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Case Report

Takotsubo Syndrome: cardiovascular complication of stroke

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ABSTRACT

An 82-year-old woman, Katz A, with history of type 2 diabetes mellitus and high blood pressure, was admitted for ischemic stroke complicated by takotsubo syndrome with subsequent readmission for atrial fibrillation after discharge. These three clinical events have criteria to be integrated as a brain-heart syndrome, which is a high-risk condition for mortality.

Keywords: Takotsubo Cardiomyopathy; Stroke; Atrial Fibrillation; Myocardial Infarction (source: MeSH-NLM).

Introduction

Brain-heart syndrome is a pathology that was first described in the 1950s and 1960s, is reported in approximately 20% of patients with ischemic stroke and is responsible for more than 1.5 million deaths around the world, including post-stroke cardiovascular complications, sudden unexpected death in epilepsy, takotsubo syndrome, and neurogenic sudden cardiac death. Thus, cardiac complications are the second leading cause of death in the first weeks after the event. It is not only limited to fatal complications, but also cardiac arrhythmias, heart failure and non-fatal coronary syndromes are common. Despite improvements in the description of the brain-heart syndrome, there is no progress in the development of specific therapies targeting the brain-heart axis to prevent cardiovascular complications and death after stroke [1,2].

Case report

An 82-year-old female patient, Katz A, with history of type 2 diabetes mellitus and high blood pressure; three hours before

admission to the emergency department, she suddenly lost muscle strength in the right side of her body associated with bradylalia, without loss of consciousness or sphincter relaxation. On examination, she presented with blood pressure: 114/70 mmHg; pulse rate: 92 beats per minute, regular; respiratory rate: 20 breaths per minute; oxygen saturation: 95%; body temperature of 36.5 °C; Glasgow Coma Scale 11/15; isochoric pupils, photoreactive; right hemiparesis; right facial paresis; bilateral Babinski sign, National Institutes of Health Stroke Scale (NIHSS): 17 points. The admission electrocardiogram (ECG) **(Figure 1)** showed sinus rhythm with enlarged left atrium and the brain computed tomography (CT) scan without contrast showed no hemorrhagic or ischemic brain injury; thrombolysis was started four hours after the onset of symptoms without improvement of NIHSS; the control brain CT scan at 24 hours showed heterogeneous hypodensity in the left basal ganglia suggestive of acute ischemia.

On the fourth day of hospitalization, an irregular pulse rate was detected without hemodynamic repercussions, the ECG showed sinus rhythm with supraventricular bigeminy and ST-segment elevation in leads V2-V5 with R-wave amputation, and ultrasensitive troponin T increased by 154 ng/L **(Figure 2).** Echocardiography **(Figure 3)** showed akinesia of the anterior, inferior, anteroinferolateral and anteroinferoseptal walls at medial and apical levels, and basal hypercontractility, with preserved left ventricular ejection fraction, suggesting Takotsubo cardiomyopathy. Coronary angiography showed no significant obstructive lesions of epicardial arteries, whereas ventriculography showed an image in the form of "Takotsubo's pot" **(Figure 4)**. With slight neurological improvement and stable cardiovascular status, she was discharged on the eighth day of hospitalization. The following medication was prescribed: acetylsalicylic acid 100 mg every 24 hours, atorvastatin 40 mg every 24 hours, enalapril 10 mg every 12 hours, metformin 850 mg every 12 hours.

Two days later, she was readmitted for sudden onset of palpitations and dyspnea at rest. On admission, blood pressure: 118/85 mmHg; tachypneic, irregular pulse rate; tachycardic with no signs of hypoperfusion or pulmonary congestion. ECG **(Figure 5)** shows atrial fibrillation (AF) with high ventricular response and ultrasensitive troponin T rose to 89 ng/L. During this hospitalization, her level of consciousness deteriorated, and a new brain CT scan showed hemorrhagic conversion at the level of the anterior ischemic injury. Subsequently, she was discharged with atorvastatin 40 mg every 24 hours, bisoprolol 2.5 mg every 24 hours and insulin glargine 30 IU every 24 hours. Finally, the patient died after two months of follow-up because of an unknown cause.

