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REVIEW

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Neurogenic Stunned Myocardium as Part of Stress Cardiomyopathy

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ABSTRACT

Stress cardiomyopathy (SCM), also called Takotsubo syndrome (TTS), is a topic of current interest that extends beyond cardiology. The neurological framework currently includes neurogenic stunned myocardium (NSM), an abnormal condition that shares many common features with TTS.

Unlike TTS, the main triggers for NSM are mostly neurological events (e.g., acute stroke, subarachnoid haemorrhage [SAH], brain trauma, etc) inducing adrenergic hyperstimulation and ultimately myocardial stunning.

Clinical examination, echocardiogram, electrocardiography, and cardiac markers share many similarities and differences between TTS and NSM. The common feature of the two conditions is their shared pathophysiological mechanisms, which ultimately lead to hypercatecholaminaemia and myocardial stunning.

Takotsubo syndrome and NSM can be seen as two phenotypes of SCM.

Treatment of SCM is based on pathophysiological data and differs according to the risk level: low or high.

The course of the disease is not always favourable; for TTS, the immediate prognosis is like that of acute myocardial infarction (MI).

Keywords: stress cardiomiopathy, Takotsubo syndrome, neurogenic stunned myocardium.

Nosological framework

The interrelation between the brain and the heart was first described by physiologists and anatomists. Experimental research revealed the brain areas and the nerve centres modulating the cardiac activity. Cardiologists and neurologists have combined observational data with fundamental science knowledge, which has led to the emergence of neurocardiology as a multidisciplinary specialty (subspecialty). Researchers from multiple specialties have defined the influence of neurologic or neuropsychiatric disorders on cardiac physiology and pathology.

In 1954, George Burch described 17 patients with "cerebrovascular accidents", transient electrocardiographic (ECG) abnormalities during the acute phase of the neurological event. The described ECG abnormalities included prolonged QT interval, negative wide T waves and U waves. They were considered as a sign of myocardial damage (ischaemia) (1).

The major observation that increased the interest in neurocardiology was reported in 1990, in Japan, by Suto *et al*, who described similar clinical features to those in acute myocardial infarction (MI), but with normal coronary angiography and

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reversible ventricular dysfunction with apical "ballooning" (2). These cardiac changes were especially noticed in women aged 55 to 60 years with important emotional (mental) stress. This condition was initially named Takotsubo syndrome (TTS) and later, Takotsubo cardiomyopathy (TCM) or stress cardiomyopathy (SCM). A large number of publications have reviewed the clinical, electrocardiographic, echocardiographic, biologic, magnetic resonance imaging (MRI), and coronographic characteristics of Takotsubo syndrome (TTS).

In recent years, TTS has been the subject of multiple overviews, *e.g.*, "Position Statement of Heart Failure Association on ESC (2016)" (3) and "International Expert Consensus Document on Takotsubo Syndrome" (Parts I and II, 2018) (4, 5).

A basic concept was formulated as early as 1982 by Braunwald and Kloner – the concept of "stunned myocardium", defined as (reversible) post-ischaemic contractile dysfunction accompanied by biochemical dysfunction (6). Myocardial stunning was detected following short periods of myocardial ischaemia and reperfusion in coronary atherosclerosis, post-thrombolysis, post-PCI. The concept of "stunned myocardium" remained a fundamental pathophysiological and clinical feature in cardiology. In fact, it can be also discussed in the context of TTS, characterised by reversible myocardial contractile dysfunction, altered ventricular motility and biological abnormalities occurring under mental, emotional, or physical stress.

Changes at the cardiac ultrasound imaging, consisting in LV systolic dysfunction and wall motion abnormalities, have also been described in intracranial haemorrhage (in particular, subarachnoid haemorrhage [SAH]) (7). Cardiac ultrasound findings of reversible regional wall motion abnormalities accompanied by ST-segment changes and/or prolonged QT-interval on the ECG, and biological markers of myocardial injury are found in approximately 20 to 30% of the SAH patients (7). Cardiac changes similar to those found in SAH also occur in other neurological events, especially in ischaemic or haemorrhagic stroke, brain trauma, epilepsy, reversible posterior encephalopathy. The combination of these findings is currently defined as neurogenic stunned myocardium (NSM) (8, 9, 10). In recent years, neurogenic stunned myocardium was better studied in patients with stroke and is referred to as "stroke–heart syndrome" (11).

