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RESEARCH ARTICLE

MANAGING CARDIOGENIC SHOCK IN TAKO-TSUBO SYNDROME: LEVOSIMENDAN AS A LIFE-SAVING SOLUTION

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Abstract

Tako-Tsubo cardiomyopathy, also known as broken heart syndrome, is an acute cardiac condition often precipitated by intense stress, leading to symptoms that mimic myocardial infarction. The management of cardiogenic shock in this context is challenging, as standard heart failure treatments, such as Dobutamine, may worsen the condition. This case report presents an 82-year-old woman who developed cardiogenic shock due to Tako-Tsubo cardiomyopathy after a prolonged fall. She was successfully treated with Levosimendan, a drug that enhances myocardial contractility and reduces cardiac workload without increasing myocardial oxygen demand. This case underscores the importance of recognizing Tako-Tsubo cardiomyopathy in patients presenting with cardiogenic shock and highlights Levosimendan as a superior treatment option due to its beneficial effects on cardiac function and patient outcomes.

Introduction:

Tako-Tsubo cardiomyopathy, also known as broken heart syndrome, is a form of acute cardiac dysfunction often triggered by intense physical or emotional stress. While this condition can mimic a myocardial infarction, it is characterized by apical ballooning observed on imaging studies. Cardiogenic shock associated with Tako-Tsubo presents specific therapeutic challenges, as standard heart failure treatments may not be appropriate. This case report highlights the crucial role of Levosimendan in managing cardiogenic shock related to Tako-Tsubo, while also emphasizing why Dobutamine is contraindicated in this context.

Case Report:

An 82-year-old independent woman living alone, with a history of hypertension managed with ARBs and atrial fibrillation treated with oral anticoagulants, was admitted to the hospital following a mechanical fall and a prolonged period of lying on the ground for approximately 6 hours, without any preceding symptoms or loss of consciousness. She was found by her son in a state of dyspnea and transported to the emergency department.

Upon admission, she was conscious but dyspneic, with a blood pressure of 70/48 mmHg, a heart rate of 100 bpm, and an oxygen saturation of 96%. Peripheral signs of hypoperfusion were noted, including cold and mottled extremities. Cardiovascular examination revealed irregular heart sounds with a systolic murmur at the tricuspid area.

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Additional tests showed atrial fibrillation with a mean ventricular conduction rate of 97 bpm, negative T waves in the anterior leads, and a prolonged QTc of 480 ms on ECG.

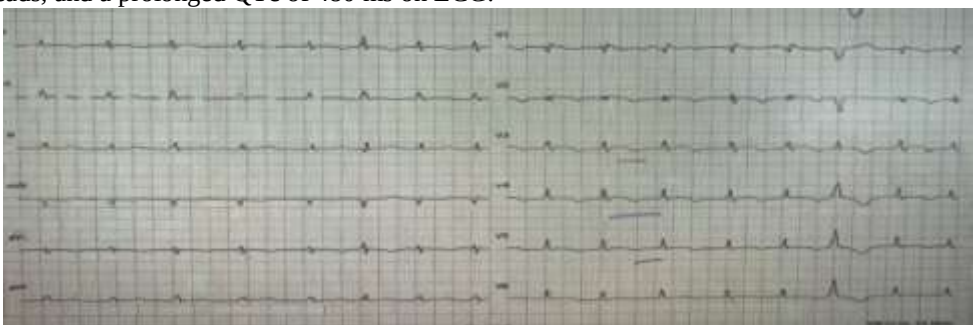

Figure 1: ECG showing negative T waves and a prolonged QT interval.

Echocardiography revealed extensive apical and mid-ventricular akinesis, with a left ventricular ejection fraction (LVEF) of 20% and a cardiac output of 2.4 l/min. Laboratory results indicated markedly elevated troponins at 11,000 pg/ml (244 times the normal level), high NT-proBNP at 26,000 pg/ml, liver dysfunction with AST at 1283 U/l and ALT at 515 U/l, renal impairment with creatinine at 206 µmol/l and an estimated glomerular filtration rate (eGFR) of 30 ml/min, and arterial blood gas analysis showing a pH of 7.25, HCO3- at 12, PCO2 at 25 mmHg, and lactates at 6.4 mmol/l.

