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## **Original Article**

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# Left ventricular longitudinal strain in the follow-up of arterial switch operation: a fingerprint of the patient's history

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## Abstract

Background: Left ventricular function after arterial switch operation for d-transposition of the great arteries is notoriously compromised because of abnormal coronary artery anatomy or altered loading conditions. We sought to longitudinally investigate the performance of the left ventricle in a cohort of d-transposition of the great artery patients after arterial switch operation, by using advanced echocardiographic deformation imaging and grouping patients according to pre- and post-surgery variables, labelled as risk factors. Methods: Longitudinal single-centre study involving 53 d-transposition of the great artery patients (81.1% male) after arterial switch operation, the latter being performed as unique surgical procedure in 39 patients (76.5%). Median follow-up was 59 months [23.5-72]. Results: Selected patients were split into two groups according to risk factors. Fifteen patients (30.6%) were grouped into high-risk class (<3 risk factors). Echocardiographic variables such as tricuspid annular plane systolic excursion, ejection fraction, and global longitudinal strain were compared between the two groups. Only global longitudinal strain reached statistical significance  $(-17.56 \pm 2.26 \text{ versus})$  $-19.82 \pm 1.97$  %; p < 0.001). To discriminate high-versus low-risk patients, a receiver operating characteristic (ROC) curve identified a global longitudinal strain cut-off value of -17.75% (sensitivity 57.1%, specificity 97%, AUC 80%). Conclusions: Several neonatal and post-surgical variables might conditionate long-term follow-up of d-transposition of the great artery patients after arterial switch operation, and global longitudinal strain best conveys the overall risk profile of these patients.

## Background

Transposition of the great arteries belongs to conotruncal CHD, and it is the second most common cyanotic CHD with a prevalence of 0.2–0.3 per 1000 live births.<sup>1</sup> Complete transposition of the great artery, also referred to as d-transposition of the great artery, is characterised by atrio-ventricular concordance and ventriculo-arterial discordance. It is defined "simple" in the case of no associated congenital anomalies, whereas it is categorised as "complex" in their presence.<sup>2</sup>

Congenitally corrected transposition of the great artery is not mentioned in this manuscript. Patients diagnosed with d-transposition of the great artery post-1980s typically undergo the arterial switch operation which provides an anatomical correction of the defect as it restores the ventriculo-arterial concordance with late complications involving the great vessels, coronary arteries, and leading to potential ventricular dilatation and dysfunction.<sup>3–5</sup>

Current perioperative mortality is around 4% and survival is >95% also after 20 years and more.  $^{6-8}$ 

Despite left ventricular systolic function in patients who have undergone arterial switch operation is within the normal range or slightly impaired, a reduced exercise capacity has been demonstrated in up to 82% of young patients later on after surgery.<sup>9–11</sup> Several efforts have been made to elucidate the nature of risk factors influencing the course of d-transposition of the great artery, nevertheless addressing this issue still deserves further elucidation.<sup>12</sup> Low-body weight, prolonged need of intensive care, age at of surgery, duration of cross clamp time, and concomitant extracardiac diagnosis (brain injury, impaired brain development) are common risk factors considered in the management.<sup>13</sup>

Accordingly, speckle tracking analysis in these patients is reduced compared to healthy subjects.<sup>14,15</sup> Coronary artery abnormalities, decreased coronary artery vasoreactivity, reduced coronary flow reserve, proximal intimal proliferation, and reversible myocardial perfusion may impact on the left ventricle function after arterial switch operation.<sup>7,9,16-18</sup>

A major issue encountered in d-transposition of the great artery patients after surgery is the impact of the coronary reimplantation on long-term heart performance, as it affects the segmental longitudinal deformation.<sup>19,20</sup> To date, most available studies only focus on left ventricle function, and there are few multimodality imaging studies involved in the assessment of biventricular function in this cohort of patients.<sup>21</sup>

Literature findings highlight the role of early surgical correction within 7 days from birth on global longitudinal strain at long-term follow-up.<sup>14</sup>