Neurogenic stunned myocardium is characterised by acute reversible ventricular (myocardial) dysfunction that occurs after various types of neurological events with brain injury and damage to the autonomic nerve centres, sympathoadrenergic hyperactivity, catecholamine surge and its cardiovascular (especially cardiac) effects (8).

Both Takotsubo syndrome and neurogenic stunned myocardium have the same pathogenetic basis – myocardial stunning that apparently occurs in different circumstances; they share multiple common and overlapping characteristics, similar pathogenetic mechanisms, and the same assessment methods and treatment approaches. Presently there is a scientific debate regarding the relationship between TTS and NSM, *i.e.*, whether they are two separate entities or represent two phenotypes of a single entity, stress cardiomyopathy (SCM) (12, 13).

Our article analyses the similarities and differences between TTS and NSM in relation to the complex assessment of patients defined as having stress cardiomyopathy.

Definition criteria for TTS, which is being considered a "primary cardiomyopathy", were formulated in the "Mayo Clinic Diagnostic Criteria", published in 2008, and include also neurogenic stunned myocardium (14). Revised Mayo criteria include the following:

- Transient hypokinesia, akinesia, or dyskinesia of the left ventricular mid segments with or without apical involvement; wall motion abnormalities that extend beyond a single epicardial vessel distribution area. Stress is an important trigger, but it is not always present.
- Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.
- New-onset electrocardiography abnormalities (ST-segment elevation and/or T-wave inversion) or moderately elevated cardiac troponin levels.
- Absence of pheochromocytoma or myocarditis.

Following the Mayo criteria, two documents were published on the same subject: "HFA/ESC Diagnostic Criteria for Stress Cardiomyopathy" (3) and "International Takotsubo Diagnostic Criteria" (InterTAK Diagnostic Criteria) (15). Both publications provide details on some of the Mayo criteria – for example:

- The presence of coronary artery disease should not be considered as an exclusion criterion for TTS; TTS may co-exist with ACS or ACS may trigger TTS.
- Rarely, wall motion abnormalities may correspond to the distribution area of a single coronary artery. In this situation, assessments are required to exclude ACS or myocarditis.

Diagnostic criteria for "neurogenic stunned myocardium" (NSM) are not defined by national Cardiology Societies in Europe and the USA, but can be partially found within the criteria used to establish the diagnosis of TTS. Key cardiac features defining NSM are particularly found in two neurological disorders: ischaemic or haemorrhagic stroke (IS, HS) and subarachnoid haemorrhage (SAH). Due to the higher incidence of stroke versus SAH, a larger number of studies are focused on identifying the clinical and exploratory features more commonly found in stroke and which define the "Stroke-Heart Syndrome".

NSM incidence during cerebral events ranges from 20 to 40%, depending on the type and severity of the neurological event. The incidence is higher in SAH (approximately 37% of the cases) and in brain trauma (20 to 40%) (16).

The incidence in stroke can be assessed based on the combination of (new-onset) changes in ECG, cardiac ultrasound, and troponin levels observed in acute stroke.

SCM assessment data – Patients with TTS and NSM have the same cardiac assessment features, which are summarised in Table 1.

The clinical circumstances under which TTS and NSM occur are partially similar and the same triggers are shared.

Typical TTS involves a psycho-emotional factor (more frequent in women), but it may also occur under physical stress. In NSM, primary triggers are acute neurological events (SAH, acute stroke), but also events with a major psycho-emotional impact (surgery, brain trauma, severe disease). In recent years, COVID-19 infection has been reported as a trigger, requiring a differential diagnosis from acute myocarditis and acute coronary syndrome (16 bis). Obstructive coronary disease is an exclusion criterion for TTS. However, some patients, especially elderly ones, may have non-obstructive coronary lesions.

Clinical cardiac symptoms similar to those of an acute MI are reported in approximately 90% of subjects with TTS; in contrast, patients with NSM are most commonly asymptomatic, and sometimes present with cardiac arrhythmias, either symptomatic or asymptomatic, and signs and symptoms of acute heart failure (8).

