Complex Congenital Heart Lesion – Should We Operate or Not?

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Abstract
Congenitally corrected transposition of the great arteries (ccTGA) is a rare congenital anomaly defined by double discordance – atrioventricular and ventricular-arterial. ccTGA frequently has associated lesions, which influence long-term survival.
The management of patients with ccTGA regarding the closure of defects and pacing strategies is often very challenging. Moreover, tricuspid valve regurgitation and its impact on the systemic right ventricle requires close monitoring and potentially timely interventions.
In this paper, we present and discuss the management challenges raised by a patient with situs inversus totalis, dextrocardia, ccTGA, Ebstein anomaly of the tricuspid valve, atrial septal defect, and complete atrioventricular block.

Keywords
congenital, transposition, block, situs inversus, dextrocardia, Ebstein-like, septal defect

Rezumat
Transpoziția de vase mari corectată congenital (TVMcc) reprezintă o anomalie congenitală rară marcată de dublă discordanță - atrioventriculară și ventriculo-arterială. TVMcc apare frecvent alături de alte malformații cardiace, acestea influențând supraviețuirea pe termen lung.
Complexitatea gestionării TVMcc, în special abordarea regurgitării tricuspide și implicațiile acesteia asupra ventriculului drept sistemic, necesită monitorizare vigilentă și potențiale intervenții la momentul potrivit. Deciziile de management legate de închiderea defectelor și strategiile de stimulare la pacienții cu TVMcc necesită evaluări personalizate,
având în vedere avantajele potențiale pe termen lung și evitarea perturbării echilibrului hemodinamic.
În acest caz, asocierea de malformații cardiace congenitale, în special TVMcc, dextrocardia, situs inversus complet, anomalie de tip Ebstein, defect septal atrial și bloc atrioventricular complet, subliniază importanța monitorizării continue și a planificării. Această abordare își propune să adreseze sistematic provocările în gestionarea transpoziției de vase mari corectată congenital și a anomaliilor asociate.

Cuvinte cheie
congenital, transpoziție, bloc, situs inversus, dextrocardie, Ebstein-like, defect septal

Case Presentation

An 18 year-old (yo) female patient diagnosed in childhood with visceral situs inversus, without known cardiac disease, presented to our hospital with a 3-month history of fatigue at light-medium intensity exercise and low heart rate at home; these symptoms persisted after a mild form of COVID-19 infection.

The clinical examination revealed a patient in good overall condition, with normal weight. The vitals were as follows: HR = 45/min and regular, RR = 18/min with no respiratory distress, BP = 115/60 mmHg, she was warm and well perfused. The saturation in room air was 95% with an unremarkable respiratory exam. The point of maximum impulse (PMI) was on the right midclavicular 5th intercostal space; there was a fixed split of the second heart sound and a 2/6 right parasternal systolic regurgitant murmur without signs of congestion. The femoral pulses were easily palpable.

The ECG (**Figure 1**) showed a complete atrioventricular block (AVB) with a junctional escape rhythm of 50/min.

NT-proBNP values and routine tests were within normal limits.

The transthoracic echocardiography (TTE) (**Figure 2**, **Figure 3**, **Figure 4**) revealed situs inversus totalis, dextrocardia, and congenitally corrected transposition of the great arteries (ccTGA) with good bi-ventricular function. There was an Ebstein-like malformation of the tricuspid (systemic) valve with grade II regurgitation; the mitral valve also had mild regurgitation.

The transthoracic windows were challenging, and interatrial communication could not be ruled out. Transesophageal echocardiography (TOE) (Figure 5, Figure 6) revealed a small secundum atrial septal defect (ASD) (8/12 mm), with a left-to-right shunt and a PFO.

The cardiac MRI confirms the diagnosis (**Figure 7**, **Figure 8**, **Figure 9**) and measures a Qp:Qs of 1.75, with signs of volume overload of the sub-pulmonary ventricle – diastolic flattening of the interventricular septum. Both ventricles demonstrate normal systolic

