

Review

An Extensive Review on Imaging Diagnosis Methods in Takotsubo Syndrome

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Academic Editor: Giuseppe Andò

Submitted: 28 March 2023 Revised: 19 April 2023 Accepted: 12 May 2023 Published: 20 October 2023

Abstract

Takotsubo Syndrome (TS) is an acute, reversible cardiac dysfunction, with complex, not entirely understood pathophysiology and heterogeneous clinical picture. Imaging methods each have a crucial role in the diagnosis, in-hospital management, short term and long term follow up. Coronary angiography needs to be performed, especially in the setting of a suspected acute coronary syndrome, in order to rule out coronary artery disease. Echocardiography plays a central role both in the acute and the chronic phase. It is the first imaging investigation performed in patients with TS, valuable to diagnose systolic dysfunction, the wall motion pattern and early complications. Cardiac magnetic resonance tissue characterization provides an essential role in the differential diagnosis of TS with other non-ischemic causes of systolic dysfunction. This review focuses on the imaging methods and the important part they play in the complex management of the disease.

Keywords: acute coronary syndrome; echocardiography; coronary angiography; cardiac magnetic resonance

1. Introduction

Takotsubo syndrome (TS) is generally regarded as a transient left ventricular systolic dysfunction caused by a precipitating factor, be it physical or psychological. The name Takotsubo comes from the resemblance of the end systolic shape of the left ventricle (LV) with a Japanese octopus trap, characterized by a narrow neck and a round apex. This is recognized as the classic Takotsubo pattern — the apical variant. This clinical instance was first described in Japan in 1990 [1]. The clinical resemblance between TS and acute coronary syndromes (ACS) makes it of utmost importance for clinicians to differentiate them in order to apply the best treatment.

International Takotsubo Diagnostic Criteria (Inter-TAK), Mayo and European Heart Failure Association of the European Society of Cardiology diagnosis criteria include transient regional wall motion abnormalities of the left (and occasionally right) ventricle in the presence of electrocardiographic dynamic changes and positive troponin and brain natriuretic peptide (BNP) levels without a culprit coronary artery lesion [2–5]. Usually, a physical or an emotional trigger preceding the event can be identified but it is not mandatory for the diagnosis. Classically known as the “broken heart syndrome”, the identifiable emotional triggers may also be of a happy nature [6,7]. Frequently described physical triggers are sepsis and neurological disease – mainly subarachnoid hemorrhage or epileptic convulsion [8–10]. An acute, transient systolic dysfunction, called neurogenic cardiomyopathy or neurogenic distress

syndrome, has been described in patients with acute neurological events [11]. At first, to meet the Initial Mayo Criteria for a positive TS diagnosis, an exclusion of serious head trauma and intracranial hemorrhage had to be established [12,13]. But the 2008 revised Mayo Criteria no longer specified these acute neurological disorders as an exclusion criteria [4,14]. Furthermore, Ghadri *et al.* [2] identified intracranial hemorrhage and other neurological instances as physical triggers in the development of TS. As a result, due to the similarities in pathophysiology, clinical and paraclinical features, we consider neurogenic cardiomyopathy as a type of TS [11].

Even though it was considered to be a self-limiting, benign disease, monitoring the TS patients in the acute and chronic phase revealed that short and long term outcome may be similar to acute coronary syndromes [3]. In the acute phase, electrical or hemodynamically instability may lead to important morbidity and mortality [15].

Two categories of Takotsubo patients have been suggested: primary and secondary [16]. The primary type is made up of mainly female patients who suffered an emotional trigger, developed mild systolic dysfunction and had a fast recovery. The secondary type does not have a female predominance, occurs after a physical trigger and has a more severe and/or prolonged myocardial dysfunction. But the main discrepancy between the two categories is the prognosis: primary TS patients have better outcome than those with secondary TS [16].



2. Pathophysiology

The pathophysiology of this syndrome is not entirely understood. Sympathetic stimulation is generally considered to play a major part, causing an adrenergic myocardial stunning. It is based on the patient's secretion of adrenaline and noradrenaline and their effect upon the cardiovascular system [17]. One theory is that of an "aborted" myocardial infarction, with spontaneous lysis of the intracoronary thrombus. Another one is based on coronary spasm. But the constriction of a single coronary artery could not explain the ventricular motion abnormalities. That leaves the possibility of smaller vessels vasospasm and microcirculatory dysfunction. Coronary microvasculature may react to high levels of catecholamines and endothelin by transient vasoconstriction [2]. Currently Takotsubo syndrome is classified as an acute coronary syndrome due to microvascular dysfunction [18].

In most Takotsubo cases, a preceding physical or a psychological trigger can be identified. Ghadri *et al.* [2] illustrated a considerable list of triggers. Perhaps the recent pandemic revealed another possible TS trigger: coronavirus Disease (COVID)-19. Studies analyzing prepandemic and pandemic incidence of TS revealed a higher incidence in the COVID pandemic [19,20]. The proposed mechanisms in COVID-19 patients are psychological stress associated with the disease, increased adrenergic response, cytokine storm and microvascular dysfunction. In the general population, social distancing and economic instability may be emotional factors leading to TS.

3. Diagnosis

The need to define and properly manage this disease led to the development of several diagnostic criteria, the most frequently used being the Mayo Clinical Criteria [14] and InterTAK Diagnostic Criteria [21]. The most common causes of hospital presentation are chest pain and dyspnea. Electrocardiographic changes are almost always present, with the most frequent one being ST segment elevation and/or T wave inversion [3]. Troponin levels in TS are usually elevated but maximum values do not generally reach those met in acute myocardial infarction [15]. A general opinion is that cardiac biomarkers (troponin and creatine kinase MB) are disproportionately low compared to the impaired wall motion [22]. The next step in the diagnostic algorithm is coronary angiography. Coronary disease is usually absent or can be present but discordant with the wall motion abnormalities. Subsequently, imaging methods bring to light the Takotsubo diagnosis.

4. Coronary and LV Angiography

Since the most frequent clinical presentation of a TS case is that of an acute coronary syndrome with ST segment elevation, the main investigation is coronary angiography in order to exclude a type 1 myocardial infarction [23,24].

Coronary arteries need to be carefully assessed, in several angiographic views. Usually, patients with TS have non obstructive epicardial coronary arteries but coronary disease unrelated to the motion anomaly of the LV may be present. However, coronary artery disease is not an exclusion criteria [25]. The main reason is that the regional wall motion abnormalities (RWMA) extend beyond the vascularization of a single coronary artery [26]. Even if the patient has coronary artery disease, it is not an exclusion criteria if the depending myocardial territory is not concordant with the wall motion abnormalities [27,28]. When coronary artery disease is found, orthogonal angiographic views of the artery and LV ventriculography help in observing the mismatch between the coronary stenosis and the wall motion abnormality. The "apical nipple sign" was described on ventriculography images: a small zone, right at the LV apex, with preserved contractility, found in approximately 30% of TS patients with apical pattern. This sign was not described in patients with acute anterior myocardial infarction and may help in differentiating the two conditions [29].

Most of the time, TS diagnosis is associated with angiographically normal or non-obstructive coronary arteries [30] (Fig. 1). In patients diagnosed with TS and coronary artery disease, intracoronary imaging techniques, like intravascular ultrasound and optical coherence tomography, revealed that coronary plaques had no sign of thrombosis, erosion or dissection [31–34].



Fig. 1. Coronary angiography in a 53 year-old female patient with Takotsubo Syndrome. Non-obstructive epicardial coronary arteries - images (A) and (B). Ventriculography showing apical akinesia and basal hyperkinesia - images (C) and (D).