TABLE 1. SCM assessment features

1	Clinical circumstances
2	Electrocardiographic changes. Arrhythmias
3	Cardiac troponin and NT-proBNP levels
4	Echocardiographic abnormalities
5	Cardiac MRI findings
6	Coronarography

TABLE 2. ECG abnormalities in TTS and NSM

Prolonged QT-interval
ST-segment depression (new-onset)
ST-segment elevation
Various arrhythmias (atrial extrasystoles, ventricular extrasystoles, atrial tachyarrhythmias, torsade de pointes)
Paroxysmal or persistent atrial fibrillation (AF)
U-waves

Changes (new-onset ECG abnormalities) are the first features suggesting TTS and NSM. They are found in over 80% of ballooning TTS cases, in 40 to 74% of subjects with SAH and in 15 to 40% of those with acute stroke (3, 17, 18). Table 2 summarises the ECG changes found in SCM.

ECG abnormalities require some comments, as follows:

- Prolonged QT-interval is one of the first new-onset ECG abnormalities and it is reported in approximately 20 to 65% of the patients at admission. It is transient and disappears rapidly, within 48 hours. Values >500 mm/sec, especially in the presence of hypokalaemia, may precede torsade de pointes and death.
- ST-segment depression is relatively common (15-25% of the patients) and it is not characteristic for NSM. A more typical feature from the diagnostic perspective is the development of negative (inverted), wide (cerebral-type) T-waves, in precordial leads, reported for the first time in SAH, but also present in 2 to 18% of the patients with ischaemic stroke (13). T-wave inversion is more pronounced and more diffusely distributed than in ACS.
- ST-segment elevation in precordial leads suggests acute MI with occlusion of the LAD, but also TTS with apical ballooning. The extent of ST-segment elevation and the number of leads

involved is lower in TTS versus STEMI. Q-wave is commonly absent. ST-segment elevation is found in 40% of subjects with TTS (19) and rarely reported in NSM. It is a manifestation of myocardial injury with ischaemic myocardial stunning. ST-segment elevation may regress in a few days, but may also persist for weeks, as can wide, negative T-waves.

- Various types of arrhythmias, *e.g.*, ventricular extrasystoles or bradyarrhythmia occur in SCM (20-40% of cases) (20).

Atrial fibrillation (AF) is the most important arrhythmia in stroke (20, 21); AF mostly precedes the neurological event, being its cause. New-onset (paroxysmal) AF, either symptomatic or asymptomatic, has an incidence of 4.6% to 10-15% in acute stroke (17). Long-term monitoring (weeks or months) may help detect AF after the stroke in approximately 25% of patients. Electrophysiological studies reported a direct relationship between the damage to the right insular cortex and the AF development.

Cardiac markers. Detection of certain ECG abnormalities, *e.g.*, in high stress circumstances (especially stroke) is an indication for assessing the levels and changes over time in cardiac markers (troponin, NT-proBNP). Both biomarkers are useful for the diagnosis of myocardial injury or ischaemia, LV dysfunction and prognosis.

The increase in hsTn levels is moderate in TTS and NSM and disproportionate relative to the magnitude and type of ECG abnormalities (8, 22). The ascending/descending curve observed in ACS (typical in acute MI) does not occur over time. Moderately increased troponin I or T levels associated with acute stroke suggest ischaemic myocardial injury and stunned myocardium. Troponin levels close to the cut-off values for ACS suggests the need for additional assessments (MRI or coronarography) in order to exclude acute MI or acute myocarditis. Even a moderate elevation of the serum troponin levels is associated with a poor functional prognosis, including death (23, 24).

Elevated NT-proBNP levels within 24 to 48 hours from the onset of an acute brain event estimate the magnitude of LV dysfunction in both TTS and NSM. LV systolic dysfunction accompanies myocardial stunning and is found in 8 to 12% of patients with stroke and TTS (25). Elevated NT-proBNP levels return to normal within five to seven days in NSM but can persist for weeks or months in TTS with apical ballooning (26). Factors associated with the severity of the ventricular dysfunction include the magnitude and localization of wall motion abnormalities, stroke severity and patient's age.

Echocardiographic assessment may provide results which are highly suggestive for SCM – it is relatively easy to perform, allows monitoring the LV wall motion abnormalities over time and, together with cardiac markers, and ensures non-invasive diagnosis of TTS.