However, these studies suffer from small sample size, singlecentre skills/policies and different anatomical settings.<sup>22</sup> Improvement in imaging techniques have allowed a better understanding of this complex congenital heart disease, being echocardiography the mainstay for first diagnosis.<sup>23,24</sup>

The purpose of this study is to assess the impact of arterial switch operation on left ventricle global longitudinal strain using advanced echocardiography imaging and to correlate changes in ventricular deformation with patients' peri- and post-operative variables. Compared to previous studies, our research aims to identify a cut-off value of ventricular longitudinal deformation and to unveil which variables (either pre- or post-surgery) have a potential diagnostic and prognostic significance in the medium term.

## **Methods**

This cross-sectional study was conducted on 53 d-transposition of the great artery patients addressed to arterial switch operation, who were regularly followed at the Paediatric Cardiology Unit of the University Hospital of Padua.

Patient selection and data collection occurred consecutively between 2013 and 2021. We included patients with follow-up length >12 months.

Exclusion criteria were extra-cardiac diseases, genetic syndromes, surgical approach without arterial switch operation, use of surgical conduits for right, or left ventricular tract reconstruction.

The study protocol was approved by our local ethics committee. All data were collected keeping confidentiality and were anonymized for statistical analysis.

Written informed consent was obtained from parents. Patients' follow-up visits included clinical examination, electrocardiography, standard Doppler echocardiography, and speckle tracking echocardiographic study.

## Clinical data

A careful clinical history was collected for all patients. Clinical data extracted from Galileo's eHealth medical platform of the Padua University Hospital included weight, height, systemic arterial pressure, heart rate, clinical evaluation and ECG. Data collected was divided into pre-surgical variables, peri-operative data, and post-surgical findings.

For variables in which a specific cut-off according to guidelines was defined, we reported the numerical value in parenthesis.<sup>25,26</sup>

The cut-off value for duration of stay in post-operative ICU was defined on internal unpublished data and previous papers.<sup>27,28</sup>

For certain items where no numerical value was established, we employed a dichotomous classification based on the presence/ absence of the item.

Pre-surgical data: weight at birth (cut-off 2500 g), gestational age (cut-off 38.0 gestational weeks), presence of coronary artery

anomalies (any coronary anomaly but circumflex artery arising from right coronary artery), need of Rashkind procedure (yes/no), use of extracorporeal membrane oxygenator support before surgery (yes/no), and age at surgery (cut-off 14 days).

Peri-operative variables: extra-corporeal circulation time (in minutes, cut-off 180 minutes), cross-clamp time (in minutes, cut-off 90 min), length of stay in ICU (in days, cut-off 4 days), need to leave chest open after surgery (yes/no), need of extracorporeal membrane oxygenator support after surgery (yes/no), post-surgical arrhythmias (yes/no), acute kidney injury (yes/no), and occurrence of post-surgical sepsis (yes/no).

Follow-up examination: need of invasive procedures on right ventricular outflow tract and pulmonary branches, right ventricular outflow tract obstruction, assessment of coronary artery anatomy by coronary angiography, cardiac-CT or cardiac-MRI, and assessment of aortic arch morphology. Patient's characteristics are depicted in Table 1.

## Cardiac imaging

Transthoracic echocardiography was performed using GE Vivid E9 machine (GE Health Medical, Horten, Norway). Standard echocardiographic study was performed according to current guidelines from American Society of Echocardiography.<sup>29</sup> Left ventricle ejection fraction was calculated using a modified Simpson's biplane method.

Using pulsed-wave Doppler, mitral inflow velocities, peak early diastolic velocity, peak late diastolic velocity, their ratio (E/A), and early diastolic wave deceleration time were measured. Tissue velocities were obtained from the apical four-chamber view. A 3-mm sample volume was placed at the septal and lateral mitral annulus. The resulting myocardial velocities were recorded for at least three satisfactory cardiac cycles. The peak velocity at the septal and lateral mitral annulus during early diastole was measured and average value was used for the analysis. The ratio of peak early trans-mitral velocity to early diastolic mitral annular velocity (E/e'avg) was calculated.