In a lot of 11 consecutive patients admitted with acute coronary syndrome but later diagnosed with TS, the wall motion abnormalities were evaluated through ventriculography [35]. Unfortunately, the diagnostic workup did not include cardiac magnetic resonance (CMR) or patient

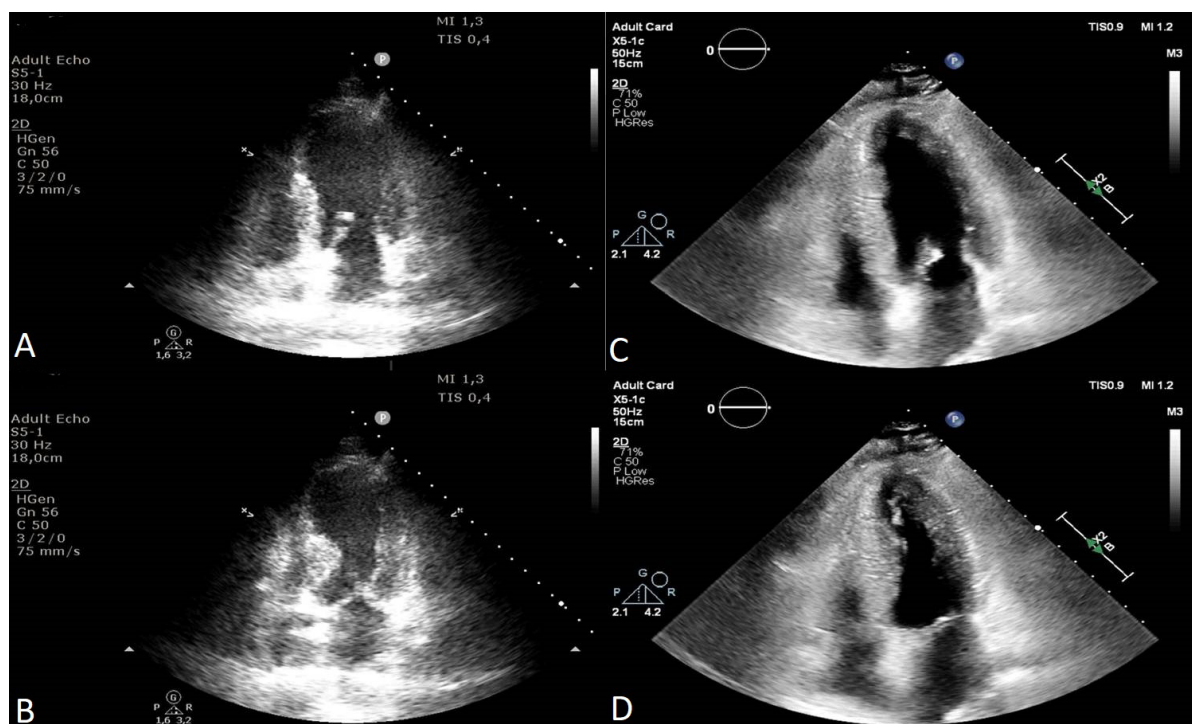


Fig. 2. Transthoracic echocardiography images apical four-chambers views of a 73 year-old female patient with Takotsubo Syndrome. Apical akinesia in the acute phase (A and B) and normalized wall motion and ejection fraction at 1 month follow-up (C and D).

follow-up after hospitalization. Even though ventriculography is a valuable tool in evaluating the circumferential pattern of ventricular motion abnormality when coronary angiography is performed, its usefulness is limited to the acute setting. Thus, in order to prove the reversible nature of the systolic dysfunction another imaging method, usually echocardiography, needs to be performed. In a retrospective study of 20 patients with TS, LV contractility was compared by assessing ventriculograms and strain derived echocardiography. The results suggest that echocardiography and strain analysis is the preferred modality in assessing the LV contractility [36].

Through catheterization, intracardiac pressures can be measured and certain complications can be detected, such as LV outflow tract obstruction (LVOTO). Elevated LV end diastolic pressure measured invasively during coronary angiography was described as a predictor of in-hospital complications [37].

Microvascular dysfunction is involved in the pathophysiology of TS. Angiography may be used in order to assess the coronary microvascular function. One of the methods is Thrombolysis in Myocardial Infarction (TIMI) frame count. Abnormal, diffusely reduced TIMI frame count values were described in TS patients compared to healthy subjects [38]. Abnormalities in microvascular circulation by altered TIMI flow grading were described in several studies [39–41]. Using an angiography-derived index of microcirculatory resistance (NH-IMRangio) during coronary an-

giography, proof of microvascular dysfunction was found in at least one of the coronary arteries in all 166 patients with TS [42].

5. Coronary Angiography by Computed Tomography

Assessment of the coronary arteries by coronary computed tomography angiography (CCTA) can be performed in patients with a high suspicion of TS and low likelihood of acute coronary syndrome [43,44]. Furthermore, in patients with terminal disease or acute, important bleeding and a high suspicion of TS, physicians may opt for this non-invasive approach. Furthermore, another type of patients that could benefit from CCTA is those with acute neurological events, especially in subarachnoid hemorrhage. Young patients with no cardiovascular risk factors, low ischemic risk and a high suspicion of TS, CCTA might be better suited for a non-invasive management. Assessing the coronaries by CCTA may also have a role in recurrent TS [3]. In case of acute hemodynamic instability of uncertain etiology, assessment by computed tomography can analyze other sections in order to exclude pulmonary embolism and acute aortic syndromes [44].

6. Standard Echocardiography

Transthoracic echocardiography (TTE) is an easily accessible and reproducible method available from the Emergency Department in order to assess patients with suspected

acute coronary syndrome or acute heart failure. It has an essential role in the management of TS cases.

It is mainly used in documenting LV systolic and diastolic function [45]. The RWMA is usually of a circumferential pattern and extend beyond the distribution of one coronary artery. The most frequent phenotype is the apical pattern — akinesia of the apical segments of the LV with basal compensatory hyperkinesis (Fig. 2). Atypical patterns are those affecting medioventricular, basal or focal myocardial territory [46–49]. Case reports have described isolated right ventricular (RV) Takotsubo [50,51].

Another important role of TTE is in patients with acute heart failure, exhibiting as acute pulmonary edema or cardiogenic shock. Assessing the biventricular function can point towards the cause of cardiac decompensation.

TTE aides in identifying TS complications (Table 1). The hyperkinesis of basal segments, sometimes associated with a septal bulging can lead to LVOTO, with or without systolic anterior motion (SAM) of the anterior mitral leaflet [52]. Mitral regurgitation can be caused by leaflet tethering due to geometrical changes in the LV (according to TS pattern) and the displacement of the papillary muscles or by SAM [53,54]. Although a rare instance, LV free wall or interventricular septal rupture may occur [55–59]. Apical akinesia may promote intraventricular thrombosis and furthermore thromboembolic events may occur [56,60]. The development of ventricular thrombosis is more frequent in older patients and in those with late presentation to the hospital [61]. Contrast echography may help in patients with poor acoustic window in identifying motion abnormalities and intraventricular thrombosis.

Table 1. Takotsubo Cardiomyopathy complications diagnosed by echocardiography.

Severe systolic dysfunction
Left ventricular tract obstruction
Moderate to severe mitral regurgitation (with or without systolic anterior motion)
Apical thrombosis
Ventricular septal defect
Free wall rupture
Right ventricular involvement
Pericardial Effusion

Cardiogenic shock in TS can be caused by severe systolic dysfunction, LVOTO, severe mitral regurgitation, and RV involvement [52,62,63]. Diagnosing TS complications is of utmost importance in order to properly treat an individual patient. TTE is particularly useful in diagnosing TS in acute clinical scenarios which are not suggestive of a cardiac event [64], such as patients with neurological disease who also present dynamic electrocardiogram (ECG) changes and elevated troponin levels [65–68]. TTE has an important role in the perioperative and periprocedural care

or in patients who become hemodynamically unstable in the Intensive Care Unit [48,69–74]. Bedside echocardiography in the Intensive Care Unit plays an important part in differentiating among different types of hemodynamic instability [9,75].

But the role of ultrasound imaging does not end here. Through its definition, TS is a reversible systolic dysfunction, thus extending the role of echocardiography from diagnosis to follow-up [76,77] [Fig. 2]. It is necessary to document the recovery of the ventricular systolic function – and the progression or regression of complications [54,78]. As diagnostic Takotsubo Criteria mention, the wall motion anomalies are transient [2,4,5]. As a result, echocardiographic follow-up is mandatory, especially if the patients cannot be evaluated by CMR. As demonstrated in this thorough study, the LV systolic function improves in the first 2 weeks and continues to recover over the next 4 weeks [79]. Documenting the left ventricular ejection fraction (LVEF) also has prognostic implications. Reduced ejection fraction ($\leq 35\%$) is a poor prognostic marker for both short and long term prognosis [80].

Alongside the LV systolic function, LV diastolic function needs to be evaluated in the acute phase and then at follow-up. Kumar *et al.* [81] revealed that LVEF improved alongside diastolic function: E value, E/A ratio and e' values improved over time (Fig. 3). Both lower LVEF and higher E/e' ratio were associated with in-hospital complications in TS patients [37,54].

Tei Index, a combined indicator of systolic and diastolic function, has limited value in Takotsubo cases. Mirna *et al.* [82] showed that Takotsubo patients had higher Tei Index as compared to patients with an acute coronary syndrome and to controls.

Surprisingly, three dimensional (3D) echocardiography has not yet been considerably used to investigate patients with TS. It might assist in a more thorough assessment of the left and right ventricle and their function [83].