Discussion

We present a patient with high cardiovascular risk factors who went through three phases. First, acute focal syndrome, in which acute ischemic stroke is the main cause, and cardioembolic events are responsible for 35% of the etiologies, among which AF is the

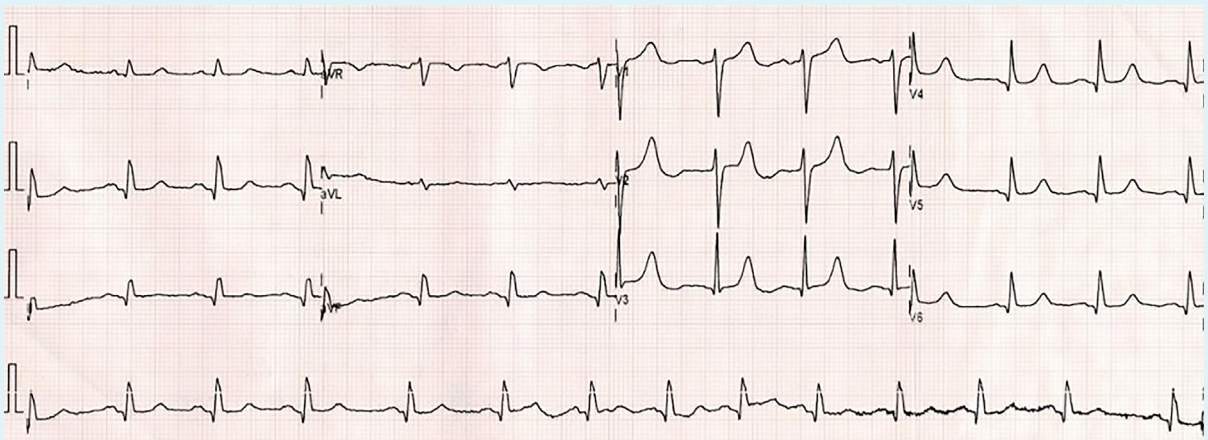

Figure 1. Admission electrocardiogram. Sinus rhythm with enlarged left atrium.

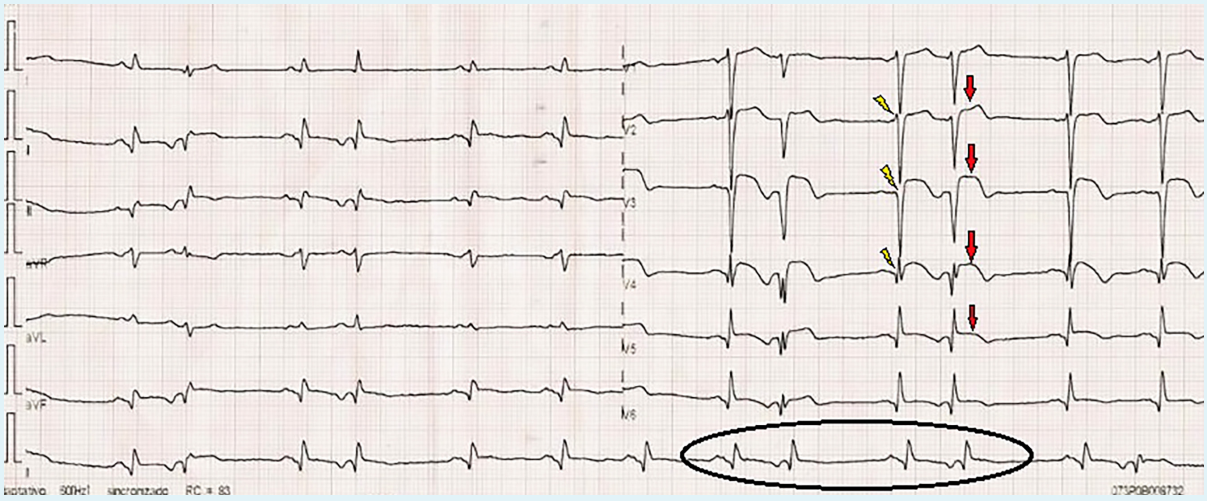

Figure 2. Electrocardiogram on the fourth day of hospitalization. sinus rhythm with supraventricular bigeminy (circle) and ST-segment elevation in leads V2-V5 (red arrow) with R-wave amputation (yellow lightning).

origin of 20 to 30% of all ischemic strokes and 10% of cryptogenic strokes [3-5]. The ischemic cause was confirmed with the brain CT; however, no signs of cardioembolic events are found in the physical examination or in the admission electrocardiogram. Thrombolytic therapy was administered, which was not effective, an expected result given that only 52% are effective when administered after four hours of illness and, in people over 80 years of age, the effectiveness is around 50% [6,7].