For the global longitudinal strain evaluation of apical four, three and two chambers views were acquired with a frame rate of 60–100 frames/s, and the best quality images were then transferred to an offline workstation (Echopac Version 202, GE Healthcare) to perform strain analysis.

#### Statistical analysis

The statistical analysis was performed using SPSS Software (version 27.0). Continuous variables were expressed as means and standard deviations. The normal distribution was verified by Shapiro-Wilk test. Qualitative data were compared using Mantel-Haenszel's test. The comparison of dichotomic variables was performed by using Chi-Square text and applying the Yates' correction or Fisher's exact test, when appropriate. Means' comparison of continuous variables was performed using unpaired Student's t-tests or Mann–Whitney U tests, when appropriate. The correlations were studied by Pearson's test or Spearman's test, when appropriate.

ROC curve was defined as the balance between sensibility and sensitivity. We performed univariate analysis for risk factors and low global longitudinal strain value, but it did not reach statistical significance.

We considered all the perinatal variables at higher risk of adverse events and echocardiographic data: weight at birth <2.5 kg, major coronaries anomalies, complex transposition of the great

**Table 1.** Pre-operative characteristics of the patients enrolled. Data were expressed as mean ± standard deviation for continue variables, in absolute number and percentage for ordinal variables. d-TGA: d-transposition of great arteries, VSD: ventricular septal defect, DORV: double outlet right ventricle, AOC: aortic coarctation, RVOTO: right ventricular outflow tract obstruction, Cx: circumflex artery; RCA: right coronary artery, PGE1: prostaglandin E1, ECMO: extra-corporeal membrane oxygenator; SpO2 pulse oximeter oxygen saturation)

Demographics	n (%); mean± sd
Male sex	43 (81.1%)
Weight at birth (g)	$3261\pm514$
Gestational weeks<38.0	6 (11.8%)
Prenatal diagnosis	42 (79.2%)
Anatomy	
d-TGA with intact ventricular septum	38 (71.7%)
d-TGA + VSD	11 (20.7%)
DORV transposition type +VSD AoC	2 (3.8%)
DORV transposition type +VSD	1 (1.9%)
d-TGA+VSD+RVOTO	1 (1.9%)
SpO2 at birth (%)	$64.4 \pm 15.3$
Rashkind procedure	41 (77.4%)
PGE1 infusion	49 (92.5%)
Pre-operative inotrope administration	8 (15.4%)
Pre-operative ECMO	3 (5.7%)
Median age at surgery (days)	10 [7-12]
Coronaries anatomy	n (%); mean± SD
Normal	29 (54.7%)
Cx from RCA	15 (28.3%)
Single ostium	4 (7.5%)
Intramural course	1 (1.9%)
Double loop	1 (1.9%)
Other/unspecified	3 (5.7%)

artery, the need of inotropes before surgery, the need of pre- or post-operative extracorporeal membrane oxygenation, age at surgery >14 days, prolonged surgery duration (extra-corporeal circulation time >180 min and/or cross-clamp time >90 minutes), major post-surgical arrhythmias, need of dialysis, post-surgical ICU stay >96 hours, and residual severe right/left ventricular outflow tract obstruction. We assigned one point for each risk factor. Therefore, we divided patients into two subgroups, based on the number of risk factors found, <3 (lower risk) and  $\geq$ 3 (higher risk). The null hypothesis was rejected for a p value <0.05.

## Results

Fifty-three patients were eligible for this study. Patients' preoperative characteristics are summarised in Table 1.

Forty-three (81.1%) were males. A prenatal diagnosis was available in 79.2% of patients.