7. Speckle Tracking Echocardiography

Strain TTE is a rigorous method of evaluating regional and global left and right myocardial function. It is angle independent and it requires a proper acoustic window. Strain images unfolded important information about patients with TS. By speckle tracking analysis, the systolic function of the left ventricle had a more delayed recovery compared to the calculated LV ejection fraction [28,84–86]. Even though it is generally accepted that in the apical and mid-ventricular variant the base of the LV is hyperkinetic, strain analysis revealed contractility impairment even in the “hyperkinetic” areas [36,87]. LV strain assessment has prognostic value in the acute phase of TS patients [88]. In TS, the motion abnormalities are not subtle, especially in the apical variant. As a result, speckle tracking echography has a more pronounced role in the follow-up part rather than in the acute, diagnostic part. Kobayashi *et al.* [85] performed

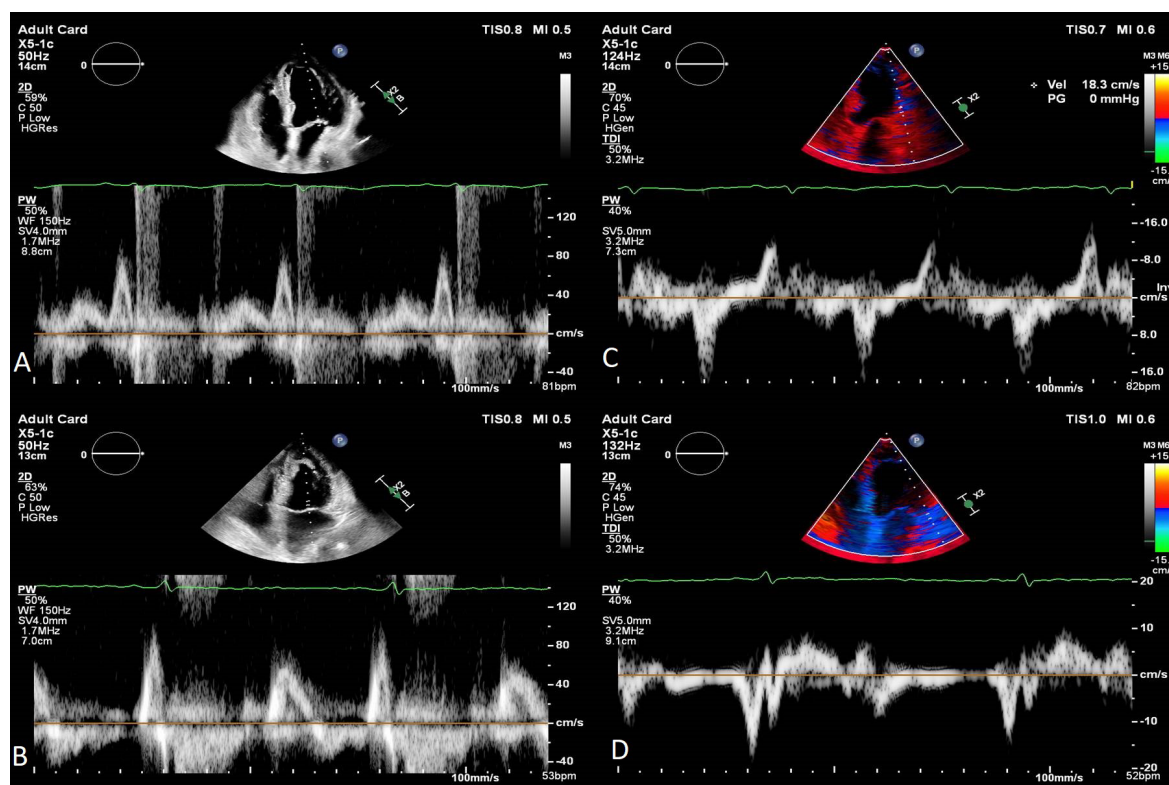


Fig. 3. Transthoracic echocardiography images apical four-chambers views of a 73 year-old female patient with Takotsubo Syndrome showing the evolution of diastolic function. E wave velocity progressed from 40 cm/s in the acute phase to 70 cm/s at one month follow-up, the E/A ratio from 0.5 to 0.8 (A and B). Lateral e' velocity increased from 4 cm/s to 8 cm/s and E/e' ratio from 10 to 8.7 (C and D). 2D, two dimensional; PW, pulsed wave doppler; TDI, tissue doppler imaging.

follow-up 3D strain echocardiography at 4 weeks and 6 months after the diagnosis. They identified that regional abnormalities by peak systolic shortening and peak systolic thickening persisted at 4 weeks despite normalized LVEF (Fig. 4). The persistence of myocardial dysfunction assessed by LV strain was described at 4 weeks follow-up in Takotsubo patients [89].

Speckle tracking echocardiography showed impaired of LV contraction and relaxation by analyzing peak systolic strain rate and early diastolic strain rate, which both improved over time [78].

In a case control study, patients with a history of TS (over 12 months prior to enrollment) were evaluated by echocardiography and CMR and compared to matched control subjects [90]. There were no differences between LVEF calculated by echocardiography and CMR, but the patients with prior Takotsubo presented impaired left ventricular longitudinal and circumferential strain, which highlights the idea that TS is not a “benign” syndrome.

Despite all the advances in ultrasound imaging, echocardiography cannot differentiate between TS and acute coronary syndrome in the acute phase, thus placing coronary angiography as a major investigation in Takotsubo diagnosis [91].

8. Dobutamine Stress Echocardiography and Takotsubo Syndrome

Dobutamine and TS have a convoluted rapport. A few cases of TS during or immediately after Dobutamine stress Echocardiography have been reported [92–97]. Coronary angiography excluded coronary artery disease in all of these patients and complete recovery of the LV systolic function was noted on follow-up echocardiography. These cases of TS in the context of Dobutamine stress test may support the important part that catecholamines play in the pathophysiology of this disease.

In a Dobutamine Stress Study in which 22 patients with a history of Takotsubo (6 months after the diagnosis) were compared to 22 control subjects, no patient developed wall motion abnormalities suggesting that the susceptibility to adrenergic stimulation did not persist after the initial diagnosis [34]. Stress echocardiography was also used in the acute phase of TS in order to unmask LVOTO. The study emphasized the need for beta blockers in patients with LVOTO or who developed LVOTO but safety of the investigation is not yet defined.

9. Contrast Echocardiography

The main utility of contrast TTE is the evaluation of the distribution of left and right ventricle wall motion ab-

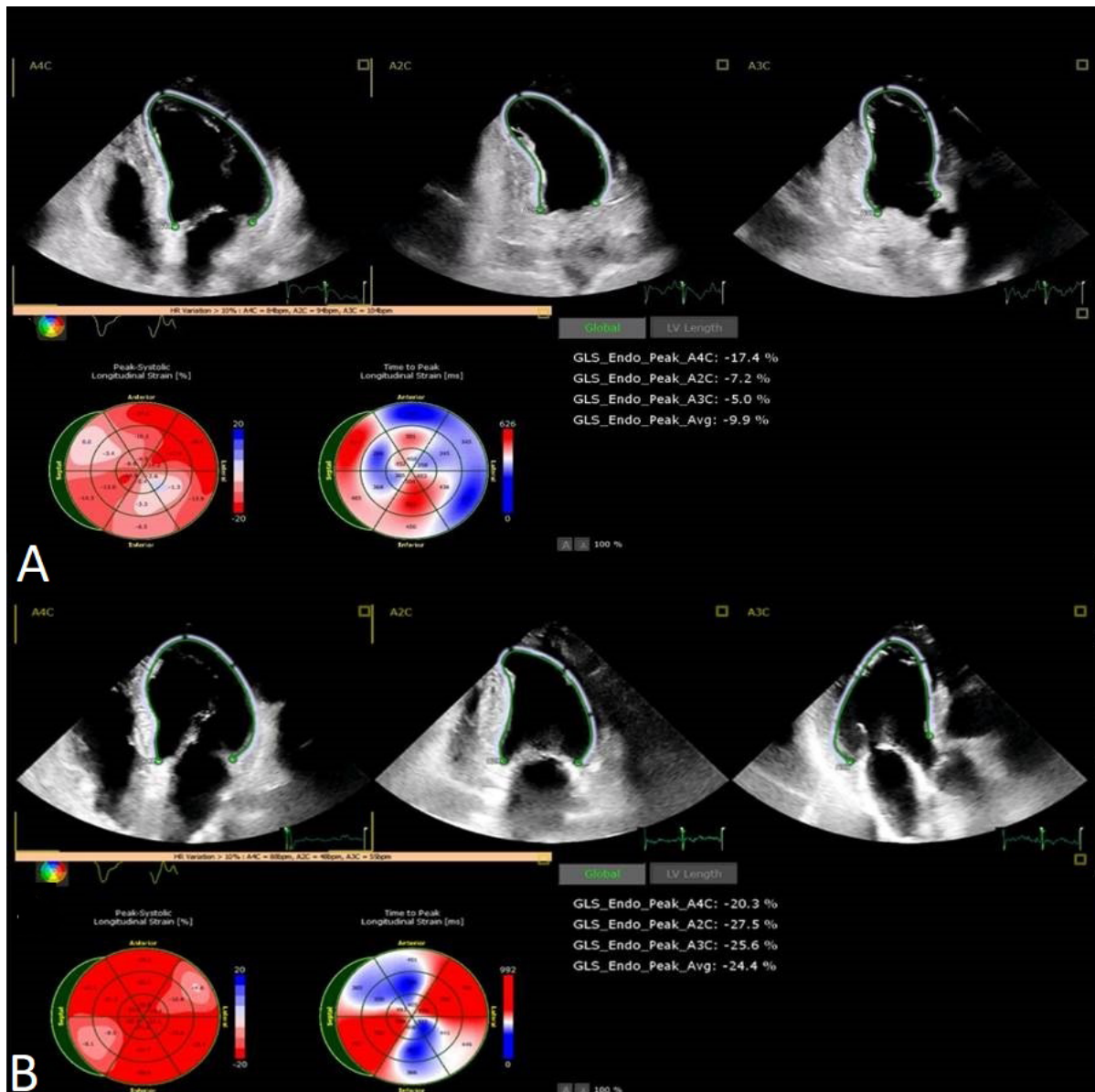


Fig. 4. Speckle tracking echocardiography showing the improvement in global longitudinal strain and time to peak longitudinal strain from the acute phase (A) to 1 month follow-up (B). GLS, global longitudinal strain.

normalities in patients with TS and poor acoustic window. Furthermore, it is useful in detecting intraventricular thrombosis. Contrast echocardiography was used in order to reveal myocardial perfusion defects in the affected areas suggesting transient microvascular dysfunction [98,99].