A second phase, when the electrocardiogram shows a clear ST-segment elevation in precordial leads **(Figure 2)** and this repolarization alteration may be secondary to ischemic stroke [8,9]; however, in the context of a patient with very high cardiovascular risk, myocardial injury must be ruled out, considering that stroke generates the release of cytokines due to a systemic inflammatory response which is capable of destabilizing coronary plaques and also causing myocardial necrosis because of the release of intracellular calcium, leading to acute coronary syndrome (ACS) or cardiomyopathy [10]. Thus, the study of cardiac enzymes played an important role [11] since it indicated acute myocardial injury that was corroborated by echocardiography, which demonstrates

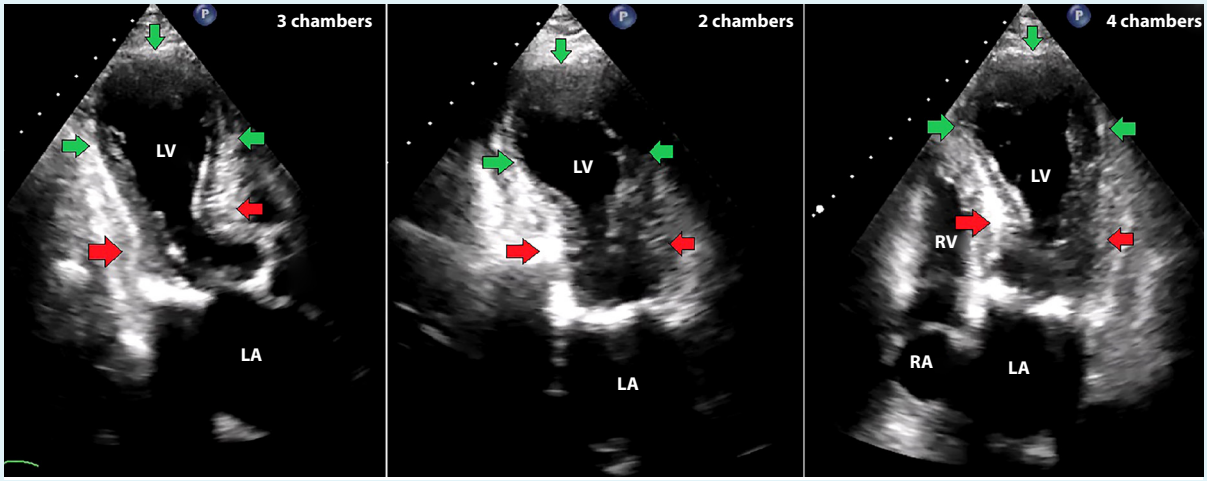

Figure 3. Echocardiography in apical view of 3, 2, and 4 chambers. Evidence of akinesia of the anterior, inferior, anteroinferolateral and anteroinferoseptal walls at medial and apical levels (green arrow) and basal hypercontractility (red arrow) (Takotsubo pattern). **RA:** right atrium. **LA:** left atrium. **Ao:** aorta. **RV:** right ventricle. **LV:** left ventricle.

