

Evaluation of left ventricular functions by speckle tracking echocardiography in coarctation patients

Tulay Demircan¹, Ozgur Kizilca², Nuh Yilmaz³, Cüneyt Zihni⁴, Mustafa Kır², and Nurettin Unal²

¹Türkiye Cumhuriyeti Sağlık Bakanlığı İzmir Tepecik Eğitim ve Araştırma Hastanesi

²Dokuz Eylül Üniversitesi Tıp Fakültesi

³Dokuz Eylül University

⁴Dr. Behçet Uz Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi

November 6, 2020

Abstract

Abstract Background/aim: Two-dimensional speckle-tracking echocardiography (2D-STE) is a novel method that allows the assessment of regional myocardial function. The aim of our study was to use 2D-STE to assess left ventricular deformation in patients with coarctation of the aorta (CoA). **Methods:** In this prospective study, patients with CoA ($n = 42$) and healthy controls ($n = 39$) were recruited. Children with CoA who visited the outpatient clinic between 2013 and 2014 were included. The data were compared with those obtained from the sex- and age-matched controls. **Results:** The mean age of the patients was 5.8 ± 4.5 years. Global longitudinal strain based on all three apical views and total global strain values did not appear to be different between the patient and the control group ($p = 0.59$, $p = 0.51$, $p = 0.15$, $p = 0.38$). Hypertension was detected in 14 (33.3%) patients with CoA. There were significant differences between the global longitudinal strain values of the normotensive CoA subgroup and the hypertensive CoA subgroup ($p < .05$). **Conclusions:** In our study, we found that 2D-STE total strain analysis of patients with CoA was not different from comparative healthy controls. However, we determined that 2D-STE parameters were lower in the hypertensive CoA subgroup compared to the normotensive CoA subgroup.

1. INTRODUCTION

Coarctation of the aorta (CoA) is a relatively common defect that occurs in the general population at a rate of 0.06%-0.08%, constituting 6%-8% of congenital heart disease.^{1,2} CoA can be clinically asymptomatic, or it may present with a shock in infancy and may present with systemic hypertension, intracranial bleeding, and heart failure in adults.³ Even if CoA is successfully treated, systemic hypertension can lead to the development of late complications such as left ventricular (LV) hypertrophy, heart failure, coronary artery disease, stroke, or sudden cardiac death.^{4,5}

LV ejection fraction (EF) is known not to be a sensitive marker for the detection of subclinical LV systolic dysfunction, and tissue Doppler imaging has its own limitations, including angle dependency.^{6,7} Two-dimensional speckle-tracking echocardiography (2D-STE) is a novel used method in terms of showing regional subclinical myocardial functions.⁸ The early detection of subclinical myocardial dysfunction in patients with CoA is essential for planning treatment. In an echocardiographic study, it was suggested that global longitudinal strain may become the optimal method for the assessment of global LV systolic function.⁹ This study aims to evaluate LV myocardial deformation using 2D-STE in young patients who underwent intervention due to CoA.

2. METHODS

2.1. Study subjects

This prospective and cross-sectional study was approved by our hospital's local ethics committee (2014 / 25-30). Signed written informed consents were obtained from all parents. The patient group included children who underwent intervention due to CoA that visited the pediatric cardiology outpatient clinic between June 2013 and June 2014. Interventions were surgical or involved percutaneous balloon angioplasty or both. Demographic and anthropometric characteristics, including patient's age, gender, body mass index, time of operation, type of operation, duration of follow-up, blood pressure, conventional echocardiography and 2D-STE were evaluated. Healthy volunteers of the same age and gender were included as a control group. These included individuals with no structural heart disease who had been referred to the pediatric cardiology outpatient clinic for cardiac evaluation with echocardiographic examination for murmurs and chest pain.

The patient group was divided into a normotensive and hypertensive CoA subgroup. Hypertension according to the standard blood pressure measurement was calculated as a mean value from three consecutive measurements obtained in 3-min intervals. Blood pressure (BP) measurements at the right arm were obtained using a cuff sphygmomanometer (Omron M1, Omron Healthcare Co, Kyoto, Japan). In addition, patients' hypertension was confirmed from previous records. In some patients, blood pressure could not be measured due to agitation and was, therefore, recorded as 'unknown'. Exclusion criteria were insufficient images and patients with additional heart disease, such as single ventricle physiology, systolic dysfunction, a pacemaker, additional chronic disease or rhythm problems.

2.2. Echocardiographic studies

The echocardiographic studies included two-dimensional, M-mode and 2D-STE. The procedures were performed by two experienced pediatric cardiologists (TD, ÖK). The both researchers were similarly blinded to the clinical condition and grouping of the patients. The echocardiography device used for these procedures was Philips (model iE33, Philips Medical Systems, Best, Netherlands) with an S5-1 MHz transducer.