Echocardiographic changes in SCM include areas of wall hypokinesia, akinesia, or dyskinesia of varied size and localization, with or without LV global systolic dysfunction. There are features that help diagnose SCM and differentiate between the different types of TTS and NSM.

Four major echocardiographic patterns have been described with regard to the regional distribution of wall motion abnormalities (4, 18).

- Apical ballooning is the most commonly found pattern (70 to 80% of patients) and it is typical for TTS. Echocardiographically, it appears as an area of hypokinesia/akinesia involving the apical segments of the LV, accompanied by basal hyperkinesia, possibly with LV outflow tract obstruction and minimal mitral valve regurgitation.
- The less frequent (10-20%) midventricular pattern is characterised by dyskinesia/akinesia of the mid LV segments and normal apical and basal segment contraction. It may occur in TTS, but is more common in NSM and it is sometimes accompanied by severe ventricular dysfunction (13).
- Less common types of echocardiographic findings have also been described (inverted basal, focal, biventricular) – therefore, the need for complex assessment (MRI, coronarography) to differentiate SCM from ACS and myocarditis.

Wall motion abnormalities occur early (up to 24 hours from the onset of the physical or mental stress factor) and may last for several days (particularly in SNM) or even weeks or months (the apical ballooning pattern).

Wall motion abnormalities may at times be accompanied by LV systolic/diastolic dysfunction in 8-12% of patients with stroke (11) and it is associated with poor prognosis (complications), particularly in TTS. For TTS, international 10-year follow-up studies have reported a similar prognosis to that of the myocardial infarction (27).

Cardiac MRI and coronary angiography are imaging assessments used in cases of overlapping signs to differentiate between SCM and ACS or myocarditis.

In the acute phase of SCM, MRI helps identifying the haemodynamic parameters, but especially localising (segmental) myocardial oedema and describing myocardial dyskinesia (3, 8). The absence of myocardial fibrosis, demonstrated by the absence of DGE (delayed gadolinium enhancement), is characteristic for SCM, unlike ACS where DGE is always present (18).

Coronary angiography is an invasive method that ensures the differential diagnosis between SCM and STEMI when non-invasive methods provide inconclusive or uncertain results.

In SCM, coronarography reveals permeable coronary arteries without a culprit lesion, including plaque rupture, thrombosis, coronary artery dissection or other conditions affecting coronary macro- and microcirculation, accompanied by regional wall motion abnormalities.

Patients who develop SCM are frequently elderly persons with multiple risk factors and asymptomatic/symptomatic coronary artery disease or other atherosclerotic disorders. Coronarography findings of non-obstructive coronary lesions and regional microcirculation changes do not exclude TTS or NSM in a challenging diagnostic setting. If troponin levels are in a grey (intermediary) area, coronarography allows to differentiate SCM from TTS.

In the TRELAS study, which included 2133 patients with ischaemic stroke, typical chest pain and high troponin T levels, coronarography was performed. A culprit coronary lesion was detected in 24% of subjects, but 48% of them had no signs of coronary artery disease (11). The combination of non-obstructive coronary arteries and high troponin levels (>20%) is currently called MI with non-obstructive coronary arteries (MINOCA).

COVID-19 associated with TTS

An increased incidence of acute myocarditis but also TTS was reported during the COVID-19 pandemic.

Typical Takotsubo syndrome, with apical ballooning and ventricular dysfunction, was also documented in COVID-19 patients since 2020. The increase in SCM incidence (2% to 4.2%) during the pandemic suggests an association between these two conditions (16 bis).

Published case studies reported TTS during the acute phase of COVID-19, predominantly in male subjects aged ≥ five years old, with or without concomitant cardiovascular disease. The clinical, biological and imaging features are similar to those observed in subjects without COVID-19, but over time, acute systolic ventricular dysfunction, cardiogenic shock, pericarditis, arrythmias and possibly death can occur (28 bis).

COVID-19-associated TTS raises various challenges regarding the differential diagnosis with acute MI (STEMI) and acute myocarditis. Similar or differential diagnostic features are revealed by echocardiography and electrocardiography, cardiac markers and inflammation markers. In cases of overlapping features, coronarographic findings of patent coronary arteries and no unstable coronary plaque settle the diagnosis.