10. Transthoracic Coronary Artery Doppler

In patients with a good acoustic window, assessment of left anterior coronary Doppler by TTE can help differentiate between acute anterior myocardial infarction and TS — apical variant [100]. Pulsed wave Doppler during dipyridamole echocardiography tests showed a decrease in the coronary flow reserve in the early days of TS and recovers alongside the systolic function [101].

11. Cardiac Magnetic Resonance

CMR has a developing role in the diagnosis of TS [102]. It is a valuable tool in differentiating between TS and other causes in patients presenting with chest pain, elevated troponin levels and coronary arteries with no significant stenoses. CMR provides a dynamic and structural assessment of the myocardium and also detects myocardial inflammation and scarring [103].

In the acute phase, the cine sequences of CMR allow the visualization of RWMA (apical, midventricular), the circumferential pattern, the RV involvement [47]. It can also show complications: pericardial effusion, systolic anterior movement mitral with mitral regurgitation, ventricular thrombosis. Maybe most importantly, CMR provides tissue characterization — it can detect myocardial

edema, necrosis, fibrosis — essential criteria for the differential diagnosis with myocardial infarction and myocarditis [103,104].

In the Stockholm Myocardial Infarction with Normal Coronaries Study I and II, patients diagnosed with myocardial infarction with non-obstructive coronary arteries (MINOCA) underwent CMR evaluation. Among them, approximately a third were diagnosed with TS, differentiating them from patients with myocardial infarction, myocarditis or other cardiomyopathies (dilated, hypertrophic cardiomyopathy) [105,106]. CMR is superior in detecting RV involvement than echocardiography and in evaluating the RV function.

CMR using T2 weighted images is a noninvasive alternative in discovering myocardial edema. The areas of myocardial edema correlated with RWMA areas [107,108] (Fig. 5). Studies who performed endomyocardial biopsies in Takotsubo patients proved there is inflammation in the motion abnormalities areas [109].

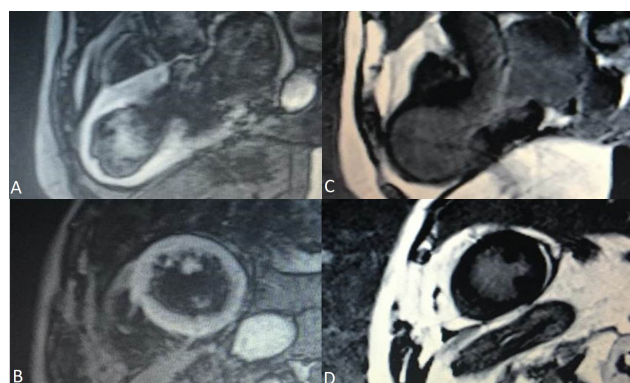


Fig. 5. Cardiac Magnetic Resonance Imaging of a 78 years old female patient in the acute phase of Takotsubo Syndrome. Myocardial edema can be observed in the apical regions of the left ventricle in T2 weighted images (A and B) and the lack of late gadolinium enhancement in C and D.

Generally, there is no fibrosis detected on late gadolinium enhancement (LGE) CMR. In the chronic phase, CMR follow up reveals normal ventricular function, normal regional wall motion, no edema, no necrosis and no fibrosis [110]. Even though in most Takotsubo cases there was no LGE present, LGE positive cardiac magnetic Resonance imaging (MRI) in TS were reported in a few cases [111–113]. A two-step recovery in the LV function in TS was described. The first step was the recovery of the LV systolic function and the latter one was the improvement of the diastolic one, assessed by LV peak filling rates and left atrial filling volumes [114]. CMR based strain analysis of the LV in the acute phase revealed that CMR does have prognostic value in TS patients. However, prognosis was mainly influenced by the patients' comorbidities [115].

Studies that enrolled patients with suspected TS patients performed CMR in order to establish the diagnosis. Thirty-seven patients with RWMA, non-obstructive coronary arteries, ECG abnormalities and elevated troponin underwent CMR evaluation. Four patients were diagnosed with myocarditis, 7 patients with myocardial infarction and the rest [26] were diagnosed with TS [110]. During the COVID-19 pandemic, there were a few cases of vaccine associated myocarditis reported [116]. In one particular case, CMR aided the medical team in discovering a case of vaccine associated TS [117].

Even though echocardiography is an extremely valuable tool in the diagnosis and management of TS, only CMR and endomyocardial biopsy can truly distinguish between myocarditis and TS [118].

In the rare instances of acute myocardial infarction and TS simultaneity, CMR is the only exploration able to describe both areas of myocardial edema suggestive of TS and areas of subendocardial or transmural ischemic necrosis [119,120].

Regarding female patients in the peripartum stage, acute systolic dysfunction requires a difficult differential diagnosis, including peripartum cardiomyopathy, acute myocarditis, TS, acute myocardial infarction and genetic cardiomyopathy. In order to differentiate among these, CMR needs to be performed [121].

When patients present with apical RWMA and non-obstructive coronary arteries, the clinical likelihood of TS is high. But when a patient presents with an atypical pattern, the TS diagnosis is so much more difficult. In such cases, CMR is of unquestionable benefit [122] (Table 2). The positive and differential diagnosis in TS is a complex one, starting from the clinical arguments of TS likelihood and ischemic risk, and oftentimes extending beyond echocardiography and coronary artery imaging to magnetic resonance myocardial description (Fig. 6).

12. Nuclear Imaging

Nuclear imaging techniques in TS patients have a limited role in clinical practice. Their importance resides in deepening the understanding of TS's pathophysiology. Nuclear techniques are used in investigating the myocardial perfusion and myocardial metabolism (using metabolites such as fatty acids and glucose). Studies using positron emitted tomography with fluorodeoxyglucose and single-photon emission computerized tomography with fatty acids revealed both metabolic and perfusion abnormalities but a more profound defect was found in the metabolic activity compared to the perfusion defect [39,123,124]. This imbalance found in the wall motion abnormalities was named "inverse perfusion-metabolism mismatch". Impaired perfusion suggests microvascular dysfunction.

Myocardial scintigraphy using ¹²³I Metaiodobenzylguanidine (a molecule which resembles noradrenaline structurally) revealed a cardiac adrenergic dysfunction in

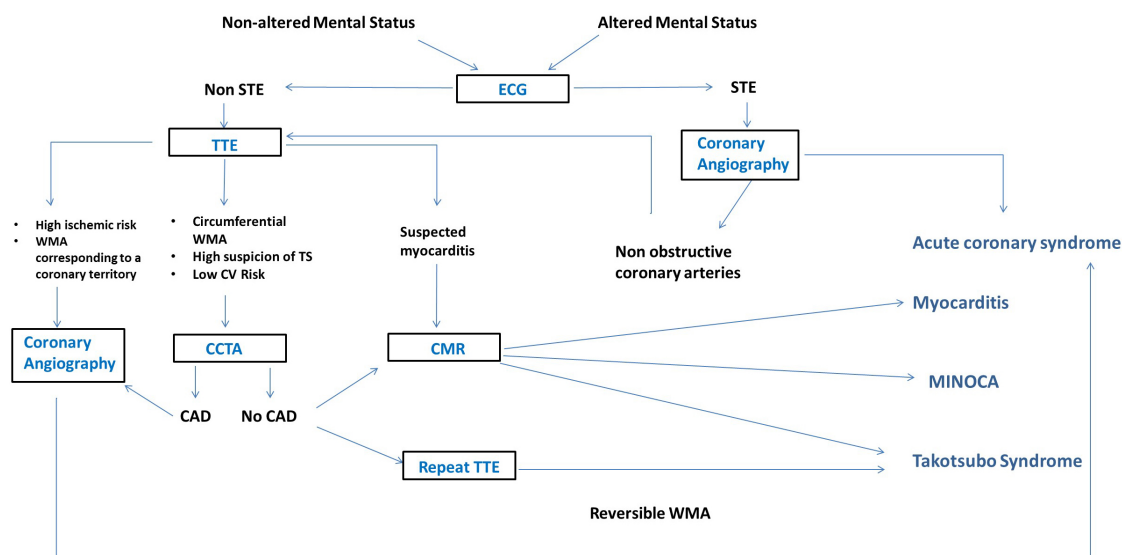


Fig. 6. Imagistic Diagnostic Flowchart of Takotsubo Syndrome (Modified after Ghadri *et al.* 2018 [3]). CAD, coronary artery disease; CMR, cardiac magnetic resonance; ECG, electrocardiogram; MINOCA, Myocardial infarction with non-obstructive coronary arteries; STE, ST segment elevation; TTE, transthoracic echocardiography; WMA, wall motion abnormalities; CCTA, coronary computed tomography angiography; TS, Takotsubo syndrome; CV, cardiovascular.