Isolated d-TGA was found in 71.7% of patients, a ventricular septal defect was present in 20.7%, double outlet right ventricle transposition type was present in 1 (1.9%), double outlet right ventricle with subpulmonary ventricular septal defect,

transposition type, aortic coarctation was present in two patients (3.8%), and d-transposition of the great artery + ventricular septal defect + right ventricular outflow tract obstruction was found in 1 (1.9%). Normal (54.7%) or minor coronary anatomy anomalies (circumflex artery from right coronary artery, 28.3%) were found in 83% of patients. The remaining nine patients had a single ostium (4; 7.5%), intramural course (1; 1.9%), double looping (1; 1.9%), and other patterns (3; 5.7%).

Mean arterial  $O_2$  saturation at birth was 64.4 ± 15.3%. Rashkind procedure was performed in 41 (77.4%). Prostaglandin E1 were used pre-operatively in 49 (92.5%) patients. A pre-operative inotropic support was used in 8 (15.4%), and an extracorporeal membrane oxygenator support was necessary in three patients (5.7%) before arterial switch operation. Median age at correction was 10 days (interquartile range 7–12 days). Surgery was performed >21 days of life in 8 (15.4%) patients. This choice was elective in two patients (due to complex anatomy). In the remaining six patients, the reasons for delay were hemodynamic instability requiring extracorporeal membrane oxygenator support (refractory desaturation due to poor lung compliance) in three patients, necrotising enterocolitis in 3.

## Surgical data and short-term morbidity and mortality

Arterial switch operation was the only surgical manoeuvrer in 39 patients (76.5%). Ventricle septal defect closure was performed in 14 patients, aortic coarctation treatment in two patients, and right ventricle outflow tract membrane resection in one patient.

Mean surgical time (from beginning to end of surgical procedure) was  $272 \pm 73$  minutes, mean extra-corporeal circulation times was  $176 \pm 65$  minutes, and mean cross clamp time was  $89 \pm 40$  minutes.

Mean ICU stay was  $6 \pm 5$  days. A delayed chest closure was provided in 20 (37.7%) patients. Further or rescue surgical or interventional procedures were necessary in 8 (15.1%) subjects. Post-operative extracorporeal membrane oxygenation was adopted in four patients (7.5%), with exitus due to multiorgan failure in all the cases.

Six patients (11.3%) developed clinically relevant tachiarrhythmias, with the need for pacemaker implantation in one patient due to iatrogenic complete atrioventricular block. Six patients experienced acute kidney injury requiring a temporary dialytic treatment. No chronic renal insufficiency was reported. Infection/sepsis were found in 9 (17.0%) patients.

#### Follow-up

Median follow-up was 59 months [23.5–72]. All patients were asymptomatic and in good clinical conditions (NYHA or Ross Class I). All patients underwent echocardiogram. Additional exams were performed in 20/49 survivors: cardiac magnetic resonance (CMR) in five patients, myocardial perfusion scan in five, lung perfusion scan in 10, and heart catheterisation in 10. In 2 patients (4%), therapy was administered: Enalapril in one (for left ventricular dysfunction) and Propranolol in one (for secondary prevention of supraventricular arrhythmias). Six patients (12.2%) underwent percutaneous balloon dilatation of right ventricle outflow tract obstruction, while surgical procedures were performed in 4 patients (8.1%) to relieve a left ventricular outflow tract obstruction in one, treat a residual right ventricle outflow tract obstruction stenosis after failing percutaneous procedures in 2, and implant an epicardial pacemaker in one.

Table 2. Echo parameters at the last follow-up. Data were expressed as mean  $\pm$  standard deviation

Variable	Mean ± standard deviation
Diastolic interventricular septum thickness (mm)	5.27 ± 1.75
Left ventricular diastolic diameter (mm)	31.29 ± 3.79
Diastolic posterior wall thickness (mm)	$6.17 \pm 1.11$
Left ventricular systolic diameter (mm)	19.41 ± 3.79
Ejection fraction (%)	67.73 ± 9.09
Tricuspid annulus systolic excursion (mm)	12.80 ± 3.10
Mitral E wave (cm/s)	109.58 ± 11.08
Mitral A wave (cm/s)	46.06 ± 10.70
Mean E' wave (cm/s)	12.25 ± 3.77
E/E' ratio	8.60 ± 3.44
Global longitudinal strain (%)	$-19.56 \pm 1.92$

Echo parameters are reported in Table 2. Ejection fraction was normal in all examined patients. Six patients presented a mild tricuspid valve regurgitation, 19 patients showed a mild pulmonary regurgitation, moderate in one, a mild aortic regurgitation was found in 17 patients (34.7%). Global longitudinal strain was below the lower normal limit value (-19%) in 14 patients (28.6%). No patient presented with right ventricular dysfunction.