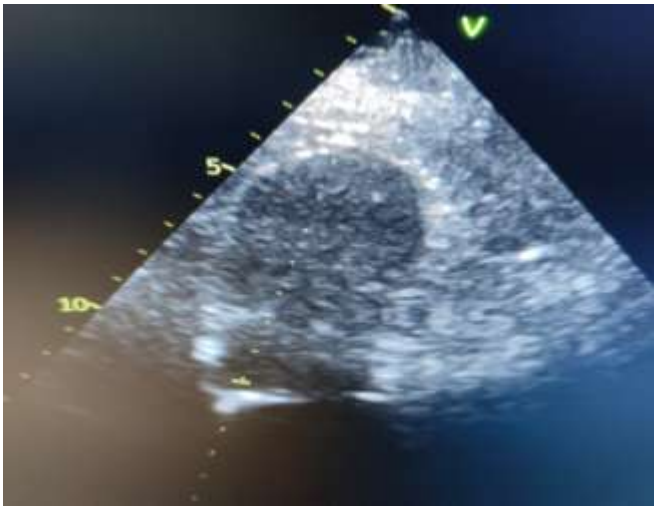

Figure 2: Echocardiography showing apical ballooning.

Coronary angiography revealed normal coronary arteries, while ventriculography showed akinesis of mid and apical segments with apical ballooning and an estimated LVEF of 20%.

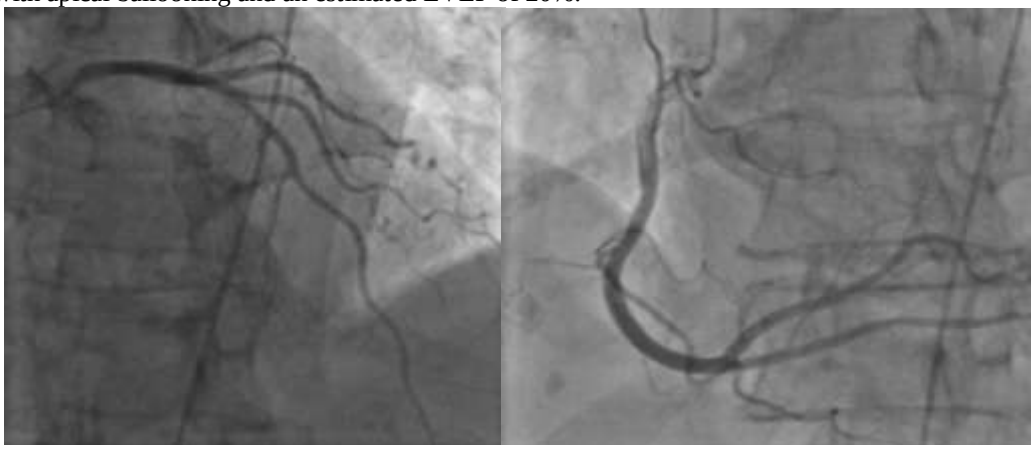

Figure 3: Coronary angiography showing normal coronary arteries.

Figure 4: Ventriculography showing apical ballooning.

A diagnosis of cardiogenic shock secondary to Tako-Tsubo cardiomyopathy was made, leading to admission to the intensive care unit. In the ICU, the patient was monitored, received cautious fluid resuscitation, anticoagulation for atrial fibrillation, and a course of Levosimendan at 0.1 µg/kg/h for 24 hours, with favorable evolution. By day 3, clinical and biological improvement was observed with blood pressure at 110/65 mmHg and regression of hypoperfusion signs. Follow-up echocardiography showed improved systolic function with an LVEF of 40%, though apical akinesis extended to adjacent segments. Biological results demonstrated improved renal function with an eGFR of 42 ml/min, a pH of 7.39, lactates at 1.1 mmol/l, a decrease in troponins to 3200 pg/ml, and NT-proBNP at 21,000 pg/ml. The patient was transferred to cardiology.

Cardiac MRI performed on day 4 confirmed the diagnosis of Tako-Tsubo cardiomyopathy, showing an LVEF of 48%, apical akinesis, diffuse mid-ventricular and apical edema confirmed by STIR and T2 mapping sequences, without late enhancement or perfusion abnormalities.