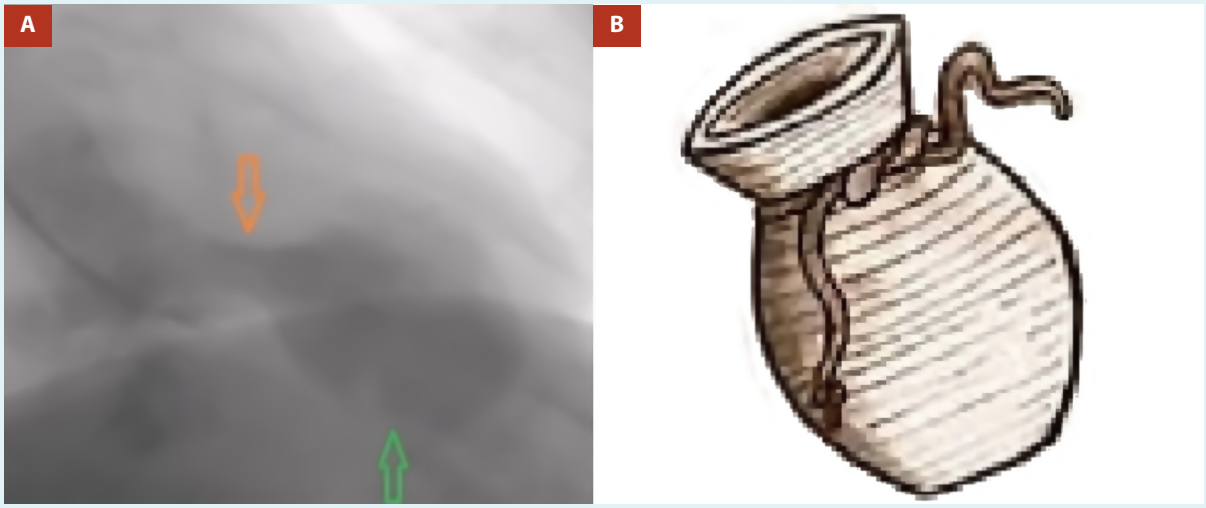

Figure 4. Ventriculography. **A:** Hypercontractility of the basal segments (orange arrow) and akinesia of the middle and apical segments of the left ventricle (green arrow). **B:** "Takotsubo" octopus capture pot.

alteration of multiple vascular territories presuming multi-vessel lesion, but, surprisingly, cardiac catheterization reports absence of significant obstructive injuries modifying the diagnosis to myocardial infarction with non-obstructive coronary arteries (MINOCA) [12], which together with the proven acute myocardial infarction and the absence of alternative diagnosis, fits the MINOCA criteria [13-15].

In the presence of MINOCA, which is a clinical syndrome with a prevalence ranging from 1 to 15% in patients with ACS, especially in young people, women and non-ST-elevation myocardial infarction (NSTEMI), a ventriculography was performed based on echocardiographic findings [15,16], which shows a ventricle in the form of a "Takotsubo's pot" **(Figure 4).** We conclude that it is a takotsubo syndrome, with controversies about the use of beta-blockers, angiotensin-converting enzyme inhibitors and single antiplatelet therapy [13,14,17].

Finally, at a third phase, it is shown that AF with high ventricular response could be an incidental event, since the patient had the conditions to develop it, such as being part of the brain-cardiac syndrome, being secondary to myocardial infarction [18] or being a pre-existing AF, which are more frequently detected after stroke; this generates a debate to demonstrate that the AF episodes are developed by the brain-heart syndrome or are the cause of the initial stroke [1,2]. These three events (ischemic stroke, takotsubo

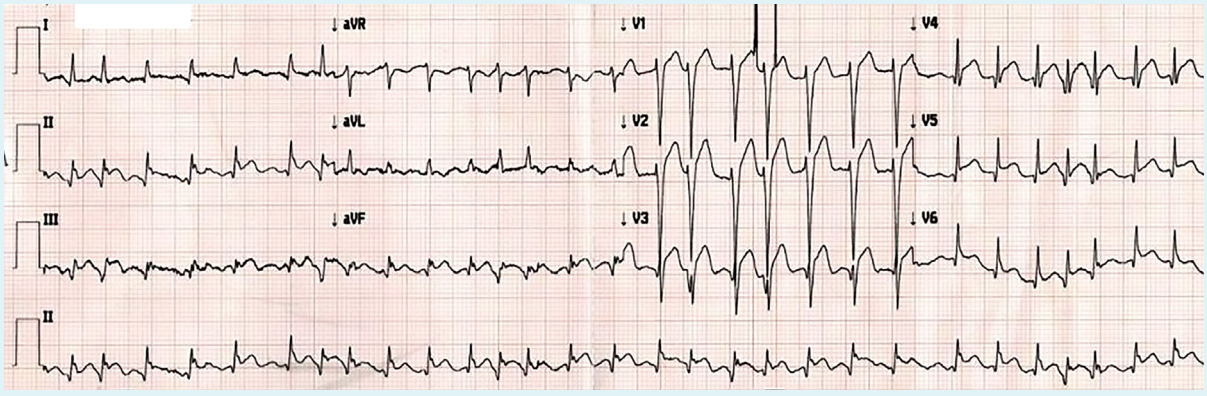

Figure 5. Electrocardiogram two days after discharge. Atrial fibrillation with high ventricular response.