Table 2. The main imaging methods in Takotsubo Cardiomyopathy — positive and negative points.

Takotsubo Cardiomyopathy					
Echocardiography		Cardiac Magnetic Resonance		Coronary Angiography	
+	–	+	–	+	–
• Easily accessible		• LV/RV function		• LV/RV function	• Invasive
• LV/RV function	• Acoustic window dependent	• Tissue characterization	• High cost	• Differential diagnosis with coronary artery disease	• Radiation exposure
• Complications		• Complications			• No follow-up
• Follow-up		• Follow-up			
		• Differential diagnosis			

LV, left ventricle; RV, right ventricle.

the acute phase in the motion abnormalities areas, which improved over time [39,125]. These methods of sympathetic nervous imaging support the idea of adrenergic mediated myocardial stunning.

13. Conclusions

Takotsubo cardiomyopathy is a condition with a wide variety of patterns and complications. Even though the reversibility of TS suggests a “benign” course, over the years many complications and poor long term prognosis were described. The complex management starts with the diagnosis and ends with a not so favorable prognosis. Echocardiography is the paramount investigation used in the diagnosis and follow up of the syndrome. Coronary angiography is of utmost importance when suspecting an acute coronary syndrome that needs urgent revascularization. CMR is most useful in the differential diagnosis with other types of acute systolic dysfunction, ischemic or non-ischemic. Strain assessment by echocardiography and CMR may provide valuable prognostic information in the near future.

Author Contributions

CP, LP and SB substantially contributed to the design of the article. CP and LP performed the research and interpreted the relevant literature. SB revised the content of the article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Publication of this paper was supported by the University of Medicine and Pharmacy Carol Davila, through the institutional program Publish not Perish. Laura Arama, MD, PhD.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Sato H, Tateishi H, Uchida T, Dote K, Ishihara M, Kodama K, *et al.* Clinical aspect of myocardial injury: from ischemia to heart failure. *Kagaku Hyoronsha*. 1990; 2: 55–64.
- [2] Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, *et al.* International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology. *European Heart Journal*. 2018; 39: 2032–2046.
- [3] Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, *et al.* International Expert Consensus Document on Takotsubo Syndrome (Part II): Diagnostic Workup, Outcome, and Management. *European Heart Journal*. 2018; 39: 2047–2062.
- [4] Scantlebury DC, Prasad A. Diagnosis of takotsubo cardiomyopathy—Mayo Clinic criteria. *Circulation Journal*. 2014; 78: 2129–2139.
- [5] Lyon AR, Bossone E, Schneider B, Sechtem U, Citro R, Underwood SR, *et al.* Current state of knowledge on Takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. *European Journal of Heart Failure*. 2016; 18: 8–27.
- [6] Qin D, Patel SM, Champion HC. “Happiness” and stress cardiomyopathy (apical ballooning syndrome/takotsubo syndrome). *International Journal of Cardiology*. 2014; 172: e182–e183.
- [7] Fazzini L, Marchetti MF, Biddau M, Aste F, Maiani S, Montisci R. The Happiness for Italy’s Victory at the European Soccer Championships Costs a “Happy Heart Syndrome”. *European Journal of Case Reports in Internal Medicine*. 2022; 9: 003572.
- [8] Morris NA, Chatterjee A, Adejumo OL, Chen M, Merkler AE, Murthy SB, *et al.* The Risk of Takotsubo Cardiomyopathy in Acute Neurological Disease. *Neurocritical Care*. 2019; 30: 171–176.
- [9] Muratsu A, Muroya T, Kuwagata Y. Takotsubo cardiomyopathy in the intensive care unit. *Acute Medicine & Surgery*. 2019; 6: 152–157.
- [10] Rowell AC, Stedman WG, Janin PF, Diel N, Ward MR, Kay SM, *et al.* Silent left ventricular apical ballooning and Takotsubo cardiomyopathy in an Australian intensive care unit. *ESC Heart Failure*. 2019; 6: 1262–1265.
- [11] Andò G, Trio O, de Gregorio C. Transient left ventricular dysfunction in patients with neurovascular events. *Acute Cardiac Care*. 2010; 12: 70–74.
- [12] Trio O, de Gregorio C, Andò G. Myocardial dysfunction after subarachnoid haemorrhage and tako-tsubo cardiomyopathy: a differential diagnosis? *Therapeutic Advances in Cardiovascular Disease*. 2010; 4: 105–107.
- [13] Bybee KA, Kara T, Prasad A, Lerman A, Barsness GW, Wright RS, *et al.* Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Annals of Internal Medicine*. 2004; 141: 858–865.
- [14] Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *American Heart Journal*. 2008; 155: 408–417.
- [15] Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jurgowski M, *et al.* Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. *The New England Journal of Medicine*. 2015; 373: 929–938.
- [16] Galiuto L, Crea F. Primary and secondary takotsubo syndrome: Pathophysiological determinant and prognosis. *European Heart Journal. Acute Cardiovascular Care*. 2020; 9: 690–693.
- [17] Lyon AR, Citro R, Schneider B, Morel O, Ghadri JR, Templin C, *et al.* Pathophysiology of Takotsubo Syndrome: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*. 2021; 77: 902–921.
- [18] Lüscher TF, Templin C. Is takotsubo syndrome a microvascular acute coronary syndrome? Towards of a new definition. *European Heart Journal*. 2016; 37: 2816–2820.
- [19] Zuin M, Mugnai G, Anselmi M, Bonapace S, Bozzini P, Chirillo F, *et al.* Takotsubo Syndrome during COVID-19 Pandemic in the Veneto Region, Italy. *Viruses*. 2022; 14: 1971.
- [20] Jabri A, Kalra A, Kumar A, Alameh A, Adroja S, Bashir H, *et al.* Incidence of Stress Cardiomyopathy During the Coronavirus Disease 2019 Pandemic. *JAMA Network Open*. 2020; 3: e2014780.
- [21] Ghadri JR, Cammann VL, Jurisic S, Seifert B, Napp LC, Diekmann J, *et al.* A novel clinical score (InterTAK Diagnostic Score) to differentiate takotsubo syndrome from acute coronary syndrome: results from the International Takotsubo Registry. *European Journal of Heart Failure*. 2017; 19: 1036–1042.
- [22] Del Buono MG, Potere N, Chiabrando JG, Bressi E, Abbate A. Takotsubo syndrome: diagnostic work-up and clues into differential diagnosis. *Current Opinion in Cardiology*. 2019; 34: 673–686.
- [23] Ibáñez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, *et al.* 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Revista Espanola De Cardiologia (English Ed.)*. 2017; 70: 1082.
- [24] Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al.* 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *European Heart Journal*. 2021; 42: 1289–1367.
- [25] Citro R, Okura H, Ghadri JR, Izumi C, Meimoun P, Izumo M, *et al.* Multimodality imaging in takotsubo syndrome: a joint consensus document of the European Association of Cardiovascular Imaging (EACVI) and the Japanese Society of Echocardiography (JSE). *Journal of Echocardiography*. 2020; 18: 199–224.
- [26] Tavakolian K, Odak M, Miller B, Mararenko A, Nightingale S, Douedi S, *et al.* Atypical Stress Cardiomyopathy: A Case Report. *Cureus*. 2022; 14: e27786.
- [27] Hurtado Rendón IS, Alcivar D, Rodriguez-Escudero JP, Silver K. Acute Myocardial Infarction and Stress Cardiomyopathy Are Not Mutually Exclusive. *The American Journal of Medicine*. 2018; 131: 202–205.
- [28] Heyse A, Anne F, Lagae B, Van Haver H, Van Durme F. Serial strain imaging in takotsubo syndrome with concomitant coronary artery disease. *Acta Clinica Belgica*. 2019; 74: 203–205.
- [29] Desmet W, Bennett J, Ferdinande B, De Cock D, Adriaenssens T, Coosemans M, *et al.* The apical nipple sign: a useful tool for discriminating between anterior infarction and transient left ventricular ballooning syndrome. *European Heart Journal: Acute Cardiovascular Care*. 2014; 3: 264–267.
- [30] Sharma V, Srinivasan M, Sheehan DM, Ionescu A. Stress cardiomyopathy: case series and the review of literature. *The Journal of Emergency Medicine*. 2013; 45: e95–e98.
- [31] Haghi D, Roehm S, Hamm K, Harder N, Suselbeck T, Borggrefe M, *et al.* Takotsubo cardiomyopathy is not due to plaque rupture: an intravascular ultrasound study. *Clinical Cardiology*. 2010; 33: 307–310.