Echocardiography measurements were performed according to the recommendations of the American Echocardiography Society standards.¹⁰ LV internal dimensions in diastole (LVIDd) and systole (LVIDs), as well as interventricular septum thickness in diastole (IVSd) and LV posterior wall thickness in diastole (LVPWd), were obtained according to the same guidelines. The EF and fractional shortening (FS) were analyzed by LV systolic function and was assessed from the parasternal long axis on the M mode tracing view using the Teichholz formula.¹¹ Devereux and Reichek formula were used to calculate LV mass (LVM, g).¹²

2D-STE evaluation was performed with simultaneous electrocardiography at frame rates of 70-100 frames / sec. The peak systolic longitudinal strain was assessed from six segments in apical long-axis (A3C), four-chamber (A4C) and two-chamber(A2C) view. GLS was calculated by averaging each value of regional peak longitudinal strain. Short-axis images, obtained at the mitral valve region basal (SAXB) images, papillary muscle region medial (SAXM), and apical levels (SAXA). These measurements were used to compute circumferential and radial strain. At least four consecutive cardiac cycles were recorded for each parameter in terms of best image quality. The recorded images were transferred from device to DVDs. A computer with QLAB software (Philips Medical Systems) was used for analysis. For longitudinal strain, mitral annulus lateral and septal planes and the LV apical endocardial planes were marked by manual. After this marking, the device automatically marks the LV wall. The software is interactive, in that the LV endocardial and epicardial contours was adjusted manually, and then the software automatically tracks the contours on the subsequent frames. F The LV algorithm was based on a 17-segment mode: AP4 (Basal septal, Mid septal, Apical septal, Apex, Apical lateral, Mid lateral, Basal lateral); AP3 (Basal inferolateral, Mid inferolateral, Apical lateral, Apex, Apical anterior, Mid anteroseptal, Basal anteroseptal); and AP2 (Basal inferior, Mid inferior, Apical inferior, apex, Apical anterior, Mid anterior, Basal anterior)(Figure1- 2)

2.3. Statistical analysis

Data were analysed using SPSS 15.0 (SPSS Inc.; Chicago, IL, USA). Descriptive statistics are given as number of units (n), percentage (%), mean $\pm$ standard deviation (mean $\pm$ SD). The relationships between

variables with categorical structure were evaluated by using the Continuity Correction Chi-Square test. The Student's t-test was used for the comparison of parametric continuous variables. Homogenous distribution of data was evaluated with Kolmogorov-Smirnov test. $p < 0.05$ was considered as statistically significant.

3. RESULTS

3.1. Patient and control finding

Patients with CoA ($n = 42$) and healthy volunteers ($n = 39$) were included in this study. The mean age of the patients was 5.8 ± 4.5 years and there were 23 boys and 19 girls included in the study. No significant differences between CoA and healthy volunteers were detected with regard to sex, age, body mass index, or heart rate ($p = 0.88$, $p = 0.59$, $p = 0.26$, $p = 0.20$). Clinical and demographic characteristics of the patients are summarized in Table 1. Among the CoA group, four patients had ventricular septal defects, one had an atrioventricular septal defect, and one had partial anomalous pulmonary venous return. In addition, two patients had mild aortic stenosis.

In CoA group was significantly higher the mean systolic blood pressure in comparison to the control group (109.41 ± 16.20 mmHg and 97.23 ± 10.10 mmHg, respectively; $p < .001$). Arterial hypertension was found in 14 (33.3%) children from the hypertensive CoA group, the remaining 22 children (52.3%) in the CoA group were normotensive. Of the 27 patients that underwent surgery, five patients underwent catheter angiography and 10 patients underwent both surgical and catheter angiography. The median time from CoA repair to the present study was 3.74 ± 2.3 years. The operating age of the patients was 7.4 ± 21 months. Repairs were performed by subclavian flap in 17 patients and by end-to-end anastomosis in 10 patients. A bicuspid aortic valve was present in 20 (47.6%) patients in the CoA group.

3.2. Echocardiographic Findings

No difference could be detected between the patients and control groups with regard to LV measurements of IVSd, LVIDd, LVIDs, LVPWd, EF, and FS. Standard echocardiographic parameters and speckle-tracking echocardiography in the study population are shown in Table 2.

3.3. 2D-Speckle Tracking Echocardiography

Global longitudinal strain values based on all three apical views (A4C, A2C, A3C) and total global strain values did not appear to be different between the patient and the control group ($p=0.59$, $p=0.51$, $p=0.15$, $p=0.38$; Table 2). LV longitudinal myocardial strain measurements indicated the following reductions in the following parameters: A2C basal inferior and basal anterior, and A3C mid inferolateral. Circumferential strain rate measurements were not different between the patient and the control group ($p = 0.68$). However, there were significant differences between the normotensive CoA subgroup and hypertensive CoA subgroup, with respect to 2D-STE longitudinal myocardial deformation properties in some segments of the LV walls ($p < .05$; Table 3).