## **Risk factors analysis**

According to the afore-mentioned risk stratification, 15 patients were considered at higher risk (30.6%). Among all the variables studied, only global longitudinal strain reached a statistical significance ( $-17.56 \pm 2.26$  versus  $-19.82 \pm 1.97$  %; p < 0.001) (Table 3, Fig 1). Successively, we built an ROC curve to find a valuable global longitudinal strain cut-off value. Based on this approach, a GLS value of -17.75% discriminated high- versus low-risk patients with a sensitivity of 57.1% and a specificity of 97%. The area under the curve value was 80% (Fig 2). On the other hand, no single risk factor was able to justify a low global longitudinal strain value.

#### Discussion

To date, arterial switch operation is the first surgical choice to manage d-transposition of the great artery physiology. In low-risk anatomies (no outflow tract obstruction, no coronary anomalies, no or single and relatively small ventricular septal defect) surgical outcome is excellent: mortality is low, patients are asymptomatic, left ventricle ejection fraction is normal, and exercise capacity is almost preserved. In complicated anatomies, morbidity and mortality are higher.<sup>30</sup> Despite all, mid-to-long-term follow-up of these patients is often very good.<sup>6,30,31</sup> On the other hand, several studies demonstrated mild or subclinical impairment in d-transposition of the great artery after arterial switch operation.<sup>32,33</sup>

In a recent metanalysis of 21 studies, van Wijk et al. reported a mild impairment in  $VO_{2max}$  after arterial switch operation (87.5 ± 2.9% of predicted values for sex and age), despite a normal ejection fraction (60.7 ± 7.2%).<sup>33</sup> About half of that studies included "complex" subtypes of d-transposition of the great

**Table 3.** Comparison of echocardiographic data between high- and low-risk patients (TAPSE: tricuspid annulus peak systolic excursion, EF: left ventricular ejection fraction, GLS: global longitudinal strain). Standard echocardiographic parameters (TAPSE, EF, E/E' ratio) did not discriminate high- versus low-risk patients. Only GLS reached statistical significance in risk stratification

Variable	High risk (15)	Low risk (24)	p value
TAPSE (mm)	$13.0 \pm 4.2$	$13.4 \pm 3.1$	NS
EF (%)	68.5 ± 9.5	67.8 ± 7.3	NS
E/E' ratio	8.0 ± 2.6	$7.4 \pm 1.6$	NS
GLS (%)	-17.56 ± 2.2	$-19.82 \pm 1.97$	<0.001

artery. The authors hypothesised that this mild impairment in exercise capacity might be due to inotropic incompetence because of aortic transection, lower physical activity compared to healthy controls, underestimated or undiagnosed coronary flow impairment, worsening of exercise-induced right ventricle outflow tract (RVOT) gradient (dynamic and stress-pressure induced), or pulmonary branch distortion. However, in this metanalysis, the considered variables were focused on VO<sub>2</sub> peak and ejection fraction, while no data were available for residual lesions (valve disease, outflow gradient, arrhythmias, etc).

