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Resynchronization and Strain Recovery Following Reimplantation of Anomalous Coronary Artery: A Tissue Doppler and Three-dimensional Echocardiographic Study

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Abstract

Resynchronization may play a significant role in recovery following surgical reimplantation of anomalous left coronary artery from the pulmonary artery (ALCAPA). Three-dimensional echocardiography and tissue Doppler may quantify this recovery. A 6-week-old infant presented with signs of congestive heart failure due to ALCAPA. Two-dimensional echocardiography showed a severely dilated left ventricular (LV) cardiomyopathy and the presence of ALCAPA was confirmed by catheterization. Three-dimensional echocardiography and tissue Doppler imaging showed severe abnormalities of systolic and diastolic synchrony and decreased contractility with a left ventricular ejection fraction (LVEF) of 13%. The infant underwent surgical coronary reimplantation and was discharged 5 weeks later with an LVEF of 54%. Serial quantitative assessment showed resynchronization and normalization of global LV function following reimplantation. However, segmental contractility improved significantly but remained depressed at discharge. The immediate recovery observed following reimplantation of anomalous coronary may be largely due to resynchronization.

Keywords

Anomalous Coronary; Synchrony; Strain Rate Imaging; 3-Dimensional Echocardiography; Segmental Contractility

Introduction

Sutherland et al. recently reported that there are few data on the use of strain rate imaging in patients with congenital heart disease, and its clinical role in these individuals has yet to be defined.¹ Strain rate imaging has, however, been used to demonstrate the benefit of surgical coronary reimplantation in patients with anomalous left coronary artery from the pulmonary artery (ALCAPA).^{2,3} This disease represents a situation of chronic myocardial hypoperfusion, suggesting that its recovery may be similar to the benefit observed following revascularization after myocardial infarction.

Adult ischemic cardiomyopathies have been associated with abnormalities in the synchrony of contraction and relaxation and revascularization has led to resynchronization.^{4,5} This

suggests that resynchronization may play an important role in the recovery of ALCAPA following reimplantation. We used tissue Doppler and real-time 3-dimensional echocardiography to assess left ventricular (LV) synchrony and segmental contractility in a 6-week-old infant with ALCAPA. Analysis was performed pre- and postoperatively to quantify recovery following surgical reimplantation of the anomalous coronary.

Methods

Patient History

The 6-week-old infant was admitted to the emergency room with tachypnea, tachycardia, and diaphoresis. Chest X-ray showed cardiomegaly. Two-dimensional echocardiography demonstrated a dilated cardiomyopathy, paradoxical motion of the lateral wall, and an ejection fraction of 13%. Coronary angiography demonstrated the origin of the left main coronary artery from the pulmonary artery. Two days after admission, the patient underwent surgical reimplantation of the left coronary to the aorta. The patient recovered and was discharged 35 days postoperatively.

Acquisition

All data were obtained on the day of admission (2 days before reimplantation) and 13 and 35 days after surgical reimplantation. Quantitative analysis was performed in MatLab (version 6.1 release 12.1, Natick, Mass, USA). Three-dimensional echocardiographic data of the LV were collected from an apical window using a Philips (Andover, Mass, USA) 2.5 MHz matrix array transducer. The final 3-dimensional image consisted of 10–12 frames spaced equally in time over 1 heart beat. Immediately following 3-dimensional acquisition, color tissue Doppler data and 2-dimensional B-mode images were collected from standard apical 2-chamber, 3-chamber, and 4-chamber views using a 5 MHz GE (Horten, Norway) Vivid 7 system. An effort was made to align the walls in each view so that they were less than 20° from parallel with the Doppler beam. We maximized tissue Doppler frame rate to a minimum of 140 Hz.

Tissue Doppler Analysis

Strain Rate—Longitudinal strain rate was calculated as the spatial gradient of tissue Doppler velocities as described in D’Hooge et al.⁶ We used GE Vingmed Ultrasound EchoPAC PC postprocessing software, version 3.1.3, to derive strain rates from the tissue Doppler data. One sample area was placed in the mid-segment of each wall of the 3 apical views. This sample area was assigned a 3 mm round shape so that its edges were entirely within the myocardium, and its position was adjusted sequentially through the cardiac cycle so that it remained in a fixed mid-myocardial position. The sample area represents the region over which strain rate is averaged in order to determine the output value. A spatial length of 8 mm was used for strain rate analysis as done previously in healthy children by Weidemann et al.⁷ This represents the length over which the velocity gradient is calculated to determine strain rate. Strain rate curves were smoothed with a Gaussian 40 millisecond filter before measuring peak systolic and early diastolic strain rates.