syndrome, and AF) are part of the brain-heart syndrome that occurs most frequently within the first three days of the cerebrovascular event, which is associated with advanced age, prevalence of cardiac comorbidities, and cardiovascular risk factors [1,2], and explains the cardiac injury by the interaction the brain-heart nerve axis causing inflammation, central autonomic dysregulation, catecholamine release, structural changes in the myocardium and vascular wall abnormalities [2,19].

Takotsubo syndrome, was first described by Sato in 1990, developed by physical or emotional stressful events which generate a "catecholamine storm" [20], that frequently affects postmenopausal women, who represent 2% of ACS or 10% if only women are considered. Its diagnosis requires alteration of transient myocardial contractility (approximately 6 weeks); evolving electrocardiographic abnormalities [21,22]; disparity between troponin elevation and dysfunctional myocardium and absence of myocarditis, pheochromocytoma or significant epicardial coronary artery disease [23]; with frequent complications, such as the presence of obstructive lesions, preferably if the triggering factor is physical, acute neurological disease, first troponin greater than 10 times the normal upper limit and the left ventricular ejection fraction is less than 45%; conditioned by a high risk of mortality [24,25].

In our opinion, the primary event was a paroxysmal AF leading to a cardioembolic ischemic stroke complicated by takotsubo syndrome, closing the circle of the brain-heart syndrome.

In conclusion, in patients with a frequent presentation such as ischemic stroke, despite not demonstrating arrhythmias on admission, it is mandatory to look for the presence of AF and to evaluate the coexistence of myocardial injury, as they are not always secondary to significant coronary injuries as in MINOCA or takotsubo syndrome, which occurs in the context of an emerging condition such as brain-heart syndrome, with high risk of mortality, the cardiologist must to look for them, and ultrasensitive troponins play a determining role in this.

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References

1. Scheitz JF, Nolte CH, Doehner W, Hachinski V, Endres M. Stroke–heart syndrome: clinical presentation and underlying mechanisms. Lancet Neurol. 2018;17:1109-20. doi: 10.1016/S1474-4422(18)30336-3.
2. Sposato LA, Hilz MJ, Aspberg S, Murthy SB, Bahit MC, Hsieh CY, *et al;* World Stroke Organisation Brain & Heart Task Force. Post-Stroke Cardiovascular Complications and Neurogenic Cardiac Injury: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;76(23):2768-85. doi: 10.1016/j.jacc.2020.10.009.
3. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, *et al.* 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52(7):e364-e467. doi: 10.1161/STR.0000000000000375.
4. Caprio FZ, Sorond FA. Cerebrovascular Disease: Primary and Secondary Stroke Prevention. Med Clin North Am. 2019;103(2):295-308. doi: 10.1016/j.mcna.2018.10.001.
5. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, *et al.* 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021 Feb 1;42(5):373-498. doi: 10.1093/eurheartj/ehaa612.
6. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, *et al*. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359(13):1317-29. doi: 10.1056/NEJMoa0804656.
7. Demaerschalk BM, Kleindorfer DO, Adeoye OM, Demchuk AM, Fugate JE, Grotta JC, *et al.* American Heart Association Stroke Council and Council on Epidemiology and Prevention. Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2016;47(2):581-641. doi: 10.1161/STR.0000000000000086. Erratum in: Stroke. 2016;47(11):e262.
8. Goldstein DS. The electrocardiogram in stroke: relationship to pathophysiological type and comparison with prior tracings. Stroke. 1979;10(3):253-9. doi: 10.1161/01.str.10.3.253.
9. Khechinashvili G, Asplund K. Electrocardiographic changes in patients with acute stroke: a systematic review. Cerebrovasc Dis. 2002;14(2):67-76. doi: 10.1159/000064733.
10. Doehner W, Leistner DM, Audebert HJ, Scheitz JF. The role of cardiologists on the stroke unit. Eur Heart J. 2020;22(Supplement_M):M3-M12. doi: 10.1093/eurheartj/suaa160.
11. Sposato LA, Hilz MJ, Aspberg S, Murthy SB, Bahit MC, Hsieh CY, *et al*. World Stroke Organisation Brain & Heart Task Force. Post-Stroke Cardiovascular Complications and Neurogenic Cardiac Injury: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;76(23):2768-2785. doi: 10.1016/j.jacc.2020.10.009.
12. Falk R, Hershberger R. Miocardiopatías dilatada, restrictiva e infiltrante. En: Braunwald's heart disease: A textbook of cardiovascular medicine. 11th edition. Capítulo 77. Elsevier; 2018. p. 1580-1601.
13. Collet J, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Deepak L. et al. 2020 ESC Guidelines for themanagement of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42(14):1289-1367. doi: 10.1093/eurheartj/ehaa575.
14. Pustjens TFS, Appelman Y, Damman P, Ten Berg JM, Jukema JW, de Winter RJ, *et al.* Guidelines for the management of myocardial infarction/injury with non-obstructive coronary arteries (MINOCA):

