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CASE REPORT
Other

Basal Takotsubo syndrome with transient severe mitral regurgitation caused by drug use: a case report

Grégoire Albenque[1], Yohann Bohbot[1,2], Quentin Delpierre[1], and Christophe Tribouilloy [1,2]*

[1]Department of Cardiology, Amiens University Hospital, Avenue René Laënnec, 80054 Amiens, France; and [2]UR UPJV 7517, CURS-UFR de pharmacie, Laboratoire UPJCV, Universite´ de Picardie, 1 chemin du Thil, 80000 Amiens, France

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Background Takotsubo syndrome (TTS) is a reversible cardiomyopathy. Little is known regarding its basal form and possible complications.

Case summary A 31-year-old woman with no medical history was hospitalized for attempted suicide by ingestion of cocaine, benzodiazepine, and methadone. Initially, the patient received intensive care for coma and bradypnoea. After naloxone administration, the neurological situation improved, but the patient developed acute pulmonary oedema. Transthoracic echocardiography (TTE) revealed left ventricular systolic dysfunction with the basal wall's akinesia associated with moderate to severe restrictive mitral regurgitation. Global longitudinal strain (GLS) was impaired mainly in the basal segments. A coronary computed tomography ruled out coronary artery disease. Symptoms improved quickly under diuretic treatment. Transthoracic echocardiography at Day 6 showed improved basal wall contraction, with a left ventricular ejection fraction (LVEF) of 50% and moderate mitral regurgitation. TTE at Day 30 confirmed the diagnosis of myocardial infarction with non-obstructive coronary arteries related to a basal TTS after complete recovery of the LVEF, normalization of the wall motion and GLS, and the absence of residual mitral regurgitation.

Discussion We report a case of acute pulmonary oedema due to basal TTS complicated by severe transient mitral regurgitation associated with moderate left ventricular dysfunction. Measuring strain by speckle-tracking can be useful to diagnose and monitor this entity. The use of coronary computed tomography is informative in young patients to rule-out coronary artery disease.

Keywords Takotsubo syndrome • Basal Takotsubo syndrome • Acute mitral regurgitation • Strain by speckle-tracking • Echocardiography • Case report

Learning points

- The basal form of Takotsubo syndrome can cause acute pulmonary oedema by left ventricular dysfunction and acute restrictive mitral regurgitation related to akinesia of the basal walls.
- Use of coronary computed tomography is informative in young patients to rule-out coronary artery disease.
- Measuring strain by speckle-tracking can be useful to diagnose and monitor this entity.

* Corresponding author. Tel: +33 3 22 45 58 83, Fax: +33 3 22 45 56 58, Email: tribouilloy.christophe@chu-amiens.fr

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Introduction

Takotsubo syndrome (TTS) is characterized by a temporary wall motion abnormality of the left ventricle and often includes emotional or physical triggers.[1] Its apical form is the most extensively studied in the literature. The basal phenotype is rare, usually occurs in younger patient than in apical type and appears commonly in patients with subarachnoid haemorrhage or pheochromocytoma or after epinephrine administration.[1] We, hereby, present a case of myocardial infarction with non-obstructive coronary arteries (MINOCAs) related to a basal TTS induced by drug use, complicated by transient severe mitral regurgitation in a pre-menopausal woman.

Timeline

Time	Events
Day 0, H0	Coma and bradypnoea after suicide attempt by ingestion of cocaine, benzodiazepine, and methadone.
Day 0, H3	Rapid response after NALOXONE administration.
Day 1	Acute pulmonary oedema.
	Transfer to the cardiology department, where the first transthoracic echocardiography is performed showing moderate-to-severe mitral regurgitation and left ventricular dysfunction with basal walls akinesia.
Day 2	Coronary computed tomography finds normal coronary arteries.
Day 6	After 4 days of monitoring, the patient left the hospital with a low dose of FUROSEMIDE.
	Echocardiography showed improvement of basal wall contraction and moderate mitral regurgitation.
Day 30	The basal form of Takotsubo syndrome is confirmed after the complete recovery of ejection fraction and the absence of residual mitral regurgitation.