- [32] Verna E, Provasoli S, Ghiringhelli S, Morandi F, Salerno-Uriarte J. Abnormal coronary vasoreactivity in transient left ventricular apical ballooning (tako-tsubo) syndrome. *International Journal of Cardiology*. 2018; 250: 4–10.
- [33] Eitel I, Stiermaier T, Graf T, Möller C, Rommel KP, Eitel C, *et al*. Optical Coherence Tomography to Evaluate Plaque Burden and Morphology in Patients With Takotsubo Syndrome. *Journal of the American Heart Association*. 2016; 5: e004474.
- [34] Fineschi M, D'Ascenzi F, Sirbu V, Mondillo S, Pierli C. The role of optical coherence tomography in clarifying the mechanisms for dobutamine stress echocardiography-induced takotsubo cardiomyopathy. *Echocardiography (Mount Kisco, N.Y.)*. 2013; 30: E121–E124.
- [35] Murthy A, Arora J, Singh A, Gedela M, Karnati P, Nappi A. Takotsubo Cardiomyopathy: Typical and Atypical Variants, A Two-Year Retrospective Cohort Study. *Cardiology Research*. 2014; 5: 139–144.
- [36] Singh M, Reddin G, Garcia-Garcia HM, Medvedofsky D, Asch FM, Kumar P, *et al*. Comparison of Contractility Patterns on Left Ventriculogram Versus Longitudinal Strain by Echocardiography in Patients With Takotsubo Cardiomyopathy. *Cardiovascular Revascularization Medicine*. 2021; 27: 45–51.
- [37] Del Buono MG, Montone RA, Meucci MC, La Vecchia G, Camilli M, Giraldi L, *et al*. Left ventricular end-diastolic pressure predicts in-hospital outcomes in takotsubo syndrome. *European Heart Journal: Acute Cardiovascular Care*. 2021; 10: 661–667.
- [38] Novo G, Quagliana A, Buccheri D, Rizzo S, Giambanco S, Giambanco F, *et al*. Characteristics of coronary microcirculatory function in patients with Takotsubo syndrome. *Journal of Thoracic Disease*. 2017; 9: 4531–4537.
- [39] Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nishioka K, *et al*. Myocardial perfusion and fatty acid metabolism in patients with tako-tsubo-like left ventricular dysfunction. *Journal of the American College of Cardiology*. 2003; 41: 743–748.
- [40] Fazio G, Sarullo FM, Novo G, Evola S, Lunetta M, Barbaro G, *et al*. Tako-tsubo cardiomyopathy and microcirculation. *Journal of Clinical Monitoring and Computing*. 2010; 24: 101–105.
- [41] Loffi M, Santangelo A, Kozel M, Kocka V, Budesinsky T, Lisa L, *et al*. Takotsubo Cardiomyopathy: One More Angiographic Evidence of Microvascular Dysfunction. *BioMed Research International*. 2018; 2018: 5281485.
- [42] Sans-Roselló J, Fernández-Peregrina E, Duran-Cambra A, Carreras-Mora J, Sionis A, Álvarez-García J, *et al*. Coronary Microvascular Dysfunction in Takotsubo Syndrome Assessed by Angiography-Derived Index of Microcirculatory Resistance: A Pressure-Wire-Free Tool. *Journal of Clinical Medicine*. 2021; 10: 4331.
- [43] Sueta D, Oda S, Izumiya Y, Kaikita K, Kidoh M, Utsunomiya D, *et al*. Comprehensive assessment of takotsubo cardiomyopathy by cardiac computed tomography. *Emergency Radiology*. 2019; 26: 109–112.
- [44] Otálvaro L, Zambrano JP, Fishman JE. Takotsubo cardiomyopathy: utility of cardiac computed tomography angiography for acute diagnosis. *Journal of Thoracic Imaging*. 2011; 26: W83–W85.
- [45] Lancellotti P, Zamorano JL, Habib G. The EACVI Textbook of Echocardiography. 2nd ed. The European Society of Cardiology Textbooks: Oxford. 2016.
- [46] Ahmed Y, Rafique M, Ahmad S, Omar B, Malozzi C. Reverse Takotsubo Cardiomyopathy in a Patient With Commotio Cordis. *Journal of Medical Cases*. 2022; 13: 414–420.
- [47] Parekh M. Change of heart: Reverse takotsubo's cardiomyopathy - A case report. *Clinical Imaging*. 2021; 69: 219–222.
- [48] Champion S, Belcour D, Vandroux D, Drouet D, Gaüzère BA, Bouchet B, *et al*. Stress (Tako-tsubo) cardiomyopathy in critically-ill patients. *European Heart Journal. Acute Cardiovascular Care*. 2015; 4: 189–196.
- [49] Song BG, Chun WJ, Park YH, Kang GH, Oh J, Lee SC, *et al*. The clinical characteristics, laboratory parameters, electrocardiographic, and echocardiographic findings of reverse or inverted takotsubo cardiomyopathy: Comparison with mid or apical variant. *Clinical Cardiology*. 2011; 34: 693–699.
- [50] Sumida H, Morihisa K, Katahira K, Sugiyama S, Kishi T, Oshima S. Isolated Right Ventricular Stress (Takotsubo) Cardiomyopathy. *Internal Medicine*. 2017; 56: 2159–2164.
- [51] Kagiya N, Okura H, Kume T, Hayashida A, Yoshida K. Isolated right ventricular takotsubo cardiomyopathy. *European Heart Journal: Cardiovascular Imaging*. 2015; 16: 285.
- [52] De Backer O, Debonnaire P, Gevaert S, Missault L, Gheeraert P, Muyldermans L. Prevalence, associated factors and management implications of left ventricular outflow tract obstruction in takotsubo cardiomyopathy: a two-year, two-center experience. *BMC Cardiovascular Disorders*. 2014; 14: 147.
- [53] Albenque G, Bohbot Y, Delpierre Q, Tribouilloy C. Basal Takotsubo syndrome with transient severe mitral regurgitation caused by drug use: a case report. *European Heart Journal: Case Reports*. 2020; 4: 1–6.
- [54] Citro R, Rigo F, D'Andrea A, Ciampi Q, Parodi G, Provenza G, *et al*. Echocardiographic correlates of acute heart failure, cardiogenic shock, and in-hospital mortality in tako-tsubo cardiomyopathy. *JACC: Cardiovascular Imaging*. 2014; 7: 119–129.
- [55] Zalewska-Adamiec M, Bachórzewska-Gajewska H, Dobrzycki S. Cardiac Rupture-The Most Serious Complication of Takotsubo Syndrome: A Series of Five Cases and a Systematic Review. *Journal of Clinical Medicine*. 2021; 10: 1066.
- [56] Akashi YJ, Tejima T, Sakurada H, Matsuda H, Suzuki K, Kawasaki K, *et al*. Left ventricular rupture associated with Takotsubo cardiomyopathy. *Mayo Clinic Proceedings*. 2004; 79: 821–824.
- [57] Jaguszewski M, Fijalkowski M, Nowak R, Czapiewski P, Ghadri JR, Templin C, *et al*. Ventricular rupture in Takotsubo cardiomyopathy. *European Heart Journal*. 2012; 33: 1027.
- [58] Sung JM, Hong SJ, Chung IH, Lee HY, Lee JH, Kim HJ, *et al*. Rupture of Right Ventricular Free Wall Following Ventricular Septal Rupture in Takotsubo Cardiomyopathy with Right Ventricular Involvement. *Yonsei Medical Journal*. 2017; 58: 248–251.
- [59] Sacha J, Maselko J, Wester A, Szudrowicz Z, Pluta W. Left ventricular apical rupture caused by takotsubo cardiomyopathy—comprehensive pathological heart investigation. *Circulation Journal*. 2007; 71: 982–985.
- [60] Herath HMMTB, Pahalagamage SP, Lindsay LC, Vinathan S, Withanawasam S, Senarathne V, *et al*. Takotsubo cardiomyopathy complicated with apical thrombus formation on first day of the illness: a case report and literature review. *BMC Cardiovascular Disorders*. 2017; 17: 176.
- [61] de Gregorio C. Cardioembolic outcomes in stress-related cardiomyopathy complicated by ventricular thrombus: a systematic review of 26 clinical studies. *International Journal of Cardiology*. 2010; 141: 11–17.
- [62] Gudenkauf B, Goetsch MR, Vakil RM, Cingolani O, Adamo L. Case Report: Steroid-Responsive Takotsubo Cardiomyopathy Associated With Cytokine Storm and Obstructive Shock. *Frontiers in Cardiovascular Medicine*. 2022; 9: 931070.
- [63] Tsugu T, Nagatomo Y, Nakajima Y, Kageyama T, Endo J, Itabashi Y, *et al*. Biventricular takotsubo cardiomyopathy with asymmetrical wall motion abnormality between left and right ventricle: a report of new case and literature review. *Journal of Echocardiography*. 2019; 17: 123–128.
- [64] Yang C, Han X, Du Y, Ma AQ. Takotsubo cardiomyopathy and pituitary apoplexy: a case report. *BMC Cardiovascular Disorders*.

ders. 2020; 20: 236.