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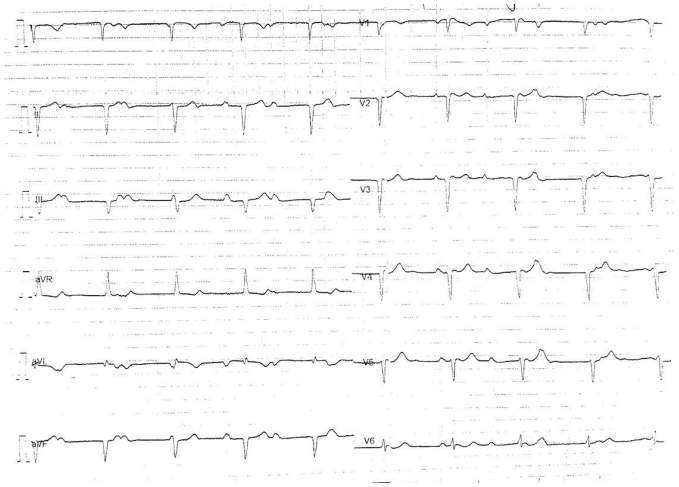


Figure 1 - ECG, complete AV block, narrow QRS, 50/min; AV, atrioventricular.

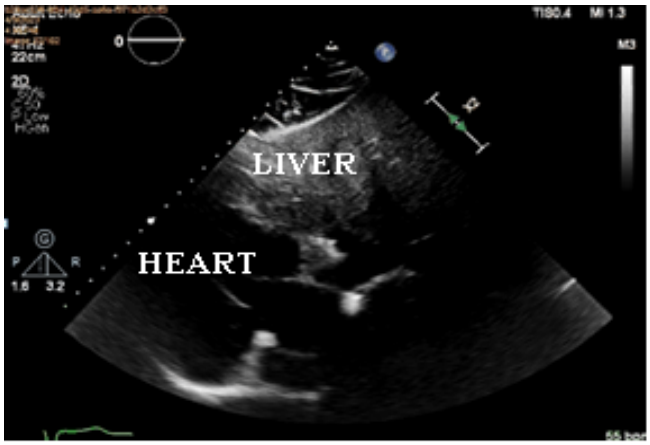


Figure 2 - TTE, subcostal view, dextrocardia, situs inversus; TTE, transthoracic echocardiography.

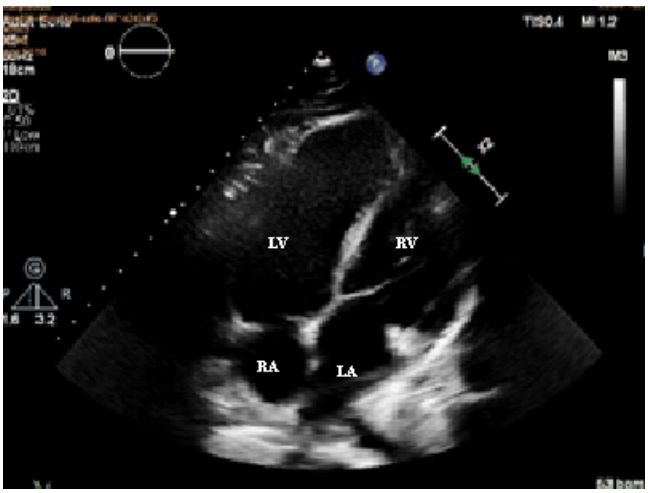


Figure 3. TTE, apical 4-chamber view, atrio-ventricular discordance; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; TTE, transthoracic echocardiography

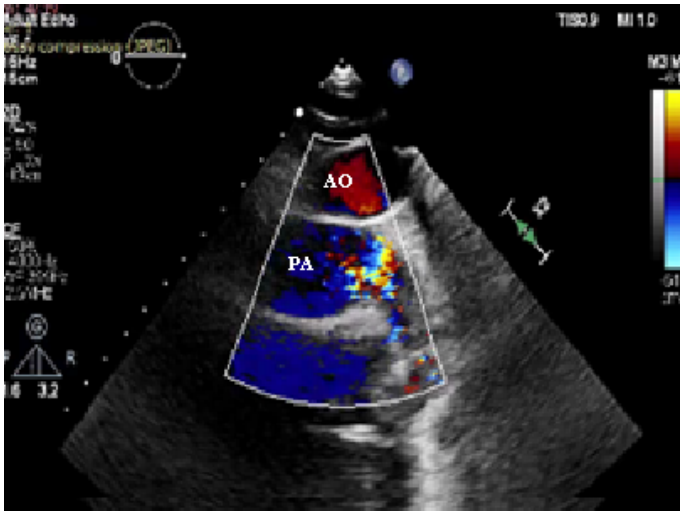


Figure 4 - TTE, suprasternal view, aorta and PA situated in parallel; AO, aorta; PA, pulmonary artery; TTE, transthoracic echocardiography.