Pathogenetic mechanisms of myocardial stunning in COVID-19-associated TTS are partly similar to those of myocarditis and include cytokine storm and exaggerated immune response, adrenergic hyperstimulation, and microvascular dysfunction.

The scientific debate of whether TTS and SNM are two separate entities or the same syndrome cannot be resolved other than by comparing assessment data (clinical status, ECG, echocardiography) between the patient groups.

Comparative studies have been conducted on a limited number of subjects (observational studies) but with appropriate scientific data processing. Two older studies based on the comparison between two groups of patients (TTS and NSM) concluded that the two CM types are the same syndrome (13, 28). A third study compared more extensive TTS versus NSM assessment data and reported significant differences. Differential fea-

TABLE 3. Differential features between TTS and NSM (after 13)

	TTS (%)	NSM (%)	P-value
Age	61.87 ± 12.3	53.00 ± 13.6	0.001
Prior coronary artery disease	31.8	0	0.01
Elevated ST-segment	59	0	0.0002
Inverted T-wave	27.3	64.3	0.04
EF (indexed)	34.7 ± 10.8	45.4 ± 12	0.009
Typical apical pattern	77.0	21.0	0.007
Basal and mid myocardial pattern	45.0	93.0	0.005
LVEF at discharge	52.2 ± 76	56.9 ± 14.6	0.21
Chest pain	100	0	-
Heart failure (clinical)	0	100	-

tures between the two groups of SAH patients are shown in Table 3 (13).

In conclusion, assessment data from comparative studies demonstrate that TTS and NSM have multiple common and overlapping features as well as differences. They provide further evidence supporting the fact that there is a single syndrome, *i.e.*, SCM, with two variants (phenotypes): TTS and NSM. Both TTS and NSM also share a common pathophysiological feature, *i.e.*, myocardial stunning.

Pathophysiological mechanisms

The pathophysiological mechanisms of TTS and NSM are largely known from neurophysiology studies, experimental data and results of clinical studies.

There are three major issues in the pathogenetic chain: 1) the initial factors: stress; brain injury; 2) the nerve centres inside the central nervous system and the beta-adrenergic axis, which are involved in sympathetic hyperstimulation and uncontrolled catecholamine release (catecholamine surge); 3) the response of the cardiovascular system to the excessive increase in catecholamines, particularly in the myocardium (function, structure) and in the cardiac microcirculation; mechanisms leading to myocardial ischaemia and ventricular dysfunction.

Factors that trigger the pathogenetic chain in SCM comprise psycho-emotional (27%) or physical (36%) stressors. In 30 to 35% of the patients with TTS, the syndrome is not preceded by any identifiable triggers (18). In NSM, more common stressors are neurological events leading to the injury of insular cortex which is involved in the cardiovascular function control and in the increase of sympathetic adrenergic tonus (29, 30).

The brain structures involved in the stress response include the neocortex, limbic system, and hypothalamus. Injury of insular cortex and parietal lobe results in catecholamine release. The main site of catecholamine synthesis in the brain, *locus coeruleus*, receives afferents from the hypothalamus. Catecholamine synthesis and release also take place in the adrenal glands and the myocardium. The final result consists of the activation of the central nervous system (CNS) structures and adrenergic autonomic nervous system (ANS), with consecutive hypercatecholaminaemia (epinephrine, norepinephrine) (31, 32).

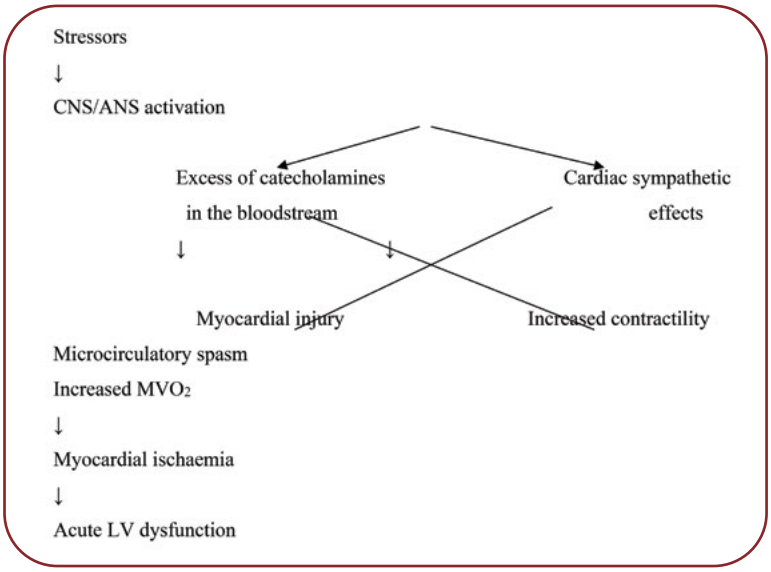

FIGURE 1. Physiopatology of stress cardiomyopathy (modified after 36)