Tissue Velocity—Tissue velocity data were collected by placing 1 basal and 1 mid-ventricular 3 mm round sample area on each wall. The sample area was again relocated so that it remained in a constant mid-myocardial position throughout the cardiac cycle. Velocity data were smoothed with a 30 millisecond averaging filter before measuring time to peak systolic tissue velocity. Global LV synchrony was quantified using the standard deviation of times to peak systolic tissue velocity in the 12 nonapical segments as described by Yu et al.⁸

Three-dimensional Analysis

TomTec 4D LV-Analysis software (version 1.2 Build 169—April 21, 2004, Unterschleissheim, Germany) was used to generate a model of the LV consisting of 16 regional volumes adjacent to each of the standard LV segments.⁹ Each of these 16 volumes changes in size throughout the cardiac cycle according to the regional deformation of the adjacent walls. The TomTec software determines the regional deformation by identifying the endocardial border of the LV in each time frame of the 3-dimensional data set.

The 3-dimensional volume of the LV was divided spatially for each time frame into 16 long-axis planes. Therefore, the 3-dimensional data set was reduced to 16 planes for each of 12 individual time points throughout the cardiac cycle, so that there were a total of 192 2-dimensional echo images to analyze. The endocardial border was automatically traced and manually adjusted for each of the 192 frames of the data set. Regional volume curves (volume of each segment vs. time throughout the cardiac cycle) for each of the 16 segments were generated using the TomTec software and exported to MatLab for analysis.

For each regional volume, time to peak ejection fraction was calculated as the time from the beginning of 3-dimensional acquisition to minimum volume. Global LV synchrony was quantified using the standard deviation of regional times to peak ejection fraction for the 12 nonapical segments. Apical segments were excluded in order to remain consistent with the methodology in Yu et al. for quantifying LV synchrony with the standard deviation of times to peak systolic tissue velocity.⁸ The numerical derivatives of the regional volume curves (change in volume per unit change in time) were calculated and plotted to visualize synchrony.

Segmental Analysis by Coronary Artery Territory

The 12 nonapical segments were grouped according to the 3 coronary artery territories⁹ for analysis. The right coronary artery (RCA) territory was defined as the inferoseptal wall from the apical 4-chamber view and the inferior wall from the apical 2-chamber view, the left circumflex (LCX) territory was defined as the inferolateral wall from the apical 3-chamber view and the anterolateral wall from the apical 4-chamber view, and the left anterior descending (LAD) territory was defined as the anterior wall from the apical 2-chamber view and the antero-septal wall from the apical 3-chamber view. Strain rate data from the 2 corresponding walls were averaged for each coronary artery territory. Peak ejection fractions for each coronary artery territory were calculated from the sum of the modeled regional volumes adjacent to the corresponding LV segments.

Ethics Approval

This study was approved by the Children's Healthcare of Atlanta Internal Review Board (IRB# 04-061).

Results

Left Ventricular Synchrony

Preoperative dyssynchrony and postoperative resynchronization were visualized by plotting the derivatives of the regional volume curves over time (Figure 1A,B). Data from a healthy control subject are shown for comparison (Figure 1C). The standard deviation of regional times to peak ejection fraction declined from 104 milliseconds (33% of mean R-R interval) preoperatively to 69 milliseconds (17% of mean R-R interval) 13 days after reimplantation to 34 milliseconds (8% of mean R-R interval) 35 days after reimplantation (Figure 2). Concurrently, the standard deviation of times to peak systolic tissue velocity declined from 51 milliseconds (16% of mean R-R interval) to 19 milliseconds (5% of mean R-R interval) to 14 milliseconds (3% of mean R-R interval) (Figure 2).