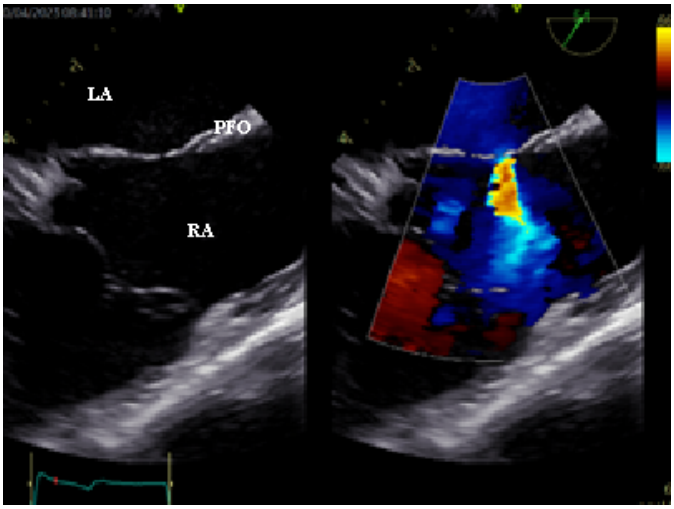


Figure 5 - TOE, PFO, left-to-right flow; LA, left atrium, PFO, patent foramen ovale; RA, right atrium; TOE, transesophageal echocardiography

function – LVEF 67%, RVEF 50%. It also described some focal fibrosis of the atrioventricular septum.

The cardiac catheterization revealed normal pulmonary pressures (mPAP of 20 mmHg) and resistances (PVR 0.8 Wu), with a Qp/Qs=1.68, consistent with the cMRI findings.

An exercise test was carried out, and the patient reached a maximum heart rate of 118/min. The test was interrupted after 6 minutes due to fatigue, and the patient achieved 7 METs, indicating a moderate level of physical capacity.

The 24-hour Holter monitoring showed complete AVB throughout the recording; heart rate ranged between 44 and 74 b.p.m., with an average of 69 b.p.m. No ventricular pauses longer than 2 seconds were detected.

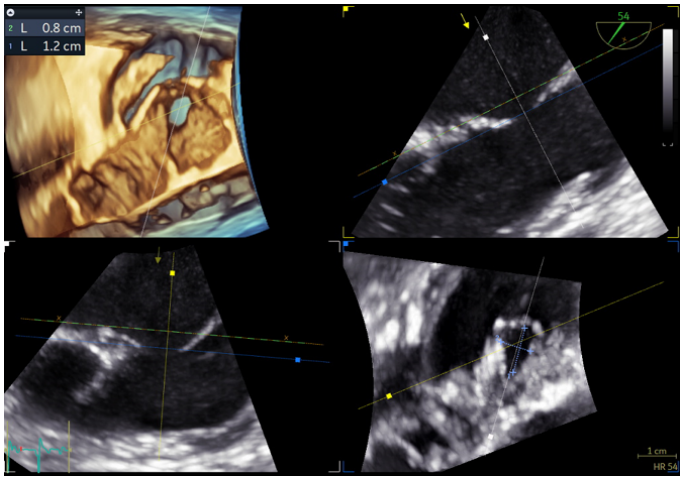


Figure 6 - 3D TOE, secundum type ASD; ASD, atrial septal defect; TOE, transesophageal echocardiography.

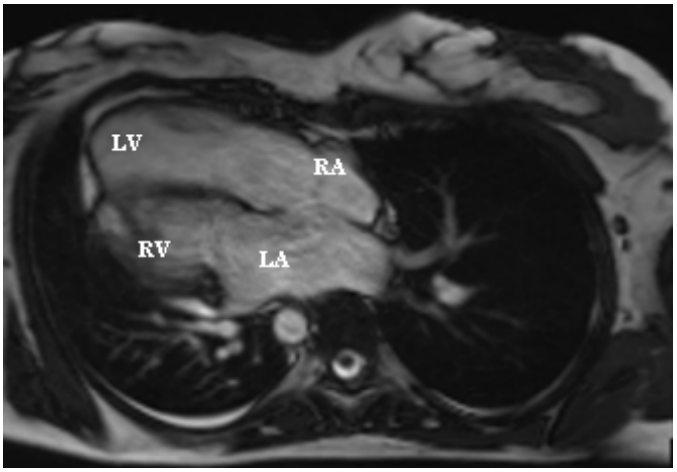


Figure 8 - CMR, 4 chamber view, atrio-ventricular discordance, small secundum type ASD; ASD, atrial septal defect; CMR, Cardiac Magnetic Resonance; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

