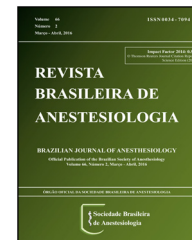




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## CLINICAL INFORMATION

# Perioperative approach of patient with takotsubo syndrome



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### KEYWORDS

Takotsubo syndrome;  
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### Abstract

**Introduction:** Takotsubo cardiomyopathy (TCM) is a stress-induced cardiomyopathy. It is characterized by an acute onset of symptoms and electrocardiographic abnormalities mimicking an acute coronary syndrome in the absence of obstructive coronary artery disease. Any anesthetic-surgical event corresponds to a stressful situation, so the anesthetic management of patients with TCM requires special care throughout the perioperative period. We describe the anesthetic management of a patient with a confirmed diagnosis of TCM undergoing segmental colectomy. **Case report:** Female patient, 55 years old, ASA III, with history of takotsubo syndrome diagnosed 2 years ago, scheduled for segmental colectomy. The patient, without other changes in preoperative evaluation, underwent general anesthesia associated with lumbar epidural and remained hemodynamically stable during the 2h of surgery. After a brief stay in the Post-Anesthesia Care Unit, she was transferred to the Intermediate Care Unit (IMCU), with epidural analgesia for postoperative period.

**Conclusion:** TCM is a rare disease which true pathophysiology remains unclear, as well as the most appropriate anesthetic-surgical strategy. In this case, through a preventive approach, with close monitoring and the lowest possible stimulus, all the perioperative period was uneventful. Because it is a rare disease, this report could help to raise awareness about TCM.

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**PALAVRAS-CHAVE**

Síndrome de takotsubo;  
Anestesia;  
Miocardiopatia;  
Estresse

**Abordagem perioperatória de doente com síndrome de takotsubo****Resumo**

**Introdução:** A miocardiopatia takotsubo (MT) é uma miocardiopatia induzida pelo estresse. Caracteriza-se por um início agudo de sintomas e alterações eletrocardiográficas que mimetizam uma síndrome coronária aguda na ausência de doença arterial coronária obstrutiva. Qualquer evento anestésico-cirúrgico corresponde a uma situação de estresse, pelo que a abordagem anestésica dos doentes com MT exige um cuidado especial em todo o período perioperatório. Descrevemos a abordagem anestésica de uma doente com diagnóstico confirmado de MT submetida a colectomia segmentar.

**Caso clínico:** Paciente do sexo feminino, 55 anos, ASA III, com antecedentes de síndrome de takotsubo diagnosticada havia dois anos, encaminhada para colectomia segmentar. A paciente, sem outras alterações na avaliação pré-operatória, foi submetida a anestesia geral associada a epidural lombar e manteve-se hemodinamicamente estável durante as duas horas do procedimento cirúrgico. Após uma breve permanência na Unidade de Cuidados Pós-Anestésicos foi transferida para a Unidade de Cuidados Intermédios (UCIM) com analgesia peridural para o pós-operatório.

**Conclusão:** A MT é uma doença rara, cuja verdadeira fisiopatologia continua por esclarecer, assim como a estratégia anestésico-cirúrgica mais apropriada. Nesse caso, por causa de uma abordagem preventiva, com monitoração rigorosa e o menor estímulo possível, todo o perioperatório decorreu sem intercorrências. Sendo uma doença rara, o seu relato poderá contribuir para o avanço do conhecimento sobre a MT.