The increase in serum catecholamine levels and adrenergic stimulation are followed by endothelial dysfunction, microvascular spasm, microthrombosis, increased contractility and, ultimately, myocardial ischaemia and acute LV dysfunction (3, 4, 11, 33, 34).

The effects of the sympathetic hyperstimulation and the excessive increase in catecholamine levels have an impact on the coronary microcirculation and on the myocardial function and structure. In terms of cardiac effects, adrenergic receptor stimulation leads to an increased cardiac contractility rate and creates conditions for an imbalance between the O_2 demand and the O_2 supply resulting in microcellular hypoxia (17). Moreover, the cardiac microcirculation spasm reduces the regional blood flow and causes or worsens the ischaemic injury, especially at a subendocardial level. The reperfusion changes that accompany the reduction of the vasospasm and the endothelial dysfunction contribute to structural damage (contraction band necrosis) and to cardiomyocyte function impairment (4, 11, 36).

Direct effects of catecholamines are also thought to contribute to the impairment of myocyte function and structure (11). In subjects with SCM (TTS) as well as in those with pheochromocytoma, the endomyocardial biopsy revealed contraction band necrosis, a unique form of myocardial injury occurring in conditions characterised by hypercatecholaminaemia.

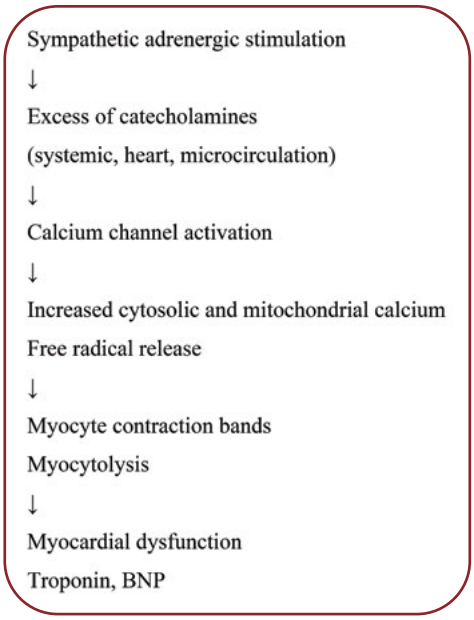

FIGURE 2. Cellular mechanisms in SCM (adapted from 11)

Cellular mechanisms ultimately leading to myocyte dysfunction in SCM are summarised in Figure 2.

Post-ischaemic myocardial stunning is a shared feature of TTS and NSM and results from the catecholamine effects on microcirculation and cardiomyocytes (37). Stunning exceeds the distribution area of a single epicardial artery and manifests with wall hypokinesia/akinesia together with LV systolic (and diastolic) dysfunction. The uneven distribution of LV microcirculation could explain the different echocardiographic patterns of regional wall motion abnormalities. The different distribution of the adrenergic receptors, which is higher in the apical region, could cause a higher vulnerability to a rapid progression of a catecholamine surge and, eventually, to apical ballooning.

Course of disease. Prognosis

There are more available data on the disease course and prognosis of TTS compared to NSM. The anatomic and echocardiographic pattern of the wall motion abnormalities and cardiac dysfunction, and the type of associated comorbidities are essential factors in the course of SCM.

The short- and long-term prognosis of SCM was at first considered to be very good and the condition was thought to be mostly benign (3, 27). The fairly quick regression of the wall motion abnormalities within a few days, especially in NSM, supports the fact that the disease course is benign.