Left Ventricular Global Function and Segmental Contractility

Global left ventricular ejection fraction (LVEF) improved from 13% preoperatively to 39% 13 days after reimplantation and further improved to 54% 35 days after reimplantation. LV end diastolic volume declined from 107 mL/m² preoperatively to 40 mL/m² 35 days after reimplantation.

Strain rate data from the inferolateral wall of the apical 3-chamber view (LCX territory) collected on day 35 were not included because the wall was greater than 20% from parallel to the Doppler beam. Systolic longitudinal strain rate improved from -1.6 to -3.1 /s for the RCA territory, 0 to -0.8 /s for the LCX territory, and 0.1 to -1.0 /s for the LAD territory (Figure 3A). Early diastolic longitudinal strain rate improved from 0.2 to 2.0 /s for the RCA, -0.3 to $+0.9$ /s for the LCX, and -0.8 to $+1.6$ /s for the LAD (Figure 3B). The RCA territory ejection fraction increased from 28% to 53%, the LCX from 13% to 62%, and the LAD from 15% to 52% (Figure 3C).

Discussion

We have quantified the occurrence and progressive resolution of severe LV dyssynchrony in an infant with presumed ischemic cardiomyopathy due to anomalous left coronary artery from the pulmonary artery who underwent surgical coronary reimplantation. The resynchronization could be visualized with a new technique of plotting the derivatives of the regional volume curves (Figure 1A,B). In a perfectly synchronous LV, we would expect negative blood flow (ejection) during systole, zero blood flow at end systole, and positive blood flow (filling) during diastole with 2 peak flows marking early and late diastolic filling (Figure 1C). This would be followed by a zero-flow representing a maximum volume corresponding to end diastole. The distance over which the lines in Figure 1A,B first cross the x-axis is a measure of synchrony and would be equal to zero in a perfectly synchronous LV: all the lines would cross zero at the same time because each regional volume of the LV would reach minimum volume, or peak ejection fraction, simultaneously. In Figure 1A we see the functional consequences of a severely dyssynchronous LV: some regions of the LV are actually gaining volume during systole, some are losing volume during diastole, and virtually all of the segments are reaching peak ejection fraction at different times.

We chose peak systolic strain rate as a measure of systolic function for several reasons. First, peak systolic strain rate is a load-independent measure of contractility.^{10,11} Second, both strain and strain rate are more reliable measures of myocardial viability than tissue Doppler velocities, perhaps due to elimination of translational effects.¹⁰ Third, strain has been shown to have some load dependence,¹¹ unlike strain rate. Similarly, peak early diastolic strain rate has been shown to be a good measure of regional relaxation.¹

Segmental analysis demonstrated that resynchronization paralleled myocardial functional improvement in specific coronary territories (Figure 3). Previous studies have similarly demonstrated dyssynchrony in adult ischemic cardiomyopathies that has resolved following revascularization.^{4,5} As expected based on the pathophysiology of ALCAPA, the RCA territory was the only segment preoperatively that was functioning normally in the timing of contraction and relaxation even though longitudinal strain rate magnitudes were depressed. Preoperative systolic strain rates were entirely abnormal in the left coronary territories (zero in the LCX and expansive or positive in the LAD). The left territories were also exhibiting postsystolic shortening (negative early diastolic strain rate) preoperatively, which is a classic marker of myocardial ischemia.¹² Right coronary territory systolic and diastolic longitudinal function appeared to recover to normal values by day 35 relative to published values (Weidemann et al. reported a mean systolic strain rate of -1.9 ± 0.6 /s and early diastolic strain rate of 2.3 ± 0.9 /s in 33 healthy children ranging from 4 to 16 years old).⁷

However, the left territory measures of systolic and diastolic function had improved but not recovered by day 35 even though peak ejection fractions in all coronary territories had returned to normal along with global LV function (LVEF = 54%). These findings are consistent with previous studies.^{2,3,13} For example, Di Salvo et al. found that patients with ALCAPA had normalized LV function as assessed by conventional echocardiographic techniques and normal radial function as assessed by strain and strain rate imaging.² However, longitudinal LV function assessed by strain and strain rate imaging remained depressed. We found a similar depression of longitudinal function in our study that, as speculated previously by Di Salvo et al., may be due to the prolonged ischemia to the subendocardium, where the fibers are predominantly longitudinally oriented.

