, described by Tsuchihashi et al again in Japan the first series of 88 patients [1,6]. The first case reported in Latin America was in 2004 in Mexico and in 2017 the first record of a series of patients in Latin America was published in Chile [7].

Although it was initially thought that this disease only affected the Japanese population, it has been proven that it really affects any race and country.

TTS is distinguished by acute contractile dysfunction, completely reversible and in most cases of the left ventricle with a typical pattern of contraction and is responsible for 1 to 2% of all acute coronary syndromes [3,4]. It most often affects middle-aged women (between 50 and 70 years old) [7], however, cases of patients between 30 and 32 years old have recently been described [4]. It is usually preceded by physical or psychological stress that acts as a trigger [7,8], although the disease has also been reported without an obvious trigger [3,9].

The pathogenesis of this syndrome is not yet clearly established; However, the serum increase in catecholamines and their myocardial toxicity is the most accepted hypothesis by the medical community. Another possibility is endothelin-mediated microvascular vasospasm

[4,5,7]. Being more frequent in postmenopausal women, estrogen deficiency has also been implicated in its genesis [7,9]. These hypotheses are still under study. The American Heart Association recognized in 2006 the cardiomyopathy of Takotsubo as a type of acquired cardiomyopathy [3,10].

Its appearance is acute and transient, normalizing ventricular function from one to three weeks, although it can be delayed up to two months. The absence of atherothrombotic disease in the coronary arteries of patients presenting with this syndrome is considered an indispensable condition for diagnosis [8]. This criterion is important, and there are authors who believe that their diagnosis cannot be made if there is no early coronary angiography, within the first 24 hours of its appearance, although at present there is no agreement on the obligation to perform explorations. invasive to carry out its diagnosis [8,10].

There are rare cases in which the regional wall motion abnormality corresponds to the distribution of a single coronary artery. This holds true for the focal TTS type mostly involving an anterolateral segment. Therefore, the criteria should not exclude cases in which the wall motion abnormalities are restricted to the distribution of a single coronary artery. In this situation, a clear differentiation of TTS, ACS, or myocarditis requires cardiac magnetic resonance imaging demonstrating myocardial oedema rather than late gadolinium enhancement in case of TTS [2].

The importance of identifying this syndrome is that its presentation simulates an acute myocardial infarction (AMI) however its evolution and prognosis are different and therefore its treatment is different, a fact that must be taken into account for the accurate diagnosis of the pathology and timely treatment.

In this cardiomyopathy, the predominant symptom is usually precordial pain, followed by dyspnea and syncope [7,11,12]. Less common manifestations are acute lung edema, cardiogenic shock and severe ventricular arrhythmias [7]. These less common manifestations are in turn complications of TTS that can even cause the death of the patient.

The electrocardiographic findings that can be observed consist of ST segment elevation, multiple wave T-wave inversion, pathological Q waves and the corrected QT interval (QTc) may be prolonged [7,9,13].

Cardiac troponin is elevated in more than 90% of patients, although at lower concentrations than acute myocardial infarction; During the acute phase the cerebral natriuretic peptide (BNP or proBNP) could be elevated, correlating with the degree of abnormal movement of the cardiac wall, low proBNP concentrations upon admission are markers of a favorable prognosis [7,9].

With the objective of timely diagnosis of TTS, the Mayo Clinic in 2008 proposed four criteria that have been widely followed for the diagnosis of the same. These criteria are included in the following table: (Table 1) [4,6-9,12,14].

Transient hypokinesia, akinesia or dyskinesia in the middle of the left ventricle, with or without apical involvement; regional wall movement abnormalities that extend beyond a single epicardial vascular distribution; and often, but not always, a stressful trigger.
Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.
New electrocardiographic abnormalities (ST segment elevation and/or T wave inversion) or modest elevation of the cardiac troponin.
The absence of pheochromocytoma and myocarditis

Table 1: Diagnostic Criteria for Takotsubo Syndrome proposed by the Mayo Clinic

After the diagnostic criteria published by the Mayo Clinic, several experts around the world have proposed different criteria. In 2018, based on current knowledge, international experts reached a consensus on new international diagnostic criteria (Inter TAK Diagnostic Criteria) (Table 2) [2], which may help to improve identification and stratification of TTS.

Patients show transient ^a left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS) ^b
An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
Neurologic disorders (e.g. subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.
New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.
Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
Significant coronary artery disease is not a contradiction in takotsubo syndrome.
Patients have no evidence of infectious myocarditis. ^b
Postmenopausal women are predominantly affected.
^a Wall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.
^b Cardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.

Table 2: International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria).

Currently there are no large studies that make clear recommendations regarding treatment. Because clinically Takotsubo Syndrome is indistinguishable from ACS, it is common to be treated as coronary ischemia until definitive diagnosis by coronary angiography, which could avoid the unnecessary use of fibrinolytics by ruling out thrombotic coronary obstruction [7]. It should be borne in mind that because not all emergency care centers have available means to perform coronary angiography, many of the patients are not properly diagnosed, so they end up being treated as an ACS.

In the treatment of TTS, platelet antiaggregation has been recommended in several cases [2,6,7]. Patients who do not have reduced ejection fraction or heart failure do not need to receive treatment; In case of ventricular dysfunction, beta blockers and angiotensin-converting enzyme (ACEI) inhibitors are used [3,4,7], however those that present, for example thrombus, anticoagulation should be performed [2,6,7]. It is recommended to keep the medication and follow up for 3 to 6 months, although the adequate duration of treatment has not yet been established [3,7].

It has been seen that the long-term evolution of this entity can be benign, with rapid recovery of the function of the left ventricle [6,7]. However, half of the patients may develop complications in the acute phase, the most frequent being systolic heart failure, in addition to 5-year recurrence rates in 5 to 25%, long-term death rate of 5.6% per patient-year and a stroke rate of 1.7% per patient-year [7]. An investigation carried out in the USA concluded that male patients have a greater predisposition to a poor prognosis with respect to

women, it also established that patients with underlying critical illness have a ten-fold higher mortality compared to a patient without concomitant disease [7,13].

This is a condition that could be under-registered, It is a latent disease, since not all emergency care centers have the necessary means for the diagnosis of certainty, this is a disease that must be thought to be able to diagnose it, because it is easily confused with the ACS being able to be badly treated with fibrinolytics with the consequent risk of bleeding. Its complications can cause the death of the patient, therefore its timely diagnosis is a vital necessity.

It is a latent disease.

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