- [65] Molnár C, Gál J, Szántó D, Fülöp L, Szegedi A, Siró P, *et al.* Takotsubo cardiomyopathy in patients suffering from acute non-traumatic subarachnoid hemorrhage-A single center follow-up study. *PLoS ONE*. 2022; 17: e0268525.
- [66] Papadis A, Svab S, Brugger N, Lanz J, von Arx R, Stamou K, *et al.* “Broken Heart” and “Broken Brain”: Which Connection? *Cardiology Research*. 2022; 13: 65–70.
- [67] Shams P, Ahmed I, Khan AH. Reverse Takotsubo Cardiomyopathy Following A Case Of Suspected Meningoencephalitis And Literature Review. *Journal of Ayub Medical College Abbottabad*. 2021; 33: 695–697.
- [68] Riaño-Ondiviela A, Escota-Villanueva J, Pinillos-Francia G, Morlanes-Gracia P, Cantero-Lozano D, Salvador-Casabón JM, *et al.* Takotsubo syndrome or stress cardiomyopathy precipitated by severe myasthenic crisis. *Archivos De Cardiologia De Mexico*. 2020; 90: 210–212.
- [69] Paraschiv C, Trasca LF, Enciu O, Balanescu SM, Miron A. Takotsubo syndrome during surgery for pheochromocytoma: an unexpected complication. *Oxford Medical Case Reports*. 2021; 2021: omab087.
- [70] Gologorsky E, Gologorsky A. Intraoperative stress cardiomyopathy. *Journal of the American Society of Echocardiography: Official Publication of the American Society of Echocardiography*. 2010; 23: 340.e3–4.
- [71] Steinecker M, Benvenuti C, Digne F, Nejari M. Case report: takotsubo cardiomyopathy after transcatheter aortic valve-in-valve replacement. *European Heart Journal: Case Reports*. 2020; 5: ytaa457.
- [72] Vieira AC, Ribeiro MFSA, Lima J, Filho JS, de Andrade Carvalho H, Mano MS. Takotsubo syndrome induced by brachytherapy in a patient with endocervical adenocarcinoma. *Cardio-oncology*. 2020; 6: 30.
- [73] Gursahaney DL, Wiktor DM, Lindquist J. Takotsubo cardiomyopathy following ultrasound-guided renal cyst aspiration. *BJR Case Reports*. 2019; 5: 20180101.
- [74] Belli O, Ardisino M, Bottioli M, Soriano F, Blanda C, Oreglia J, *et al.* Emergency cardiac imaging for coronavirus disease 2019 (COVID-19) in practice: a case of takotsubo stress cardiomyopathy. *Cardiovascular Ultrasound*. 2021; 19: 31.
- [75] Pancholi P, Emami N, Fazzari MJ, Kapoor S. Stress cardiomyopathy in critical care: A case series of 109 patients. *World Journal of Critical Care Medicine*. 2022; 11: 149–159.
- [76] Naser N, Buksa M, Kusljagic Z, Terzic I, Sokolovic S, Hodzic E. The role of echocardiography in diagnosis and follow up of patients with takotsubo cardiomyopathy or acute ballooning syndrome. *Medicinski Arhiv*. 2011; 65: 287–290.
- [77] Perera I, Rajapakse S, De Silva ST. Severe Hyponatremia-Induced Stress Cardiomyopathy: A Case Report and Review of Literature. *Case Reports in Cardiology*. 2020; 2020: 2961856.
- [78] Ishigaki D, Okuyama H, Yuki K, Sato Y, Ogawa N, Hirono O, *et al.* Serial evaluation of left ventricular contraction and relaxation in Takotsubo cardiomyopathy by 2D speckle tracking echocardiography. *Journal of Medical Ultrasonics (2001)*. 2012; 39: 265–269.
- [79] Lee M. Time Course of Functional Recovery in Takotsubo (Stress) Cardiomyopathy: A Serial Speckle Tracking Echocardiography and Electrocardiography Study. *Journal of Cardiovascular Imaging*. 2020; 28: 50–60.
- [80] Citro R, Radano I, Parodi G, Di Vece D, Zito C, Novo G, *et al.* Long-term outcome in patients with Takotsubo syndrome presenting with severely reduced left ventricular ejection fraction. *European Journal of Heart Failure*. 2019; 21: 781–789.
- [81] Kumar S, Waldenborg M, Bhumireddy P, Ramkissoon K, Loiske K, Innasimuthu AL, *et al.* Diastolic function improves after resolution of takotsubo cardiomyopathy. *Clinical Physiology and Functional Imaging*. 2016; 36: 17–24.
- [82] Mirna M, Vogl F, Schmutzler L, Rezar R, Boxhammer E, Topf A, *et al.* Tei Index Complements Conventional Echocardiographic Parameters in Diagnostic Workup of Suspected Takotsubo Syndrome. *Medical Principles and Practice*. 2022. (Online ahead of print)
- [83] Hwang HJ, Sohn IS. A case of biventricular involvement of Takotsubo cardiomyopathy: 3D echocardiographic imaging. *Journal of Echocardiography*. 2014; 12: 48–49.
- [84] Wierzbowska-Drabik K, Marcinkiewicz A, Hamala P, Trzos E, Lipiec P, Kurpesa M, *et al.* Takotsubo cardiomyopathy in the case of 72-year-old teacher after work-related psychological stress. Evolution of left ventricular longitudinal strain - Delayed but complete recovery in automated function imaging (AFI). *International Journal of Occupational Medicine and Environmental Health*. 2017; 30: 681–683.
- [85] Kobayashi Y, Okura H, Kobayashi Y, Fukuda S, Hirohata A, Yoshida K. Left ventricular myocardial function assessed by three-dimensional speckle tracking echocardiography in Takotsubo cardiomyopathy. *Echocardiography*. 2017; 34: 523–529.
- [86] Schwarz K, Ahearn T, Srinivasan J, Neil CJ, Scally C, Rudd A, *et al.* Alterations in Cardiac Deformation, Timing of Contraction and Relaxation, and Early Myocardial Fibrosis Accompany the Apparent Recovery of Acute Stress-Induced (Takotsubo) Cardiomyopathy: An End to the Concept of Transience. *Journal of the American Society of Echocardiography*. 2017; 30: 745–755.
- [87] Heggemann F, Weiss C, Hamm K, Kaden J, Süselbeck T, Papavassiliu T, *et al.* Global and regional myocardial function quantification by two-dimensional strain in Takotsubo cardiomyopathy. *European Journal of Echocardiography: the Journal of the Working Group on Echocardiography of the European Society of Cardiology*. 2009; 10: 760–764.
- [88] Dias A, Franco E, Rubio M, Bhalla V, Pressman GS, Amanullah S, *et al.* Usefulness of left ventricular strain analysis in patients with takotsubo syndrome during acute phase. *Echocardiography*. 2018; 35: 179–183.
- [89] Hung MJ, Kao YC, Chen WS, Mao CT, Chen TH, Yang NI, *et al.* Layer-specific quantification of myocardial deformation in sepsis-induced Takotsubo cardiomyopathy: Three case reports of a serial 2-dimensional speckle-tracking echocardiographic study. *Medicine*. 2016; 95: e5250.
- [90] Scally C, Rudd A, Mezincescu A, Wilson H, Srivanasan J, Horgan G, *et al.* Persistent Long-Term Structural, Functional, and Metabolic Changes After Stress-Induced (Takotsubo) Cardiomyopathy. *Circulation*. 2018; 137: 1039–1048.
- [91] Wilk A, Król W, Anna ŻS, Ziemska-Gorczyca M, Tetera W, Konopka M, *et al.* Can longitudinal strain analysis differentiate between Takotsubo syndrome and acute coronary syndrome? *Echocardiography*. 2023; 40: 174–179.
- [92] Kumar A, Jenkins LA, Perez-Verdia A, Roongsritong C. Transient left ventricular apical ballooning during dobutamine myocardial perfusion imaging. *International Journal of Cardiology*. 2008; 124: 378–380.
- [93] Margey R, Diamond P, McCann H, Sugrue D. Dobutamine stress echo-induced apical ballooning (Takotsubo) syndrome. *European Journal of Echocardiography*. 2009; 10: 395–399.
- [94] Mosley WJ, 2nd, Manuchehry A, McEvoy C, Rigolin V. Takotsubo cardiomyopathy induced by dobutamine infusion: a new phenomenon or an old disease with a new name. *Echocardiography*. 2010; 27: E30–E33.
- [95] Shah BN, Simpson IA, Rakhit DJ. Takotsubo (apical ballooning) syndrome in the recovery period following dobutamine stress echocardiography: a first report. *European Journal of Echocardiography*. 2011; 12: E5.
- [96] Silberbauer J, Hong P, Lloyd GW. Takotsubo cardiomyopathy (left ventricular ballooning syndrome) induced during dobu-