Despite normal ejection fraction, reduced global longitudinal strain values were found in enrolled patients. However, the grading of that impairment was quite large (van Wijk:  $-15.4 \pm 1.1\%$ vs.  $-23.2 \pm 0.9\%$ ; Di Salvo:  $-19.2 \pm 2.9\%$  vs.  $-22.7 \pm 2.4\%$ ).<sup>14,33</sup> In addition, several studies demonstrated stress-induced hypokinesia after arterial switch operation. Also in this case, many variables were evocated to justify these discrepancies: timing to surgery, coronary anomalies, suboptimal coronary perfusion, reduced coronary flow reserve, progressive dilation of neoaortic root, gothic aortic arch, aortic stiffening causing elevated LV afterload, significant aortic regurgitation, and altered ventricular-ventricular interaction due to right ventricular hypertrophy.9,10,15,18,34-37 Another important (but unstressed) point might be the age of surgical correction. Van Wijk et al. reported a decline in global longitudinal strain over the age, despite in normal subjects global longitudinal strain values should be stable over the time.<sup>38</sup> On the other hand, it might also be due to different single-operator surgical skills, tools and Centre-expertise (older patients were operated in '80s, still in the learning curve of this "new approach" to d-TGA).<sup>32</sup> In addition, older patients might experience iatrogenic and acquired coronary diseases, which should be carefully assessed in adult patients.<sup>38</sup>

O'Byrne et al. compared the management of arterial switch operations in 40 different hospitals of United States.<sup>39</sup> They found significant differences between the involved centres, regarding the use of Rashkind procedure, pre-operative care, and age at surgery. On the other hand, prematurity, genetic syndromes, the need of Rashkind manoeuvre, and low number of CHD surgery/year were associated with higher mortality rate. In this article, the age at surgery seems to have a prognostic relevance. On the other hand, it might reflect different care-setting policies. Larger centres generally treat these patients in the first 5 days of life, significantly reducing the need for balloon atrial septostomy. Thus, the largest centres have higher experience and lower morbidity and mortality rates than smaller centres. Nevertheless, early surgery and no need for atrial septostomy might mask a selection bias due to different approaches for d-TGA patients.<sup>39</sup>

In summary, several variables and confounding factors might impact the outcome of arterial switch operation: extra-cardiac



Figure 1. Boxplot of comparative global longitudinal strain across the two risk groups. High risk versus low risk p < 0.001.



Figure 2. ROC curve for global longitudinal strain value in the presence of 3 or more risk factors. The ROC curve identifies a sensitivity of 57.1%, a specificity of 97%, and area under the curve of 0.80 for a cut-off of -17.75%, standard error = 0.070.

factors, pre-operative events, anatomic features, post-surgical events, residual defects, and events during follow-up.

In our single-centre study, we evaluated the effect of different perinatal variables on the function of the left ventricle in newborns with d-transposition of the great artery undergoing corrective cardiac surgery to rebuild their clinical history.

The results obtained suggest that even in the presence of good clinical conditions and good haemodynamic compensation, patients who presented three or more risk factors among those identified in the study have a significantly higher risk of presenting an alteration of cardiac function and lower global longitudinal strain in the medium term. In addition, as reported in a retrospective metanalysis by Al-Sarraf et al., surgical variables (aortic cross clap time) strongly impact post-surgical morbitidty.

Most importantly, patients with low global longitudinal strain values and an unremarkable peri-operative history had one or more residual defects and/or peri-operative risk factors, explaining this finding.

A worse global longitudinal strain value was confirmed to have a high negative predictive value. On the other hand, unexplained low global longitudinal strain values should be a trigger for physicians to investigate further, looking for other relatively hidden causes, such as coronary arterial abnormalities, reduced coronary flow reserve, increased aortic stiffness, stress induced by right ventricle outflow tract obstruction, and so on.

d-transposition of the great artery patients with ventricular dysfunction short after surgery can be addressed with pharmacological treatment to restore left ventricular function and prevent deterioration of global longitudinal strain. Literature findings describe that after arterial switch operation, the left ventricle might present an altered contraction pattern, due to subtle myocardial fibrosis.<sup>40</sup> In our cohort, newborns following surgery were admitted to the ICU, and they were treated according to guidelines. In case of reduction of left ventricular function and low cardiac output, patients were addressed to inotropic infusion with milrinone and dopamine; angiotensin-converting enzyme inhibitors were administered to institute reduction of afterload.