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**Introduction**

Takotsubo cardiomyopathy (TCM), first described in 1990 in the Japanese population, is a cardiomyopathy induced by physical or emotional stress.<sup>1</sup> It is characterized by an acute onset of symptoms and electrocardiographic abnormalities mimicking an acute coronary syndrome (ACS). Although there may be a slight rise in enzymes of myocardial injury, there is no obstructive coronary artery disease (CAD) and the clinical presentation reverts completely in days or weeks.<sup>2-4</sup> TCM designation comes from the occurrence of transient dysfunction of the left ventricle (LV). The appearance of the LV during systole resembles a takotsubo (Japanese ceramic pot with rounded base and narrow neck, tsubo; used to trap octopus, tako). This morphology is due to mesoventricular akinesis and apical and basal ventricular hyperkinesis (narrow at the base and with apical bulging).<sup>2,5</sup>

With the growing number of cases reported worldwide, other names has been proposed, justified by the cardiac morphology and clinical presentation context: apical bulging syndrome, transient left ventricular dysfunction with apical bulging, broken heart syndrome, and, more recently, transient left ventricular apical akinesia/dyskinesia or stress-induced cardiomyopathy are some of a total of 75 different names. However, the initial name seems to be the most appropriate, as it is comprehensive enough to allow the addition of new variants, reminds us of the changes in LV morphology and is recognition of the investigators who first described it.<sup>5</sup>

The true prevalence of TCM remains unclear, but it is estimated to correspond to 1%–2% of cases in which there is clinical suspicion of ACS; it predominantly affects

women in the postmenopausal period, between 62 and 76 years.<sup>2,4,6</sup>

For TCM diagnosis, a high index of clinical suspicion is needed as well as diagnostic tests such as echocardiography and cardiac catheterization, in addition to ECG and myocardial injury markers that are essential. Echocardiography allows the verification of the typical changes in LV segment contractility. And cardiac catheterization proves the absence of significant coronary changes.<sup>2,6</sup> Several diagnostic criteria have been proposed. The most widely used are the Mayo Clinic criteria (Table 1).<sup>7</sup>

Despite the lack of a clear, singular, and unambiguous explanation of the TCM pathophysiology, the underlying etiologic mechanisms have been the subject of many studies

**Table 1** Diagnostic criteria (Mayo Clinic).<sup>7</sup>

- Hypokinesia, transient dyskinesia or akinesia in LV mid and apical segments, with or without apical involvement, with impaired contractility of the vascularization area corresponding to more than one coronary artery
- No obstructive CAD or angiographic evidence of acute plaque rupture
- Electrocardiographic changes *de novo* (ST segment elevation and/or T-wave inversion) and/or slight increase in serum troponin levels
- No pheochromocytoma and myocarditis

It does not include criteria such as age, gender and presence of triggering factor, as well as documentation of the reversibility of LV systolic dysfunction

and several theories have been proposed, such as the cardiotoxicity associated with catecholamine, the occurrence of coronary spasm, microvascular ischemia, cardiac autonomic instability, isolated plaque rupture in the anterior descending coronary artery, and/or acute obstruction and dynamic LV outflow tract.<sup>2</sup>

There is no standard treatment for these patients because of its reversibility and pathophysiological uncertainty. In the acute phase, the treatment is symptomatic with supportive therapy according to the degree of systolic dysfunction and directed to the acute complications that occur in approximately 20% of patients, which include acute lung edema, arrhythmia, embolism, cardiogenic shock, and death.<sup>2,6</sup>

In the absence of complications, the prognosis is usually benign, with full recovery of ventricular function, complete disappearance of symptoms and electrocardiographic changes and ventricular motion abnormalities and normalization of myocardial injury markers. Although this recovery occurs in a period of about 6–8 weeks, the electrocardiographic tracing can take years to normalize.<sup>2,5</sup> In patients whose recovery is complete, long-term survival is similar to the general population. Recurrence of TCM is less than 10%, and a prolonged follow-up is recommended.

Any anesthetic-surgical event being defined as a physical and emotional stress situation requires that all patients with confirmed diagnosis of takotsubo syndrome have close monitoring and special care during the perioperative period.