- tamine stress echocardiography. *European Journal of Echocardiography*. 2008; 9: 136–138.
- [97] Chia PL, Lee E. Reverse Takotsubo pattern stress cardiomyopathy in a male patient induced during dobutamine stress echocardiography. *Annals of the Academy of Medicine, Singapore*. 2012; 41: 264.
- [98] Jain M, Upadaya S, Zarich SW. Serial evaluation of microcirculatory dysfunction in patients with Takotsubo cardiomyopathy by myocardial contrast echocardiography. *Clinical Cardiology*. 2013; 36: 531–534.
- [99] Abdelmoneim SS, Mankad SV, Bernier M, Dhoble A, Hagen ME, Ness SAC, *et al.* Microvascular function in Takotsubo cardiomyopathy with contrast echocardiography: prospective evaluation and review of literature. *Journal of the American Society of Echocardiography*. 2009; 22: 1249–1255.
- [100] Meimoun P, Clerc J, Vincent C, Flahaut F, Germain AL, Elmekies F, *et al.* Non-invasive detection of tako-tsubo cardiomyopathy vs. acute anterior myocardial infarction by transthoracic Doppler echocardiography. *European Heart Journal: Cardiovascular Imaging*. 2013; 14: 464–470.
- [101] Rigo F, Sicari R, Citro R, Ossena G, Buja P, Picano E. Diffuse, marked, reversible impairment in coronary microcirculation in stress cardiomyopathy: a Doppler transthoracic echo study. *Annals of Medicine*. 2009; 41: 462–470.
- [102] Nakamori S, Matsuoka K, Onishi K, Kurita T, Ichikawa Y, Nakajima H, *et al.* Prevalence and signal characteristics of late gadolinium enhancement on contrast-enhanced magnetic resonance imaging in patients with takotsubo cardiomyopathy. *Circulation Journal*. 2012; 76: 914–921.
- [103] Kohan AA, Levy Yeyati E, De Stefano L, Dragonetti L, Pietrani M, Perez de Arenaza D, *et al.* Usefulness of MRI in takotsubo cardiomyopathy: a review of the literature. *Cardiovascular Diagnosis and Therapy*. 2014; 4: 138–146.
- [104] Jensch PJ, Stiermaier T, Eitel I. Takotsubo Syndrome-Is There a Need for CMR? *Current Heart Failure Reports*. 2021; 18: 200–210.
- [105] Collste O, Sörensson P, Frick M, Agewall S, Daniel M, Henareh L, *et al.* Myocardial infarction with normal coronary arteries is common and associated with normal findings on cardiovascular magnetic resonance imaging: results from the Stockholm Myocardial Infarction with Normal Coronaries study. *Journal of Internal Medicine*. 2013; 273: 189–196.
- [106] Sörensson P, Ekenbäck C, Lundin M, Agewall S, Bacsovcics Brodin E, Caidahl K, *et al.* Early Comprehensive Cardiovascular Magnetic Resonance Imaging in Patients With Myocardial Infarction With Nonobstructive Coronary Arteries. *JACC: Cardiovascular Imaging*. 2021; 14: 1774–1783.
- [107] Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, Carbone I, Muellerleile K, Aldrovandi A, *et al.* Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. *JAMA*. 2011; 306: 277–286.
- [108] Subbaraman S, Rajan SC, Veeraiyan S, Natarajan P. Takotsubo Cardiomyopathy: Role of Cardiac MRI. *Journal of Radiology Case Reports*. 2021; 15: 26–32.
- [109] Iacucci I, Carbone I, Cannavale G, Conti B, Iampieri I, Rosati R, *et al.* L'edema miocardico come marker di danno acuto nella cardiomiopatia di Takotsubo: Valutazione con risonanza magnetica cardiaca. *Radiol Medica*. 2013; 118: 1309–1323.
- [110] Eitel I, Lücke C, Grothoff M, Sareban M, Schuler G, Thiele H, *et al.* Inflammation in takotsubo cardiomyopathy: insights from cardiovascular magnetic resonance imaging. *European Radiology*. 2010; 20: 422–431.
- [111] Bohl S, Schulz-Menger J. Cardiovascular magnetic resonance imaging of non-ischaemic heart disease: established and emerging applications. *Heart, Lung & Circulation*. 2010; 19: 117–132.
- [112] Bruder O, Hunold P, Jochims M, Waltering KU, Sabin GV, Barkhausen J. Reversible late gadolinium enhancement in a case of Takotsubo cardiomyopathy following high-dose dobutamine stress MRI. *International Journal of Cardiology*. 2008; 127: e22–e24.
- [113] Haghi D, Fluechter S, Suselbeck T, Borggrefe M, Papavassiliu T. Delayed hyperenhancement in a case of Takotsubo cardiomyopathy. *Journal of Cardiovascular Magnetic Resonance*. 2005; 7: 845–847.
- [114] Ahtarovski KA, Iversen KK, Christensen TE, Andersson H, Grande P, Holmvang L, *et al.* Takotsubo cardiomyopathy, a two-stage recovery of left ventricular systolic and diastolic function as determined by cardiac magnetic resonance imaging. *European Heart Journal: Cardiovascular Imaging*. 2014; 15: 855–862.
- [115] Stiermaier T, Busch K, Lange T, Pätz T, Meusel M, Backhaus SJ, *et al.* Prognostic Value of Different CMR-Based Techniques to Assess Left Ventricular Myocardial Strain in Takotsubo Syndrome. *Journal of Clinical Medicine*. 2020; 9: 3882.
- [116] Cordero A, Cazorla D, Escribano D, Quintanilla MA, López-Ayala JM, Berbel PP, *et al.* Myocarditis after RNA-based vaccines for coronavirus. *International Journal of Cardiology*. 2022; 353: 131–134.
- [117] Crane P, Wong C, Mehta N, Barlis P. Takotsubo (stress) cardiomyopathy after ChAdOx1 nCoV-19 vaccination. *BMJ Case Reports*. 2021; 14: e246580.
- [118] Caforio ALP, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, *et al.* Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *European Heart Journal*. 2013; 34: 2636–2636–48, 2648a–2648d.
- [119] Blazak PL, Holland DJ, Basso T, Martin J. Spontaneous coronary artery dissection, fibromuscular dysplasia, and biventricular stress cardiomyopathy: a case report. *European Heart Journal: Case Reports*. 2022; 6: ytae125.
- [120] Menezes MN, Silva D, Almeida AG, Pinto FJ, Brito D. A rare case of concomitant stress (takotsubo) cardiomyopathy and acute myocardial infarction. *Revista Portuguesa De Cardiologia: Orgao Oficial Da Sociedade Portuguesa De Cardiologia*. 2015; 34: 499.e1–e3.
- [121] Tomida M, Fujimoto N, Moriwaki K, Nii M, Ishida M, Imanaka-Yoshida K, *et al.* Peripartum Mid-Ventricular-Type Takotsubo Cardiomyopathy After Cesarean Delivery. *International Heart Journal*. 2022; 63: 782–785.
- [122] Nash E, Roberts DM, Jamshidi N. Reverse Takotsubo Cardiomyopathy Precipitated by Chronic Cocaine and Cannabis Use. *Cardiovascular Toxicology*. 2021; 21: 1012–1018.
- [123] Bybee KA, Murphy J, Prasad A, Wright RS, Lerman A, Rihal CS, *et al.* Acute impairment of regional myocardial glucose uptake in the apical ballooning (takotsubo) syndrome. *Journal of Nuclear Cardiology*. 2006; 13: 244–250.
- [124] Feola M, Chauvie S, Rosso GL, Biggi A, Ribichini F, Bobbio M. Reversible impairment of coronary flow reserve in takotsubo cardiomyopathy: a myocardial PET study. *Journal of Nuclear Cardiology*. 2008; 15: 811–817.
- [125] Ito K, Sugihara H, Kinoshita N, Azuma A, Matsubara H. Assessment of Takotsubo cardiomyopathy (transient left ventricular apical ballooning) using 99mTc-tetrofosmin, 123I-BMIPP, 123I-MIBG and 99mTc-PYP myocardial SPECT. *Annals of Nuclear Medicine*. 2005; 19: 435–445.