Case presentation

A 31-year-old woman with no medical history was hospitalized for attempted suicide by ingestion of cocaine, benzodiazepine, and methadone. Initially, the patient received intensive care for coma and bradypnoea. The initial electrocardiogram (ECG) recorded sinus tachycardia (*Figure 1*) and the first blood sample analysis revealed a troponin Ic concentration at 0.56 µg/L (normal range < 0.045 ng/mL), creatinine kinase at 182 IU/L (normal range 20–200 IU/L), a white blood cell count of 6000 10.3/mm^3 (normal range 4000–10 000 10.3/mm^3), and a normal level of C reactive protein. After naloxone administration, the neurological status quickly improved, whereas the patient developed acute pulmonary oedema with no fever or ECG changes. After a rapid response to intravenous diuretic therapy, the patient was transferred to the cardiology department. The measurement of cardiac biomarkers showed troponin Ic at 2.5 µg/L and brain natriuretic peptide (BNP) at 929 ng/L (normal range <100 ng/L).

The first TTE (Supplementary material online, *Video S1*) showed moderate systolic dysfunction with a left ventricular ejection fraction (LVEF) of 40%, hyperkinesia of the apical segments, and akinesia of the basal segments associated with moderate to severe functional mitral regurgitation (*Figure 2*). Global longitudinal strain (GLS) was abnormally low at -16.1%. Longitudinal strain was mainly impaired in the basal segment (*Figure 3*). A MINOCA related to a basal TTS was suspected in this stable patient with an interTAK diagnostic score of 81.[1] The patient refused cardiac magnetic resonance because of claustrophobia and we choose to perform coronary computed tomography the next day, which revealed healthy coronary arteries and confirmed the diagnosis of MINOCA (*Figure 4*).

In the assessment of this probable basal TTS, 24-h urine stress hormones were measured, showing: noradrenaline at 1206 nmol/24 h (normal range 135–620 nmol/24 h), adrenaline at 136 nmol/24 h (normal range 21–109 nmol/24 h), dopamine at 1351 nmol/24 h (normal range 404–2912 nmol/24 h), normetanephrine at 4.1 µmol/24 h (normal value < 3 µmol/24 h), metanephrine at 0.9 µmol/24 h (normal value < 1.4 µmol/24 h). Based on these biological results, a pheochromocytoma was suspected but ruled out after a normal thoracoabdominal computed tomography scan.

At Day 6, TTE revealed an improvement in basal wall contraction and LVEF (50%) and a reduction of mitral regurgitation, which was now moderate (Supplementary material online, *Video S2*). No rhythm disorder was recorded by ECG telemetry and cardiac biomarker levels decreased (BNP at 335 ng/L and troponin at 0.103 µg/L). The patient left the hospital with 20 mg of FUROSEMIDE.

At 30 days, the patient was asymptomatic and TTE (Supplementary material online, *Video S3*) showed complete recovery of LVEF (60%), normalization of wall motion and of GLS (-21.1%) (*Figure 5*), and the absence of residual mitral regurgitation. These results confirmed the diagnosis of basal TTS and the FURO SEMIDE was discontinued.

Discussion

There are several aetiologies responsible for MINOCA: epicardial coronary artery disorders such as plaque rupture, ulceration, or coronary dissection with non-obstructive or no coronary artery disease; inequation between oxygen supply and demand such as coronary spasm or coronary embolism; coronary endothelial dysfunction; and myocardial disorders without involvement of the coronary arteries such as TTS or myocarditis.[2] Drug abuse, might account for, at least, 10% of acute coronary syndromes[3] and cocaine may induce vasospasm through adrenergic stimulation of the coronary arteries. Provocative spasm testing has demonstrated inducible spasm in 27% of MINOCA, especially in the context of drug abuse, suggesting that it is an important pathogenetic mechanism in MINOCA.[4] However, in the present case, the topography of the wall motion abnormality was not evocative of a coronary spasm.

Basal TTS, which is a rare and reversible form of MINOCA, represents only 2% of all TTSs and usually occurs in younger patients,