## Case report

Female patient, 55 years old, white, 60 kg, scheduled for elective segmental colectomy for angiodysplasia of the colon, with recurrent episodes of lower gastrointestinal bleeding. The patient reported history of ischemic stroke with right hemiparesis sequela of brachial predominance, hypertension, type 2 diabetes mellitus, dyslipidemia, and takotsubo syndrome diagnosed two years earlier after suspected ACS without ST elevation (excluded by cardiac catheterization with normal coronary arteries and complete clinical resolution after three days). The patient was taking allopurinol 300 mg, omeprazole 20 mg, gabapentin 400 mg, simvastatin 40 mg, amlodipine 5 mg, aspirin 100 mg, carvedilol 25 mg, lisinopril 20 mg, hydrochlorothiazide 12.5 mg, furosemide 20 mg, and glimepiride 60 mg—medication maintained until the day of surgery.

In pre-anesthetic evaluation, no significant changes were detected on physical examination or auxiliary diagnostic tests. She was classified as ASA III.

Intraoperative monitoring included 5-lead ECG, invasive blood pressure, peripheral oxygen saturation, capnography, esophageal temperature, BIS<sup>®</sup>, neuromuscular block, and urine output.

After premedication with midazolam (1 mg) and fentanyl (0.05 mg), a lumbar epidural catheter was placed, as well as an arterial line in the left radial artery. General anesthesia was induced using fentanyl (0.02 mg kg<sup>-1</sup>) and propofol (2 mg kg<sup>-1</sup>), and neuromuscular blockade with rocuronium (0.6 mg kg<sup>-1</sup>). Anesthesia was maintained with sevoflurane for BIS<sup>®</sup> between 40 and 60, bolus of intravenous

rocuronium, and 0.2% ropivacaine epidurally. Anesthesia was supplemented by bolus followed by infusion of esmolol for heart rates of 60–70 beats per minute.

The patient remained hemodynamically stable throughout the procedure, which was uneventful and lasted two hours. At the end of surgery, neuromuscular block was reversed with sugammadex (2 mg kg<sup>-1</sup>), and the patient was extubated without incident.

After uneventful 2 h at Post-anesthesia Care Unit (PACU) esmolol was suspended and the patient was transferred to the Intermediate Care Unit (IMCU). Postoperative analgesia was performed with epidural infusion of ropivacaine 1 mg mL<sup>-1</sup> and sufentanil 0.008 mcg mL<sup>-1</sup> (10.4 mL h<sup>-1</sup>) for 24 h.

## Conclusion

Despite the good prognosis and low recurrence, TCM should not be overlooked due to its serious complications.<sup>2,8</sup> Of the acute complications, systolic heart failure is the most common, followed by heart failure (fatal if not treated surgically), and other less common, such as cardiogenic shock (requiring vasopressor and/or intensive inotropic treatment or intra-aortic balloon placement), acute pulmonary edema, atrial or ventricular arrhythmias, ventricular septal defect, or thrombus formation at the LV level with possible embolism.<sup>9,10</sup> These complications are responsible for prolonged and recurrent hospitalizations, as well as mortality associated with this syndrome.<sup>2,8</sup>

The physiological mechanism relating the perioperative stress with TCM is still unclear because of its multifactorial pathogenesis and because its true etiology remain unknown.<sup>2</sup> Although sometimes no triggering factor is identified, the association with emotional and/or physical stress arises in about two-thirds of patients who develop TCM.<sup>11–13</sup>

Currently, the most accepted etiology related stress stimuli to the significant increase in catecholamine release by increased sympathetic stimulation. This can cause myocardial adrenergic stimulation and consequent change in contractility and transient heart dysfunction.<sup>2,3,8</sup> The stress inducing stimulation of the limbic system can lead to excitation of medullary centers of autonomic nervous system, which will encourage presynaptic and postsynaptic neurons and lead to the release of noradrenaline and its neuronal metabolites; at the same time that stimulation of the adrenal medulla occurs and the release of adrenaline is induced. Through cardiac and extra-cardiac sympathetic nerves, as well as bloodstream, these catecholamines stimulate the heart by binding to adrenergic receptors of the vessels and induce toxicity in cardiomyocytes. Toxicity may be exercised in an indirect way by coronary spasm and/or microvascular alterations, or directly by excess of calcium and free radical production.<sup>2,3,14</sup> Patients with TCM have supra-physiological levels of plasma catecholamines, with significant increases of epinephrine and norepinephrine, among others neurotransmitters, consistent with increased synthesis and reuptake.<sup>11,14</sup>