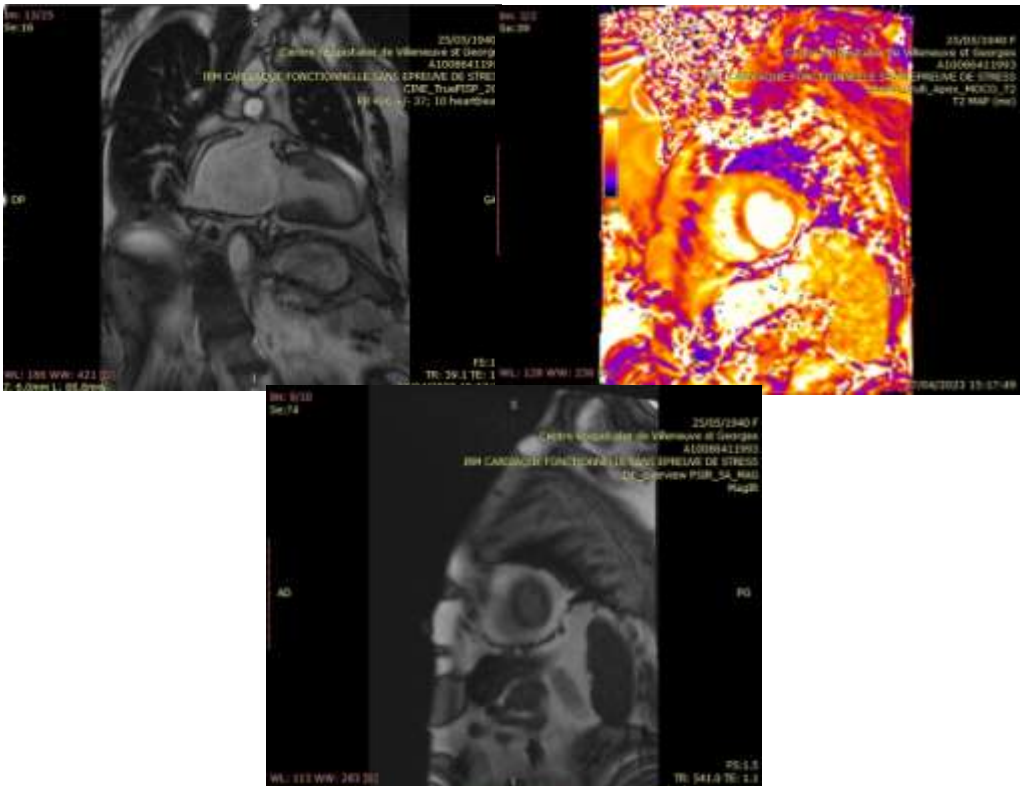

Figure 5: MRI showing apical akinesia and oedema, without late gadolinium enhancement.

The patient was discharged home on day 8 with complete regression of clinical signs, improved overall condition, normalized renal function, and an LVEF estimated at 55%. She was placed on apixaban, irbesartan, and bisoprolol.

Discussion:

Tako-Tsubo cardiomyopathy, also known as broken heart syndrome, is an acute form of cardiac dysfunction that can lead to cardiogenic shock. This case underscores the importance of appropriate management for this condition, particularly in the context of shock. In our 82-year-old patient, a prolonged fall resulted in cardiogenic shock associated with Tako-Tsubo cardiomyopathy, necessitating a specific therapeutic approach.

Diagnostic Criteria for Tako-Tsubo Syndrome:

The diagnosis of Tako-Tsubo is based on a combination of clinical, electrical, biological, and imaging criteria. For our patient, the following diagnostic criteria were applied[1,2]

1. **Clinical Criteria**:
   - Presence of acute symptoms such as dyspnea and marked elevations in cardiac biomarkers (troponins and NT-proBNP).
2. **Electrical Criteria**:
   - ECG showed negative T waves in the anterior leads and a prolonged QT interval.
3. **Imaging Criteria**:
   - **Echocardiography**: Revealed apical ballooning with significant systolic dysfunction.
   - **Cardiac MRI**: Confirmed apical akinesis and diffuse edema without late enhancement or perfusion abnormalities, distinguishing Tako-Tsubo from myocardial infarction.
4. **Exclusion Criteria**:
   - Absence of significant coronary lesions on coronary angiography.

Table I International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)

1.	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]
2.	An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
3.	Neurologic disorders (e.g. subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.
4.	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.
5.	Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
6.	Significant coronary artery disease is not a contradiction in takotsubo syndrome.
7.	Patients have no evidence of infectious myocarditis.[b]
8.	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.

Figure 6: International Takotsubo diagnostic criteria (InterTAK diagnostic criteria)[3].

Ghadri and al. have developed expert consensus defining the diagnostic criteria for Tako-Tsubo known as the InterTAK Diagnostic Criteria (figure 6). They have also developed a diagnostic probability score for Tako-Tsubo (figure 7). Our patient had a high probability score of 79.8%. Furthermore, Ghadrians al. have simplified diagnostic management through a decision tree (figure 8).