In-hospital follow-up of the SCM patients revealed various complications in 20% to 52% of cases (34). LV systolic dysfunction to acute heart failure (HF), cardiogenic shock, arrhythmias, intraventricular thrombosis are the most common complications that change the course of the disease, even to death. The reported in-hospital mortality rate ranges from 2% to 5%, the cause of death being cardiogenic shock and VF (38). According to a report based on SWEDEHEART Registry, the mortality rate in TTS patients was similar to that in patients with MI (39). Parameters associated with poor in-hospital outcomes include physical trigger, neurological (or mental) disorder, initial troponin level 10-fold higher than the upper limit of normal, LVEF <45% (at admission), elderly patients, and apical ballooning pattern. The disease course and prognosis of neurogenic stunned myocardium (NSM) mainly depend on the severity of the neurological event. Persistent wall motion abnormalities, elevated troponin and NT-proBNP levels, and inverted wide T-waves are associated with poor prognosis and mortality (41).

Patients with SAH or acute stroke and brain death are potential heart donors. Recognising the cardiac stunning and its rapid reversibility is an essential condition for using the heart for transplant.

Treatment

The treatment for TTS and NSM and for SCM in general is not standardized and no special guidelines have been developed. Treatment recommendations are based on the experience of physicians and experimental data.

In practice, treatment begins with risk stratification – low risk: asymptomatic or minimally symptomatic patients, mild wall motion abnormalities; and high risk: patients with complications; ventricular dysfunction to acute heart failure, haemodynamic instability – cardiogenic shock, arrhythmias, intraventricular thrombosis (3).

A proportion of TTS and NSM patients are mildly symptomatic and need ECG and echocardiographic monitoring in the intensive care unit (ICU) (for at least 24 hours) and early detection of complications. Especially in NSM, but also in TTS, cardiac changes are rapidly reversible and the patients do not need any specific therapy other than for the associated conditions. In cases of adrener-

gic overstimulation, beta-blockers may be given (5, 18). In high-risk patients, the treatment choice is based on the type of complications, which are more common in TTS with apical ballooning; ICU monitoring is required for several days.

If cardiac dysfunction is moderate to severe and there are obvious clinical signs of heart failure, treatment recommendations are similar to those in heart failure, according to guidelines, including ACEI/ARB, MRA, beta-blockers, etc. The use of beta-blockers in TTS "is reasonable, although there is insufficient evidence to support their benefits" (42). Calcium channel blockers appear to be associated with faster recovery. Beta-blocker therapy, possibly associated with ACEI/ARB, may be continued until the regression of the apical ballooning.

In patients initially assessed as having ACS, who were using anti-platelet therapy, aspirin may be continued (3, 27).

In TTS patients without LV outflow tract obstruction who develop haemodynamic instability (persistent hypotension, cardiogenic shock), inotrope agents may be administered (dobutamine, levosimendan) (18). If haemodynamic instability is not corrected, low doses of vasoconstrictor agents (norepinephrine, vasopressin) may be used in an attempt to stabilise haemodynamic parameters for the possibility to use mechanical circulatory support.

Intraventricular thrombosis is a common complication, in particular in apical TTS or in patterns with large areas of wall motion abnormality. It occurs within the first three to six days from the symptom onset, when the systolic function of the LV is still depressed and may complicate with cardioembolic stroke in 2% to 5% of subjects (3). Intraventricular thrombosis is an indication for anticoagulant therapy for approximately 90 days, or possibly longer in patients with extensive areas of wall akinesia, until the recovery of the LV function.

Patients who develop SCM require long-term cardiologic (clinical, imaging) follow-up until the complete recovery of the ventricular (cardiac) function. Recurrent TTS, reported in up to 30% of the cases, is preferably treated with ACEI/ARB, which are associated with a lower recurrence rate compared to beta-blockers, which do not prevent recurrence (5).

Neurogenic stunned myocardium associated with an atherosclerotic event requires long-term secondary prevention with statins, acetylsalicylic acid, and neurological rehabilitation. ❑

CONCLUSION

Stress cardiomyopathy is a generic term which includes two conditions: Takotsubo syndrome and neurogenic stunned myocardium. The etiologic conditions are different, but their mechanism is similar: hypercathecolaminemia, coronary micro spasm and transitory myocardial hypokinesia. Clinical data, imagistic and evolution are partially common. Differentiation from acute coronary syndromes necessitates the use of coronarography. Medication includes calcium blockers and partially beta blockers, ACEI and antiplaquetaire. ❑

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