In summary, 35 days after reimplantation we have an infant with depressed regional LV strain rates, normal LVEF, and normal LV synchrony. The best clinically attainable measure of regional contractile function is strain rate,¹ and ejection fraction is the most widely used clinical measure of global LV function. The data from this infant suggest that these 2 measures of contractility may be independent: global function has recovered while regional contractility has remained depressed. Alternatively, LVEF may be a gross measure of global cardiac function that is insensitive to localized reduction in strain rates. This further underscores the value of segmental analysis of myocardial deformation as we have presented it.

The recovery of global function following reimplantation of anomalous coronary may be largely due to resynchronization. The energetic cost of dyssynchrony needs to be defined independent of dysfunctional myocardium in order to quantify the benefit of resynchronization. This may provide insight into better selection criteria for resynchronization therapies^{14,15} in patients with severe, drug-refractory heart failure or idiopathic dilated cardiomyopathy.

Limitations

The commercially available 3-dimensional software (TomTec 4D LV-Analysis) does not model the entire cardiac cycle. The cycle is divided into an equal number of frames and there are no model data generated from the last frame back to the first frame of the cycle. In a normal heart it would be expected that the regional volume curves would be linear throughout this unmodeled segment and thus no information would be lost. However, in a severely dyssynchronous heart, this assumption may not be valid.

Although the techniques used in this study are on the verge of readiness for routine clinical use,^{1,16} standard values and methodology for neonates or children under the age of 4 have yet to be defined. We compared strain rate values with normal values reported in 33 healthy children ranging from 4 to 16 years of age.⁷

Strain rate imaging and 3-dimensional echocardiographic modeling of the LV both require a significant amount of postprocessing time, which may limit their clinical applicability. The strain rate analysis performed in this study took approximately 30–60 minutes to complete for each acquisition while the 3-dimensional modeling took nearly 8 hours.

The RCA distribution was normal by angiography. However, the left territories are assumed for segmental analysis, as they were unable to be identified due to the anomalous origin of the left coronary from the pulmonary artery.

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Figure 1.

Left ventricular synchrony before and after reimplantation. A–B: Derivatives of each of the 16 left ventricular regional volume curves plotted versus time. Time zero marks the beginning of three-dimensional acquisition and corresponds to the peak of the electrocardiogram R-wave. Solid vertical lines correspond to minimum volume and maximum volume, respectively from left to right, calculated from the global volume curve of the left ventricle. Only 91% of the cardiac cycle is shown because the three-dimensional analysis software does not model the time period from the last to the first frame of the three-dimensional data set. C: Derivatives of the 16 left ventricular regional volume curves in a healthy control subject. The healthy control had normal two-dimensional echocardiography, normal 12-lead EKG, and no history of cardiac disease. Systolic (S), early diastolic (E), and late diastolic (A) waves are shown.

Figure 2.

Standard deviation of times to peak ejection fraction of the 12 nonapical regional LV volumes calculated from real-time three-dimensional echocardiography data (left y-axis) and standard deviation of times to peak systolic tissue velocity of the same segments calculated from tissue Doppler data (right y-axis). Both are measures of global LV synchrony. Pre = pre-operative, D13 = 13 days postoperative, D35 = 35 days post-operative, 3DE = three-dimensional echocardiography, SD = standard deviation, EF = ejection fraction, TDI = tissue Doppler imaging, Sys = systolic, TV = tissue velocity.

Figure 3.

Segmental contractility before and after reimplantation. A–B: Peak systolic longitudinal strain rate as a measure of systolic function and early diastolic longitudinal strain rate as a measure of diastolic function. Standard apical views were used to sample a point in the mid-segment on each of the 6 walls of the LV. Data from the 2 corresponding walls were averaged for each coronary artery territory. Data from the inferolateral wall of the apical 3-chamber view (LCX territory) collected on day 35 is not included because the wall was greater than 20% from parallel to the Doppler beam. C: Peak ejection fractions for the coronary artery territories, derived from TomTec three-dimensional echocardiographic modeling of the LV. SR = strain rate, Pre = pre-operative, D13 = 13 days post-operative, D35 = 35 days post-operative, RCA = right coronary artery, LCX = left circumflex artery, LAD = left anterior descending.