4. DISCUSSION

In this study, we shown that 2D-STE total strain analysis of patients with CoA did not differ from the healthy controls. Only the A2C basal inferior and basal anterior and A3C mid inferolateral regions had local deterioration. The circumferential strain was normal. Like many other study; we showed normal total global LV function in patients who underwent CoA repair many years earlier and who had blood pressure control.^{13,14} Kowalski et al. also showed normal global LV function and LV longitudinal strain in CoA patients using 2D-STE, suggesting only the anterior LV walls were impaired.¹⁵ In another study, patients with ventricular outflow tract stenosis (with CoA and aortic stenosis) made an 2D-STE preoperatively and postoperatively, and there was a marked improvement in both groups.¹⁶ Postoperative improvement was considered better in the group operated for CoA between the two groups. In this study, the follow-up period was 18 months and the mean follow-up period of our patients was 3.74 ± 2.3 years. This study has no long-term results, but the future results of our study may be similar to those of Kowalski et al.

We determined that 2D-STE parameters were lower in the hypertensive CoA subgroup compared to the normotensive CoA subgroup. One of the most important problems for these patients following the operation is hypertension. According to 26 articles published between 1987 and 2012, hypertension remains a common complication following aortic coarctation repair was found to be 32.5% (range 25-68%).¹⁷ Kowalik et al. evaluated 26 cases patients with CoA that underwent operation with three dimensional speckle-tracking echocardiography D-STE and, despite preservation of the EF, the global strain measurement was found to be decreased compared with controls.¹⁸ Similar to our study, they observed that the total global strain decreased as the mean blood pressure increased. A meta-analysis LV global longitudinal strain in healthy cases showed that only blood pressure was independently associated with strain values.¹⁹

In contrast to our study, Florianczyk et al. compared global longitudinal strain in a healthy group with tissue Doppler strain analysis higher than in operated for CoA.²⁰ There were no significant differences in global longitudinal strain between the hypertensive CoA group and the normotensive CoA group. In our patients, we found the global longitudinal strain analyses to be impaired in the hypertensive CoA subgroup. We thought that this difference may be caused by the higher number of patients with hypertension in our study. In contrast, Menting et al. showed that LV dysfunction, which cannot be detected by M mod echocardiography, deteriorated in the late period after CoA repair with 2D-STE and LV global longitudinal strain.²¹ In their study, there were additional diseases, such as aortic insufficiency and valve replacement, which impair LV function.

Kutty et al. showed that global longitudinal strain reduction is more pronounced in the presence of LV hypertrophy.²² Our patients did not have LV hypertrophy and there was no reduction in global longitudinal strain. Shang et al. reported increased LVM and decreased myocardial deformation in hypertensive CoA patients compared to healthy controls.²³ According to Salva et al., 2D-STE analysis on obese and lean young patients revealed abnormal myocardial deformation properties along longitudinal, radial, and circumferential planes in the obese CoA patients.²⁴ However, there was no obesity among our patients.

Impaired global strain was shown after CoA repair that correlated with the systolic blood pressure, which matches our observations.

5. CONCLUSION

In conclusion, LV function tends to decrease in cases complicated by hypertension despite successful treatment of coarctation. LV structural and functional change in response to CoA do exist and tend to normalize after correction of the obstruction, although not completely. Hypertension is an important complication in these patients and its treatment and follow-up is important. In addition, further research is needed to propose the most accurate parameter for function and prognosis.

Study Limitations

First, our study had a relatively small sample size and a single-center study design. Second, blood pressure measurements of the patients were done manually and 24-hour ambulatory blood pressure was not obtained.

REFERENCES

1. Baumgartner H, Bonhoeffer P, De Groot NM, et al. Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology Association for European Paediatric Cardiology (AEPC) ESC Committee for Practice Guidelines (CPG) ESC guidelines for the management of grown-up congenital heart disease. *Eur Heart J.* 2010;31:2915-57.
2. Singh S, Hakim FA, Sharma A, et al. Hypoplasia, pseudocoarctation and coarctation of the aorta - a systematic review. *Heart Lung Circ.* 2015;24:110-8.
3. Ward KE, Pryor RW, Matson JR, et al. Delayed detection of coarctation in infancy: implications for timing of newborn follow-up. *Pediatrics.* 1990; 86:972-6.