We did not evaluate the effect of single pharmacological therapy on outcome, but we can speculate that the group of highrisk patients may benefit from inotropic infusion and/or diuretic medications, adjusting dose according to clinical response. There are no specific guidelines regarding pharmacological management in d-transposition of the great artery patients after arterial switch operation, and currently, treatment is based on clinical course.

Unfortunately, a consensus on the long-term follow-up of dtransposition of the great artery patients after arterial switch operation is still lacking despite the search for residual coronary artery disease should be assessed over time.<sup>2</sup>

In the management of the young patient, therefore, it is necessary to pay particular attention to the risk factors previously identified and their presence should be clearly indicated in the discharge letter. This is because the proportion of patients with three or more positive variables has a greater probability of developing subclinical sequelae in the medium term that can be identified in the early phase by studying the indices of myocardial deformation.

The evaluation of risk factors allows, therefore, to discriminate a group of patients associated with a higher risk of developing ventricular dysfunction despite the good clinical condition at discharge. In this category of patients, it is therefore appropriate to consider a more careful and targeted follow-up path to identify any acquired coronary alterations, which may be the basis of the altered myocardial contraction pattern. Interestingly, Wang et al. published a 16-year experience after arterial switch operation, exploring risk factors for late complications.<sup>41</sup> They mainly focused on the assessment of risk factors (both echocardiographic and demographics, such as low body weight and age at surgery) that can address patients to reintervention. In this perspective, it emerges the need to pursue multicentric studies with homogeneous standard of care to verify and refine a weighted risk scoring system. Nevertheless, a decline in global longitudinal strain value should be addressed in a multimodality imaging to search for hidden or undiagnosed residual defects.

For this purpose, it is possible in the longitudinal follow-up to use invasive and non-invasive investigation methods, such as early haemodynamic study, echo-stress, myocardial scintigraphy, choro-CT, or more in-depth investigations compatible with the age of the patient and the invasiveness of the tests. Our study outlines the role of advanced imaging in the follow-up of dtransposition of the great artery patients to early recognise the presence of subclinical alterations that cannot be detected through the use of standard echocardiography.

On the other hand, we failed to find a correlation between global longitudinal strain and age at surgery. In our Institution, arterial switch operation is electively performed between 5 and 12 days of life. In patients with adequate  $SpO_2$  values, surgery is planned in an available slot in the second week of life (median 10 days). Late corrections were due to cardiac or extracardiac reasons in about 15% of patients. Global longitudinal strain was impaired in all these patients, included in the high-risk group.

This study suffers from some limitations. First, it is a retrospective single-centre study. The analysis of risk factors must therefore consider local hospital policies, and our findings cannot be transversely applied to other settings. In addition, the results of a single-centre study are influenced by heart team composition, and the presence of paediatricians alongside with experienced paediatric cardiologists adds a worthwhile contribution to the detection and management of extra-cardiac issues, which can have relevant implications in the patient's outcome.

Follow-up length range was large because patients were enrolled in a span time of 8 years. The presence of residual or iatrogenic lesions was only assessed by echocardiography; therefore, pulmonary branch lesions or coronary stenoses might have been underdiagnosed. However, 61.2% of patients were addressed to further imaging modalities, the discussion of which outlines the purposes of the present manuscript

In conclusion, despite the outcome of arterial switch operation is usually excellent, a subclinical left ventricular dysfunction can be found in a significant percentage of patients. The magnitude of left ventricular global longitudinal strain impairment is related to the number of risk factors. Speckle tracking demonstrated a significant negative predictive value. In patients without known risk factors, a drop of global longitudinal strain value during follow-up or a relatively low absolute value than expected might address to further explore undiagnosed diseases through cross-sectional imaging.

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#### Competing interests. None to declare.

**Ethical standard.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines.

Ethical review and approval were waived for this study as only deidentified compliant data were used in the analysis. Patient consent was waived due to the retrospective nature of the study. All the information being collected were part of the routine care.

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