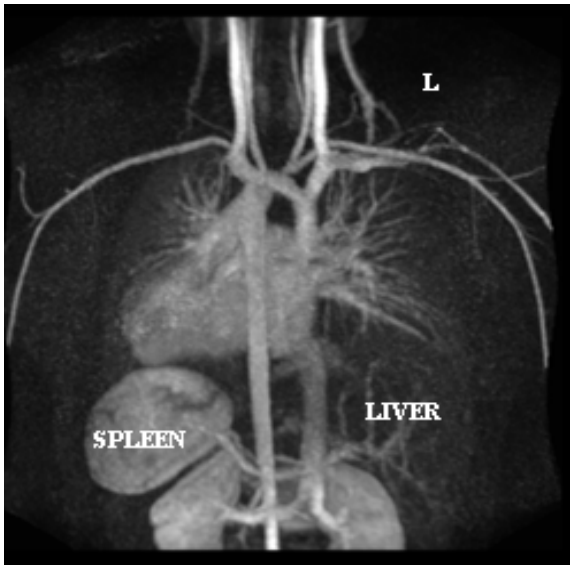


Figure 7 - MR angiography, dextrocardia, situs inversus; MR, magnetic resonance.

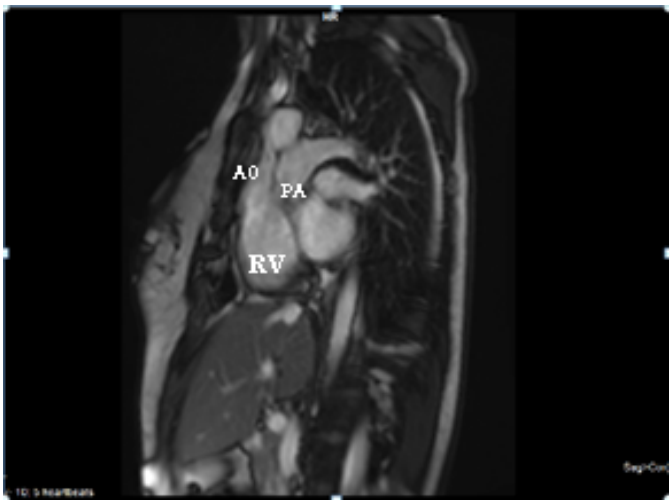


Figure 9 - CMR lateral view, ventriculo-arterial discordance, AO anterior and to the right of PA; AO, aorta; CMR, Cardiac Magnetic Resonance; PA, pulmonary artery; RV, right ventricle.

1. Summary of the case

18 yo woman with situs inversus totalis, dextrocardia, ccTGA, mild Ebstein malformation of the left AV valve with mild regurgitation, small secundum ASD with mildly significant L-R shunt. There was a complete heart block with a junctional ER of more than 50/min average heart rate/24 hours and mildly decreased exercise tolerance.

2. Management

Given the atrial septal defect, the non-hemodynamically significant nature of the communication, and the supportive role of the shunt in mitigating volume overload resulting from primary systemic valve regurgitation, the decision was made to postpone the closure of the defect.

The complete atrioventricular block was well-tolerated, with consistent and acceptable heart rate throughout the day and satisfactory exercise tolerance. Consequently, we decided to defer the implantation of a permanent cardiac pacemaker.

During the 6-month follow-up and later at 1 year, the patient was asymptomatic, so we concluded that the initial symptoms could have been due to the COVID-19 infection. Also, the oxygen levels were improved. No deterioration was noted in ventricular dimensions or function on transthoracic echocardiography, with mild tricuspid regurgitation at the one-year follow-up.