4. Presbitero P, Demarie D, Villani M, et al. Long term results (15-30 years) of surgical repair of aortic. *Br Heart J*. 1987; 57:462-467.
5. Roifman I, Therrien J, Ionescu-Ittu R, et al. Coarctation of the aorta and coronary artery disease: fact or fiction? *Circulation* 2012;126:16-21.
6. Sanderson JE, Fraser AG. Systolic dysfunction in heart failure with a normal ejection fraction: echo-Doppler measurements. *Prog Cardiovasc Dis*. 2006;49:196-206.
7. Teske AJ, De Boeck BWL, Melman PG, et al. Echocardiographic quantification of myocardial function using tissue deformation imaging, a guide to image acquisition and analysis using tissue Doppler and speckle tracking. *Cardiovasc Ultrasound* 2007;5:27.
8. Kleijn SA, Aly MF, Terwee CB et al. Three-dimensional speckle tracking echocardiography for automatic assessment of global and regional left ventricular function based on area strain. *J Am Soc Echocardiogr*. 2011; 24: 314-321.
9. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. *Circ Cardiovascular Imaging*. 2009;2(5):356-64.
10. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2010;23:685-713.
11. Teichholz LE, Cohen MV, Sonnenblick EH. Study of left ventricular geometry and function by B scan ultrasonography in patients with and without asynergy. *N Engl J Med*. 1974;291:1220-26
12. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in men: anatomic validation of the method. *Circulation*. 1997;55:13-8.
13. Kimball TR, Reynolds JM, Mays WA, et al. Persistent hyperdynamic cardiovascular state at rest and during exercise in children after succesful repair of coarctation of the aorta. *J Am Coll Cardiol*. 1994;24:194-200.
14. Gentles TL, Sanders SP, Colan SD. Misrepresentation of left ventricular contractile function by endocardial indexes: Clinical implications after coarctation repair. *Am Heart J*. 2000;140:585-595.
15. M. Kowalski, E Kowalik, K, Kotlinski et al. Regional left ventricular myocardial shortening in normotensive patients late after aortic coarctation repair - normal or impaired? *Ultrasound Med Biol*. 2009;35:1947-52.
16. Van der Ende J, Vazquez Antona CA, et al. Left ventricular longitudinal strain measured by speckle tracking as a predictor of the decrease in left ventricular deformation in children with congenital stenosis of the aorta or coarctation of the aorta. *Ultrasound Med Biol* 2013;39:1207-14.
17. Canniffe C, Ou P, Walsh K et al. Hypertension after repair of aortic coarctation a systematic review. *International Journal of Cardiology*. 2013;167:2456-61.
18. Kowalik E, Kowalski M, Klisiewicz A, et al. Global area strain is a sensitive marker of subendocardial damage in adults after optimal repair of aortic coarctation: three-dimensional speckle-tracking echocardiography data. *Heart Vessels*. 2016;31:1790-97.
19. Yingchoncharoen T, Agarwal S, Popovic ZB, et al. Normal ranges of left ventricular strain: a meta-analysis. *J Am Soc Echocardiogr*. 2013;26:185-191.
20. Florianczyk T, Werner B. Assessment of left ventricular diastolic function in children after successful repair of aortic coarctation. *Clin Res Cardiol*. 2011;100:493-499.

21. Menting M, van Grootel R, van den Bosch A, et al. J Quantitative assessment of systolic left ventricular function with speckle-tracking echocardiography in adult patients with repaired aortic coarctation. Intern J Cardiovasc Imaging. 2016; 32:777-787.

22. Kutty S, Rangamani S, Venkataraman J,et al. Reduced global longitudinal and radial strain with normal left ventricular ejection fraction late after effective repair of aortic coarctation: a CMR feature tracking study. Int J Cardiovasc Imaging. 2013;29:141-150.

23. Shang Q, Sarikouch S, Patel S et al. Assessment of ventriculo-vascular properties in repaired coarctation using cardiac magnetic resonance-derived aortic, left atrial and left ventricular strain. Eur Radiol. 2017; 27(1):167-177.

24. Di Salvo G, Gala S, Castaldi B, et al. Impact of obesity on left ventricular geometry and function in pediatric patients after successful aortic coarctation repair. Echocardiography 2011;28(8):907-912.

Figure Legends

Figure 1 . Schematic diagram (A) of the LV segmentation, in apical four chamber (B), three-chamber (C), and twochamber (D)

Figure 2. Left ventricular longitudinal strain measurements in CoA patients. The left ventricle was traced in the apical four, three, and two chamber views at end-diastole. AP2 = apical two chamber; AP3 = apical three chamber; AP4 = apical four chamber; GL = global longitudinal

LV= left ventricle, RV= right ventricle, RA= right atrium, Ao= Aorta

Table 1. Clinical data of the study population.

Table 2. Standard echocardiographic parameters and speckle-tracking echocardiography in the study population

Table 3. Two-dimensional speckle-tracking echocardiography parameters in the normotensive and hypertensive coarctation of the aorta (CoA) group.