a position paper from the Dutch ACS working group. Neth Heart J. 2020;28(3):116-130. doi: 10.1007/s12471-019-01344-6. Erratum in: Neth Heart J. 2020;28(1):59.

15. Sucato V, Testa G, Puglisi S, Evola S, Galassi AR, Novo G. Myocardial infarction with non-obstructive coronary arteries (MINOCA): Intracoronary imaging-based diagnosis and management. J Cardiol. 2021;77(5):444-451. doi: 10.1016/j.jjcc.2021.01.001.
16. Kosmas N, Manolis A, Dagres N, Iliodromitis E. Myocardial infarction or acute coronary syndrome with non-obstructive coronary arteries and sudden cardiac death: a missing connection. EP Europace. 2020;22(9):1303-10. doi: 10.1093/europace/euaa156.
17. Nordenskjöld AM, Agewall S, Atar D, Baron T, Beltrame J, Bergström O, *et al.* Randomized evaluation of beta blocker and ACE-inhibitor/angiotensin receptor blocker treatment in patients with myocardial infarction with non-obstructive coronary arteries (MINOCA-BAT): Rationale and design. Am Heart J. 2021;231:96-104. doi: 10.1016/j.ahj.2020.10.059.
18. Bhatia GS, Lip GY. Atrial fibrillation post-myocardial infarction: frequency, consequences, and management. Curr Heart Fail Rep. 2004;1(4):149-55. doi: 10.1007/s11897-004-0002-y.
19. Budnik M, Piątkowski R, Ochijewicz D, Zaleska M, Grabowski M, Opolski G. Pathophysiology of Takotsubo Syndrome as A Bridge to Personalized Treatment. J Pers Med. 2021;11(9):879. doi: 10.3390/jpm11090879.
20. Goico A, Chandrasekaran M, Herrera CJ. Novel developments in stress cardiomyopathy: From pathophysiology to prognosis. Int J Cardiol. 2016;223:1053-1058. doi: 10.1016/j.ijcard.2016.08.241.
21. Johnson NP, Chavez JF, Mosley WJ 2nd, Flaherty JD, Fox JM. Performance of electrocardiographic criteria to differentiate Takotsubo cardiomyopathy from acute anterior ST elevation myocardial infarction. Int J Cardiol. 2013;164(3):345-8. doi: 10.1016/j.ijcard.2011.07.029.
22. Kosuge M, Kimura K. Electrocardiographic findings of takotsubo cardiomyopathy as compared with those of anterior acute myocardial infarction. J Electrocardiol. 2014;47(5):684-9. doi: 10.1016/j.jelectrocard.2014.03.004.
23. Akashi YJ, Nef HM, Lyon AR. Epidemiology and pathophysiology of Takotsubo syndrome. Nat Rev Cardiol. 2015;12(7):387-97. doi: 10.1038/nrcardio.2015.39.