Discussion

Congenitally corrected transposition of the great arteries (ccTGA) is a rare anomaly, accounting for roughly 0.5% of all congenital

heart defects. It is defined by atrioventricular (AV) discordance and ventriculo-arterial (VA) discordance.[1]

In ccTGA, the cardiac architecture deviates from the typical anatomical configuration. The right atrium connects to the morphologic left ventricle, supplying blood to the lungs through the pulmonary artery. Meanwhile, the left atrium connects to the morphologic right ventricle, providing blood to the body via the aorta. The presence of dual discordance results in a scenario where the blood is adequately oxygenated. However, both the morphological right ventricle and the systemic atrioventricular valve experience elevated systemic pressures.[2]

Over 90% of cases of ccTGA have associated lesions. These include abnormalities of the tricuspid valve in 9 out of 10 patients, pulmonary outflow obstruction, and dextro/mesocardia – in up to 20% of cases.[3] In a study conducted at the Mayo Clinic involving 44 adult patients with ccTGA, 32% had high-grade atrioventricular block at the time of diagnosis, while an additional 14% already had a cardiac pacemaker implanted.[4] ccTGA is frequently associated with ventricular septal defects (3 out of 5 patients), while the presence of an atrial septal defect (ASD), either isolated or in conjunction with other defects, is less common.[5] The associated lesions and their hemodynamic impact determine the clinical manifestations and long-term outcomes.[6]

In unoperated patients and those who undergo physiological repair, the anatomically right ventricle serves as the systemic ventricle. This can lead to the later development of systemic atrioventricular regurgitation, consequently resulting in right ventricular dysfunction.[7] Additional late complications include left ventricular outflow tract obstruction (LVOTO) and the risk of complete AVB, with the yearly risk of progressing to complete atrioventricular block being approximately 2% in this group.[8] Rarely, patients may have ventricular arrhythmias (VTs).

Reduced life expectancy is notable: about half of patients with associated lesions survive to 40 years, while those without associated lesions usually survive to their 60s. However, ccTGA is compatible with normal life expectancy if associated with the right amount of pulmonary outflow tract obstruction.

Patients usually die of heart failure but may also die suddenly, possibly via VT/VF, irrespective of the presence of advanced heart failure.[9]

The majority of ccTGA cases are found in individuals with situs solitus, but a pediatric series reported situs abnormalities in around 34% of patients.[10] The clinical distinctions between individuals with ccTGA and situs inversus versus situs solitus haven't been thoroughly studied.

In a case series comprising 38 adult patients from Spain with ccTGA followed over a period of approximately seven years, an observation indicated that the association with situs inversus may represent a potentially protective factor for these patients.[11] It has been speculated that patients with situs inversus, due to the improved alignment between the interatrial and interventricular septa, might experience a reduced likelihood of both atrioventricular (AV) block and tricuspid Ebstein-like anomalies.[12] This better septal alignment could potentially prevent AV conduction disorders and abnormalities in the tricuspid valve.[11] Consequently, in patients without these issues, the long-term outcome is expected to be more favorable. We did not find this in our patient. Despite her situs inversus, she does have an Ebstein anomaly of the tricuspid valve and a complete atrioventricular block.

In the adult population, it is customary to close atrial septal defects (ASDs) with Qp/Os > 1.5, or if larger than 10 mm in the absence of pulmonary hypertension (PVR < 3 Wu). In the setting of ccTGA, however, the decision-making process is more nuanced.[9] These individuals typically develop progressive tricuspid regurgitation, consecutive RV dysfunction, and eventually, escalation in pulmonary pressures.[13] In this scenario, opting not to close the defect and maintaining a left-to-right shunt may have a potential benefit by reducing the volume and pressure overload on the failing systemic RV over time. However, this is not a long-term benefit to look forward to, and careful follow-up to avoid it is paramount.

Nevertheless, this underscores the importance of careful assessment of associated lesions, as some of them may produce real hemodynamic advantages in the long run.

In the case of congenital AVB, permanent cardiac pacing presents slightly different criteria compared to acquired blocks. Proactive pacing is recommended for asymptomatic patients who exhibit specific risk factors, such as a low daytime heart rate, prolonged pauses, broad QRS escape rhythm, prolonged QT interval, and complex ventricular ectopy. These risk factors were absent in our case. Symptoms like syncope or chronotropic incompetence further highlight the need for pacemaker implantation. These indications are outlined in the 2021 ESC Guidelines for cardiac pacing and resynchronization therapy.[14] In ccTGA patients, biventricular pacing is advisable in instances of complete atrioventricular block or a requirement for more than 40% ventricular pacing.[9,15] Univentricular (dual-chamber) pacing has been identified as a notable risk factor for ventricular dysfunction, whereas biventricular pacing (BiVP) seems to maintain systemic ventricular function. These findings indicate that ventricular dyssynchrony significantly contributes to the functional decline of the systemic ventricle in patients with ccTGA.[16]