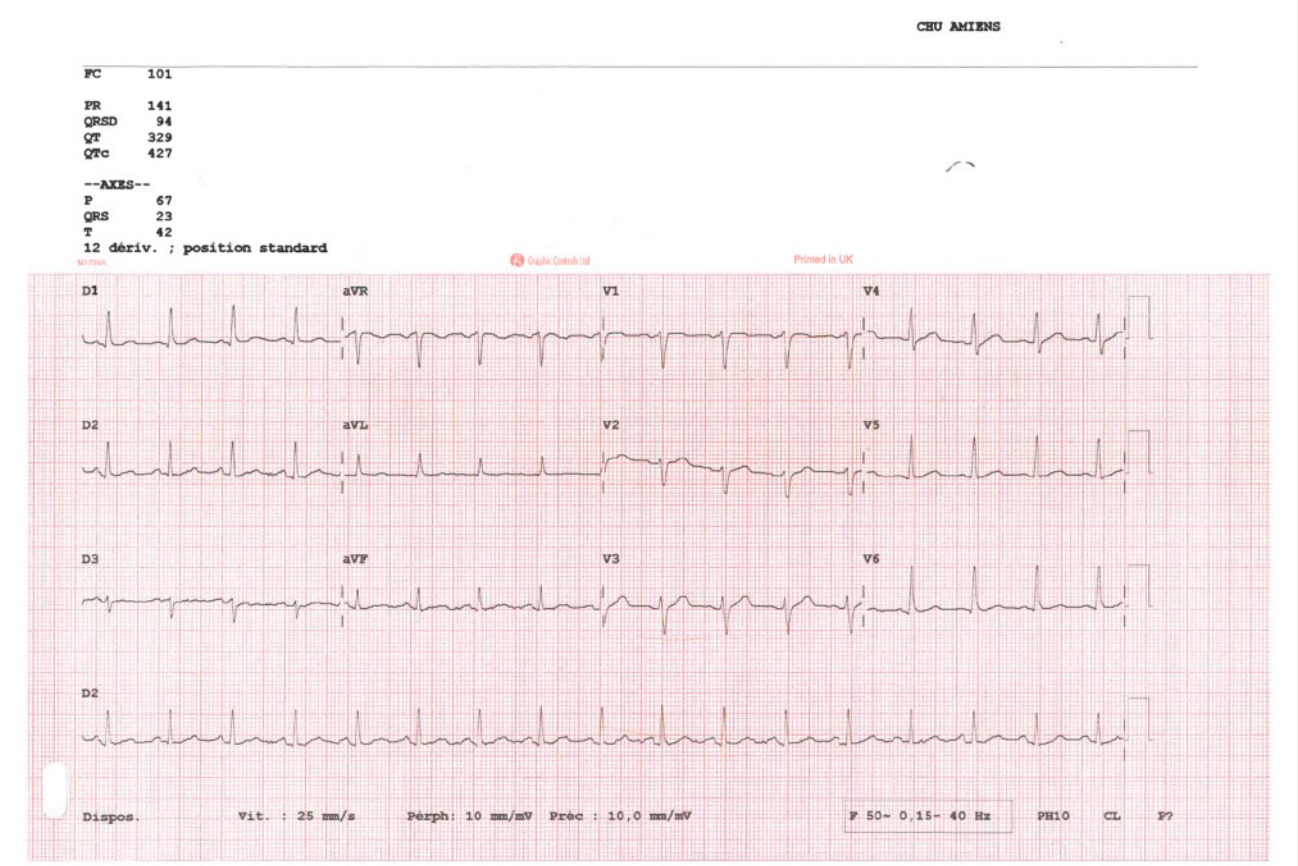

Figure 1 Electrocardiogram.

more often with neurological disorders, with lower values of BNP, less altered LVEF, and more frequent ST-segment depression than the typical form.[5] Otherwise, it has been reported that basal TTS can be associated with the presence of a pheochromocytoma, induced by epinephrine, or occur in the context of subarachnoid haemorrhage,[6] emotional stress,[7] or drug use.[8] The 24-h urine stress hormones were high, but the thoracoabdominal computed tomography scan was normal and consequently, we did not retain the pheochromocytoma diagnosis, which may be responsible for this cardiomyopathy.[9,10]

Pulmonary oedema was favoured by acute functional mitral regurgitation. The mechanism of the regurgitation was the restrictive movement of both mitral leaflets related to basal wall akinesia. Mitral regurgitation decreased on Day 6, with improved contractility, and completely disappeared on Day 30, with full recovery of cardiac function, making mitral regurgitation a transient complication of basal TTS.

Based on the clinical context and the diagnostic algorithm of TTS that was proposed in the recent International Expert Document,[1] we diagnosed a basal TTS without using coronary angiography or cardiac magnetic resonance. Indeed, in this specific case of a young patient with a typical echocardiographic aspect of TTS, coronary computed tomography can be very useful to eliminate coronary artery disease. Cardiac magnetic resonance can also be very useful for suspected cases of TTS. It can find oedema as in myocarditis, but its main utility is to rule-out an ischaemic event or a myocarditis by showing no enhancement after gadolinium injection. Our patient was claustrophobic. Thus, we could not perform magnetic resonance. However, the age of the patient and the topography of the wall motion abnormality were not evocative of an ischaemic process. Moreover, the echocardiographic follow-up of wall motion abnormalities, LVEF, and strain pattern allowed us to confirm the TTS by showing a full recovery.