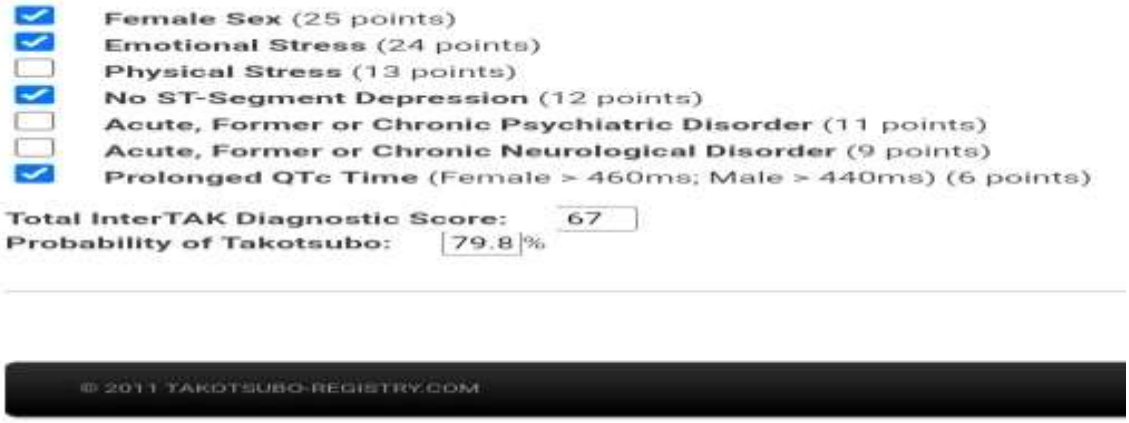

Figure 7: Diagnostic probability score for Takotsubo[3].

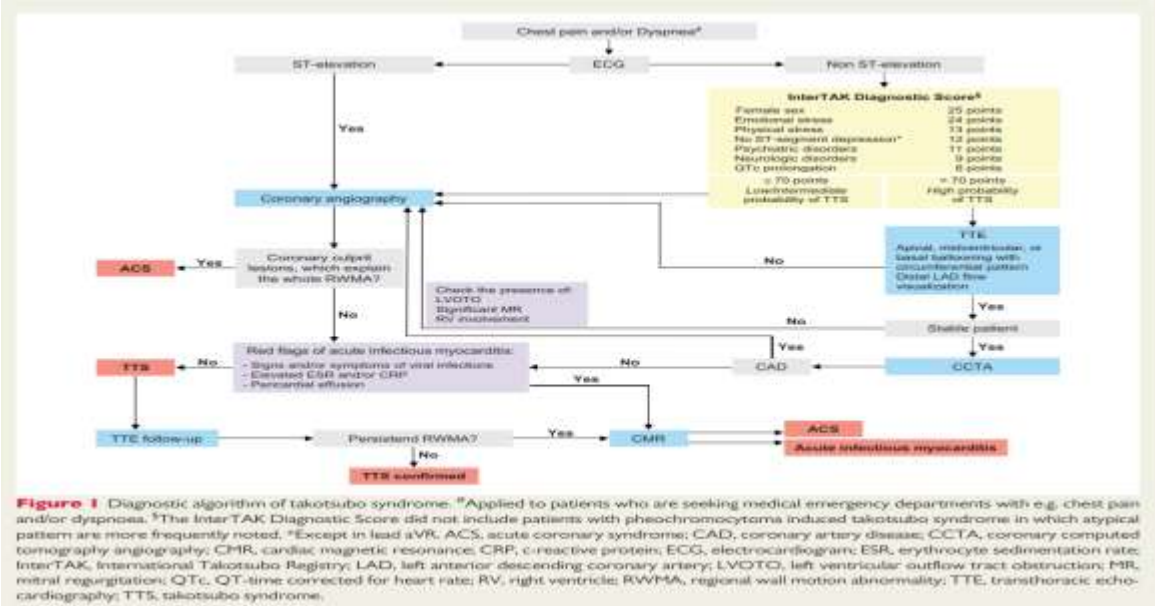

Figure 8: Simplified diagnostic management of Takotsubo[4].

Therapeutic Management of Cardiogenic Shock Related to Tako-Tsubo: [4,5,6]

Management of cardiogenic shock in the context of Tako-Tsubo requires thorough evaluation of underlying mechanisms, including left ventricular dysfunction (LVD) and obstruction of the LV outflow tract. The expert consensus by Ghadri et al. outlines treatment orientation, emphasizing the avoidance of Dobutamine

1. **Shock Due to Left Ventricular Dysfunction (LVD)**:
   - **Recommended Treatment**: Levosimendan is particularly suitable as it enhances myocardial contractility and reduces preload and afterload, thus improving cardiac function without exacerbating myocardial stress. In our patient, Levosimendan treatment led to significant cardiac improvement.
   - **Avoid Dobutamine**: Although Dobutamine is commonly used in cardiogenic shock, it is contraindicated in Tako-Tsubo as it can increase myocardial oxygen demand and worsen cardiac dysfunction, as observed in our case.
2. **Shock Due to LV Outflow Tract Obstruction**:
   - **Appropriate Treatment**: If dynamic obstruction is suspected, management includes cautious fluid resuscitation based on left ventricular tolerance and the use of short-acting intravenous beta-blockers to relieve LV outflow tract obstruction.