Our patient had an asymptomatic complete heart block, and the 24-hour ECG Holter monitoring showed an average heart rate of 69 bpm. Moreover, during the exercise stress test, she achieved a satisfactory maximum heart rate with good exercise tolerance. The procedure for implanting biventricular cardiac stimulation is inherently complex in a ccTGA patient with dextrocardia and complete situs inversus. Currently, we decided that there's no immediate benefit from permanent cardiac pacing. Rather, periodic reassessment was preferred, and close follow-up played a crucial role in this patient.

Studies indicate that timely replacement of the tricuspid valve before the SRV ejection fraction declines below 40% correlates with improved survival. Recent guidelines support the early replacement of the tricuspid valve in adults with severe TR, aligning with the objective of preserving SRV function and preventing potential deterioration.

Another possibility of management would be pulmonary artery banding. In ccTGA, pulmonary stenosis appears to confer a favorable natural history, with relief of this stenosis leading to

worsened tricuspid valve function. Pulmonary stenosis improves the pressure ratio between ventricles, optimizing interventricular septum positioning and preventing distortion of the subvalvular apparatus, thus reducing tricuspid regurgitation and the subsequent cycle leading to the morphological right ventricle (mRV) failure. Pulmonary artery banding has emerged as a therapeutic option for mRV dysfunction and TR, demonstrating improvements in mRV and morphological left ventricle (mLV) geometry, TR reduction, mRV ejection fraction enhancement, and functional class improvement in cases of failing systemic mRV. There are also centers that perform pulmonary artery banding as a prophylactic measure with good results.[17,18]

The patient's short and medium-term prognosis appears favorable. She is currently asymptomatic, maintains normal biventricular function, and has mild tricuspid regurgitation. However, given the natural history and survival data of patients with ccTGA discussed earlier, close follow-up of TV regurgitation and RV function is critical.[13] To that end, tricuspid valve replacement may become necessary, likely accompanied by biventricular cardiac pacing or even epicardial pacing, given the anatomical variations. Also, pulmonary artery banding represents an option for rescuing the failing morphological right ventricle. This illustrates the potential future challenges and necessary interventions in the journey of the patient with congenitally corrected transposition of the great arteries with or without associated lesions.

Conclusion

Congenitally corrected transposition of the great arteries (ccTGA) is a highly diverse cardiac malformation, often presenting a multitude of associated lesions. The case we presented displays the importance of individualized and thoughtful strategies tailored to the individual nuances of the patient with ccTGA. In our Adult Congenital Heart Disease (ACHD) center, we engaged a Heart Team consisting of a cardiologist, interventional cardiologist, cardiac surgeon, and electrophysiologist.

Given the rarity and diversity of the condition, large studies to derive robust data that would then guide decision-making cannot be done. Therefore, it is important for physicians to share such experiences as they may offer valuable insights that supplement the existing data and help future patients.

Compliance with ethics requirements

The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as national law. Informed consent was obtained from all the patients included in the study.

Abbreviations

ACHD, Adult Congenital Heart Disease
ASD, atrial septal defect
AV, atrioventricular
AVB, atrioventricular block
b.p.m., beats per minute
BiVP, biventricular pacing BiVP
BP, blood pressure
ccTGA, congenitally corrected transposition of the great arteries
COVID-19, coronavirus disease
ECG, electrocardiogram
LA, left atrium
LV, left ventricle
LVOTO, left ventricular outflow tract obstruction
METs, metabolic equivalent of task
mLV, morphological left ventricle
mPAP, medium pulmonary artery pressure
MRI, magnetic resonance imaging
mRV, morphological right ventricle
NTproBNP, N-terminal pro-Brain Natriuretic Peptide
OS, ostium secundum
PA, pulmonary artery
PFO, patent foramen ovale
PVR, pulmonary vascular resistance
Qp, pulmonary flow
Qs, systemic flow
RA, right atrium
RV, right ventricle
SRV, systemic right ventricle
TOE, transesophageal echocardiography
TR, tricuspid regurgitation
TTE, transthoracic echocardiography
TVMcc, transpoziția de vase mari corectată congenital
VA, ventricular-arterial
VF, ventricular fibrillation
VT, ventricular tachycardia
Wu, Woods unit

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