The interest of GLS has already been investigated in apical TTS.[1,11]

Some authors have suggested that GLS may also have a prognostic value.[11] In our case, GLS was initially impaired, with apical sparing in the bullseye. Transthoracic echocardiography at 1 month showed complete normalization, with homogenization of segmental values.

In the present case, the transient severe mitral regurgitation was related to basal TTS. Indeed, the akinesia of the basal walls could explain the pathophysiology of such regurgitation by increasing tethering forces and reducing closing forces, as in ischaemic mitral regurgitation. Moreover, the complete recovery of contractility allowed complete correction of the regurgitation.

Conclusion

The basal form of TTS is a rare and reversible cause of MINOCA that can cause acute pulmonary oedema by left ventricular dysfunction and acute restrictive mitral regurgitation related to akinesia of the

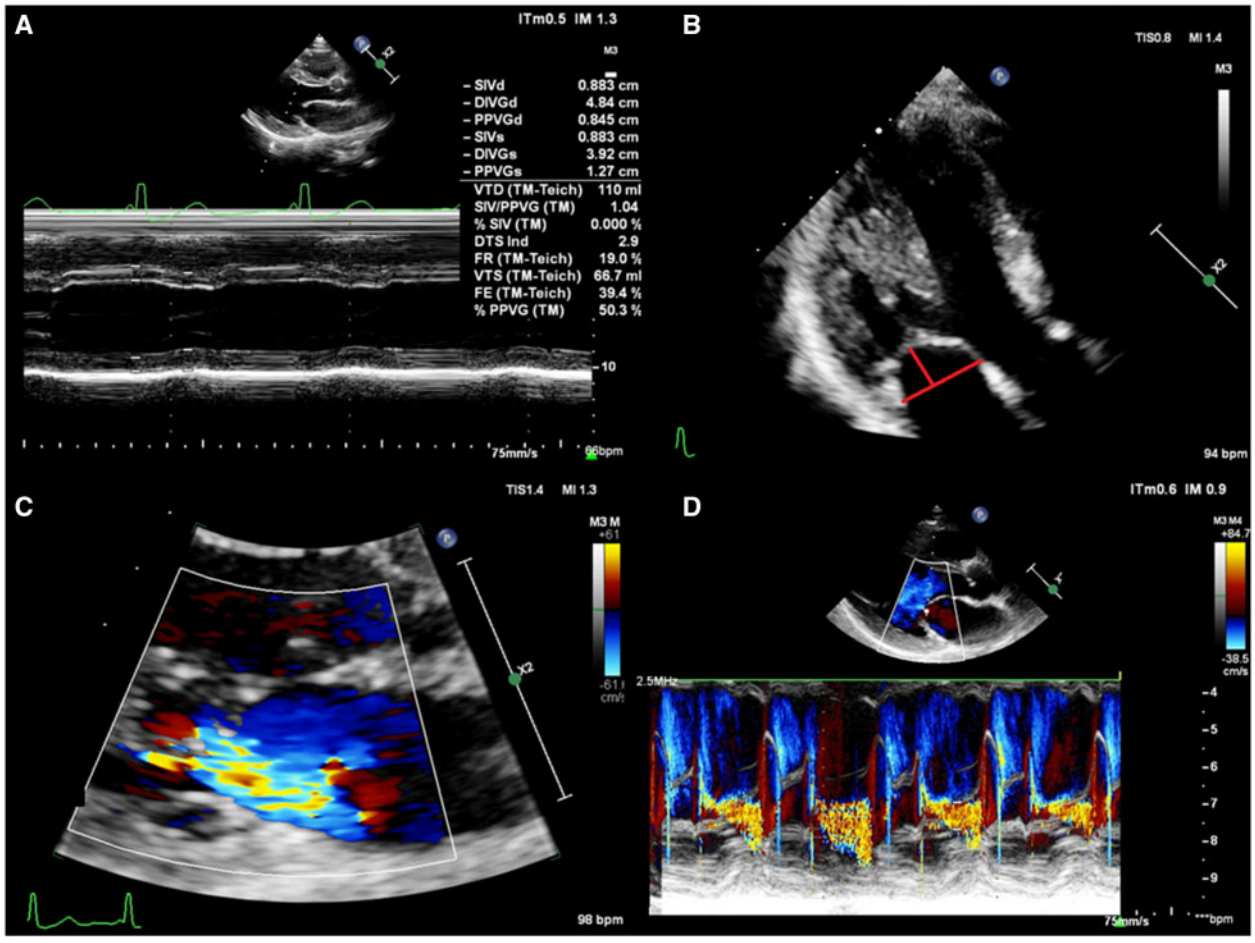

Figure 2 (*A*) Parasternal long-axis views by two-dimensional-guided M-mode showing left ventricular dilatation and dysfunction. (*B*) Apical three-chamber view showing significant mitral tenting. (*C* and *D*) Parasternal long-axis view showing holosystolic mitral regurgitation in two-dimension and in the colour M-mode.

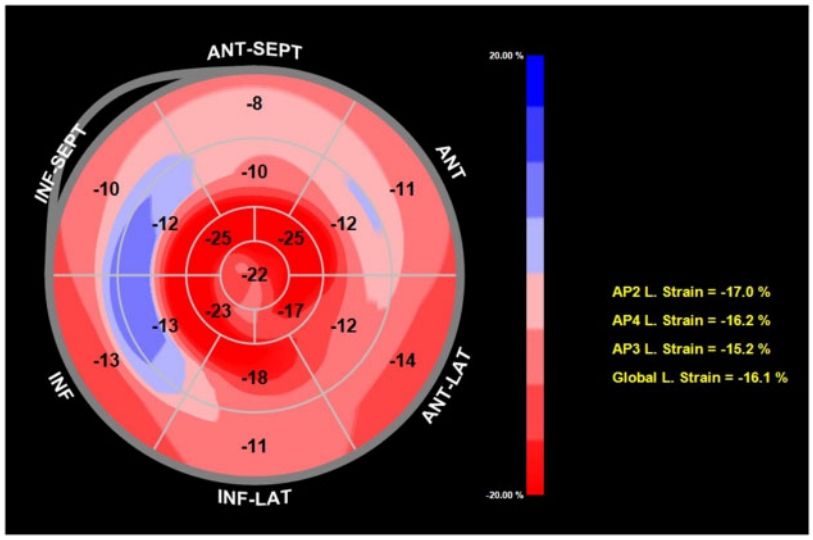

Figure 3 Global longitudinal strain at Day 1.