- **Evaluation and Management**: In our patient, dynamic obstruction was not observed; however, appropriate management of symptoms and cardiac function was essential.

Mode of Action of Levosimendan: [7,8]

Levosimendan is a unique inotropic agent with distinct properties compared to other treatments. Unlike Dobutamine, which primarily increases cardiac contractility by stimulating beta-adrenergic receptors, Levosimendan works through two complementary mechanisms:

1. **Calcium Sensitization**: Levosimendan enhances the sensitivity of myocardial filaments to calcium, improving myocardial contractility without increasing intracellular calcium levels. This effect is particularly beneficial in Tako-Tsubo, where stress and adrenergic activation may already burden the heart.
2. **Vasodilation**: The drug also has vasodilatory effects due to its action on ATP-sensitive potassium channels. This vasodilation reduces preload and afterload, decreasing vascular resistance and cardiac workload, thus improving myocardial perfusion.
3. **Myocardial Protection**: Levosimendan opens similar ATP-sensitive potassium channels in the mitochondria of cardiomyocytes, providing additional myocardial protection.

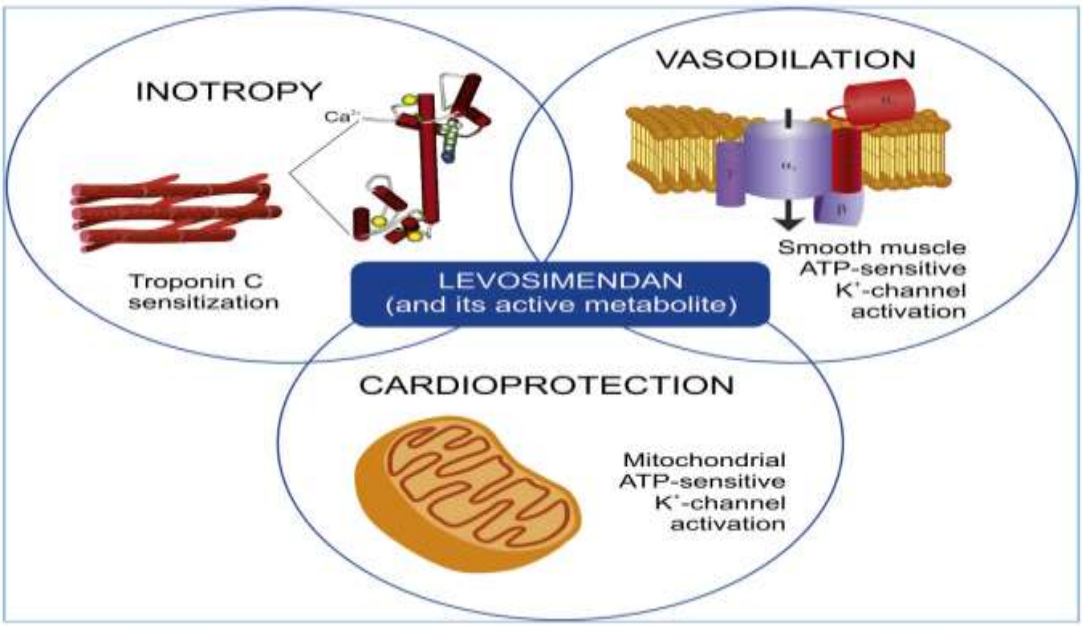

Figure 9:- Mechanisms of action of levosimendan[8].

All these effects of Levosimendan result in a rapid onset of action within an hour and durable effects lasting up to 3 weeks.

Conclusion:

This case clearly demonstrates that Levosimendan is a preferred therapeutic option for managing cardiogenic shock in Tako-Tsubo syndrome, due to its beneficial properties of positive inotropy and vasodilation. The use of Dobutamine is contraindicated in this context, as it can worsen the clinical state by increasing the workload on an already compromised heart. Prompt recognition of Tako-Tsubo and targeted treatment with Levosimendan are essential for optimizing outcomes and improving patient prognosis.

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