Any anesthetic-surgical event is a stress event for these patients, and initiates the cascade of physiological and metabolic events by direct activation of the sympathetic and somatic nervous system with a significant increase in plasma

catecholamines, which begins in the preanesthetic period and ends within three to four days postoperatively.<sup>15,16</sup> However, a clear explanation for this individual susceptibility to cardiomyopathy after exposure to a similar degree of stress is unknown; it is possible due to a genetic heterogeneity associated with adrenergic receptors, which makes them more or less sensitive to stimuli.<sup>16</sup>

There is no anesthetic-surgical strategy clearly defined in the literature to prevent the recurrence of takotsubo cardiomyopathy in patients requiring surgical intervention. However, the lowest possible stimulation and rigorous monitoring for early diagnosis of a probable acute complication during the perioperative period appear to be the safest options.<sup>17,18</sup>

Ideally, this type of patient should only be operated upon in hospitals with cardiology service, with hemodynamic unit and intensive coronary care. Although there is no absolute consensus, one should choose regional anesthesia, which can mitigate the release of catecholamines associated with the surgical stress, intubation and extubation, in addition to provide excellent postoperative analgesia. General anesthesia, which has the advantage of patient's unconsciousness, may be replaced by supplementation of regional anesthesia with sedation.<sup>15,19</sup>

In the preoperative period, the time before the surgical procedure itself and the emotional imbalance should be minimized to provide a deeper level of anxiolysis, using pharmacological and psychological approaches, before the patient is taken to the operating room.<sup>15,17–20</sup> Prophylactic  $\beta$ -blocker therapy appears to be useful to prevent acute stress, reducing the emotional impact of surgery in the functional status of the patient. Thus, if there are no contraindications, it should be given to these patients; however, it remains unclear what dosage is required to block the high levels of catecholamines and if there is any significant difference between different  $\beta$ -blockers.<sup>8,15,19</sup> Studies in animals suggest that both  $\alpha$  and  $\beta$ -blocking agents may normalize the electrocardiographic changes induced by stress.<sup>21</sup>

Intraoperative and postoperative monitoring should be careful. It is recommended continuous monitoring of invasive blood pressure via arterial catheter and, if possible, intraoperative monitoring of left ventricular function with transesophageal echocardiography when using general anesthesia. ECG monitoring should be performed with 5-lead.

In order to prevent sympathetic stimulation and excessive release of catecholamines, laryngoscopy should be brief, awakening and extubation should be smooth, and residual neuromuscular blockade should be avoided. The anesthetic agents of choice, both for induction and maintenance, should be those with less potential of myocardial depression to avoid hemodynamic instability. An adequate control of fluid avoiding volume overload is recommended, as well as a good pain control.<sup>15,19</sup>

In the above mentioned clinical case, the anesthetic plan included a balanced general anesthesia combined with thoracic epidural. The objective was to decrease the sympathetic response inherent to this type of abdominal surgery, classically classified as major. All preoperative care was performed, including  $\beta$ -blocking, a medication that the patient was already taking. Postoperatively, there was constant monitoring in IMCU, and it was found that epidural infusion of a local anesthetic has provided an effective analgesia.

There is question about if this was a successful case, given the perioperative approach, or just a fluke. However, it is important to note that any patient diagnosed with TCM undergoing surgery requires an individualized perioperative approach to avoid a possible recurrence and fatal outcome caused by one of its acute complications.

Given the rarity of TCM, it is important to expose and discuss the anesthetic management of any patient with this disease and contribute to clarifying the best prophylactic and anesthetic approach in such patients.

## Conflicts of interest

The authors declare no conflicts of interest.

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