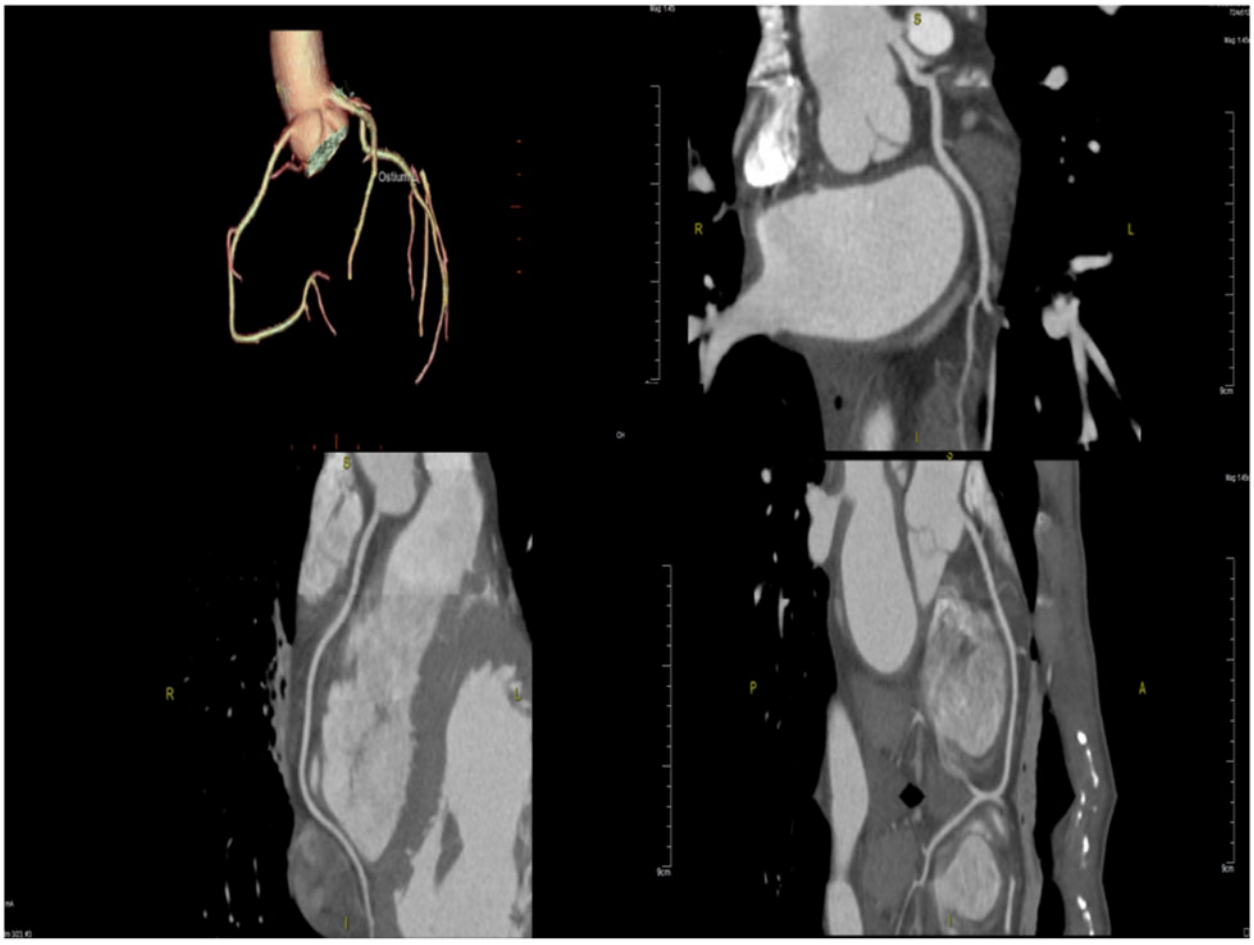

Figure 4 Coronary computed tomography showing normal coronary arteries.

basal walls. Measuring strain by speckle-tracking can be useful to diagnose and monitor this entity. The use of coronary computed tomography is informative in young patients to rule-out coronary artery disease.

Lead author biography

Grégoire Albenque is currently a French cardiology resident at the Amiens University Hospital in France.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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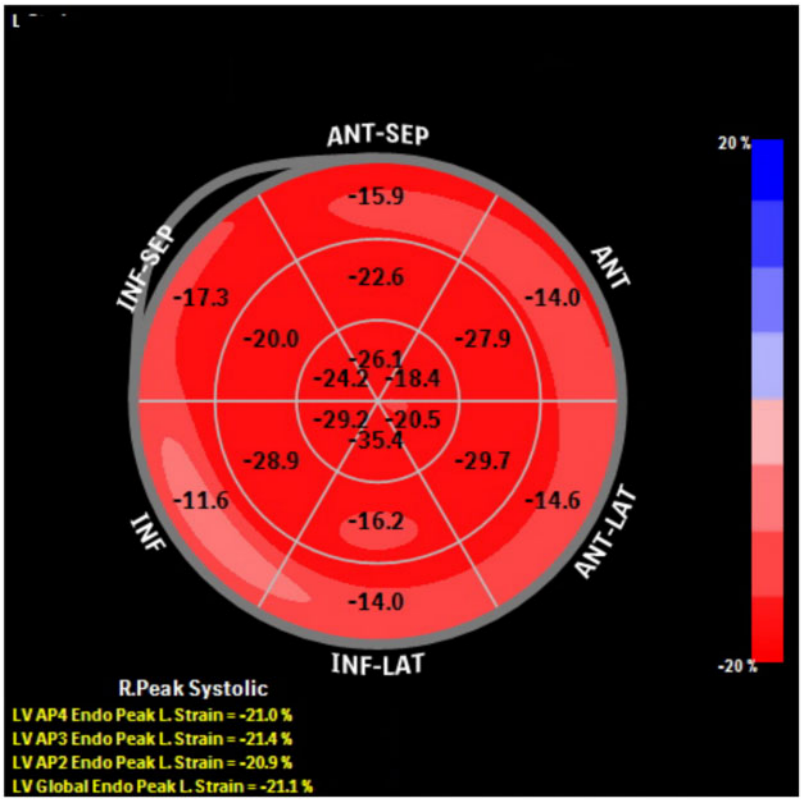

Figure 5 Global longitudinal strain at Day 30.

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