Cardiol Young 2005; 15 (Suppl. 3): 45–50
© Cambridge University Press
ISSN 1047-9511

Findings from new echocardiographic techniques concerning ventricular remodelling and function in the functionally univentricular heart

Giuseppe Pacileo, Giovanni Di Salvo, Alessandra Rea, Raffaele Calabrò

Paediatric Cardiology, Second University, A.O. Monaldi, Naples, Italy

Keywords: Fontan circulation; strain; strain rate; cavo-pulmonary connections

THOSE PATIENTS WITH FUNCTIONALLY univentricular hearts are the ones in which surgical repair so as to produce biventricular circulations is deemed impossible, despite the fact that in most instances there are two ventricles within the ventricular mass. Before the era of the Fontan procedure, the typical course of patients with such functionally univentricular arrangements consisted of cardiac failure and death within the first year of life. Despite the advent of effective palliative therapy, ventricular dysfunction remains a significant clinical problem for these patients.[1]

The physiology of patients with functionally univentricular hearts, both before and after palliative surgery, is characterized by the combination of cyanosis and ventricular volume loading.[2–4] Under the circumstances of complete mixing of the systemic and pulmonary venous flows, the flow of blood to the lungs must be at least one and a half times greater than the systemic flow so as to achieve an acceptable saturation of oxygen, greater than 85%.[2] This means that total ventricular output must be at least two to three times greater than normal. If ejection fraction is normal, this implies that end-diastolic volume must also be two to three times greater than normal.[1–3] If ventricular function is depressed, even greater ventricular dilation is required to achieve this level of output. The chronic volume overload state is characterized by progressive ventricular dilation, with transition to a more spherical ventricular shape.[5,6] The onset of inadequate hypertrophy with afterload excess, manifest as elevated mural stress, portends the ultimate appearance of myocardial contractile failure.[3] Creation of a direct connection between the systemic venous pathways and the pulmonary arteries, with either a partial anastomosis such as the Glenn shunt, or complete cavo-pulmonary diversion to produce the Fontan circulation, reduces the volume load, and sometimes reduces cyanosis, but may not improve ventricular function.[4,7–9]

The evaluation of ventricular function in patients after conversion to the Fontan circulation still relies on parameters requiring geometrical assumptions, which may not be valid in such patients. Imaging of strain and strain rate ultrasonically is a new non-invasive technique able to quantify the properties of regional myocardial deformation.[10–13] Strain is the total amount of regional deformation, and strain rate is the rate at which this regional deformation takes place. Significantly, both of these parameters are free of geometrical assumptions.[10–14] The aim of our study, therefore, was to evaluate the properties of regional myocardial deformation in patients with a dominant left ventricle before and after their conversion to the Fontan circulation, and to correlate these parameters with standard echocardiographic indexes of systolic function. We also took the opportunity to compare the indexes of myocardial deformation with the age at conversion to the Fontan circulation.

Methods

We studied 20 consecutive patients, with a mean age at the time of the study of 17 plus or minus 6 years, with double inlet left ventricle or tricuspid atresia who underwent a Fontan operation. The mean age at the time of the Fontan operation had been 7 plus or

Correspondence to: Giuseppe Pacileo MD, Via Romaniello, 12, Napoli 80129, Italy. Tel: +39 81 706 2852; Fax: +39 81 706 4275; E-mail: gpacile@tin.it

https://doi.org/10.1017/S1047951105001630 Published online by Cambridge University Press

minus 5 years, with a range from 2.5 to 12 years. They had been followed regularly at our tertiary referral centre, and from their records we chose images deemed acceptable for quantitative analysis. We excluded patients with obstruction of the systemic outflow tract, or uncontrolled dysrhythmia. Data was compared to those obtained in 20 healthy controls matched for gender and age.

Standard echo-Doppler study

Transthoracic echocardiography was performed using the General Electrics Vingmed System Seven ultrasound machine (Horten, Norway). The standard parasternal short-axis view was used to derive the M-mode measurements of left ventricular systolic and end-diastolic dimensions. Using the apical views, we calculated the end-systolic and end-diastolic volumes according to a modified biapical Simpson's rule, using one four-chamber and one two-chamber long-axis view in orthogonal planes. Left ventricular ejection fraction was calculated according to the standard formula.[15]

Colour Doppler myocardial imaging

Colour Doppler myocardial imaging data to assess longitudinal function was recorded from the anterior and posterior walls from the standard apical view. Radial function for the left ventricular posterior wall was recorded using the parasternal long-axis view. All data was acquired at a frame rate of 200 plus or minus 15 frames per second using a transducer of 3.5 megahertz. This frame rate was necessary to

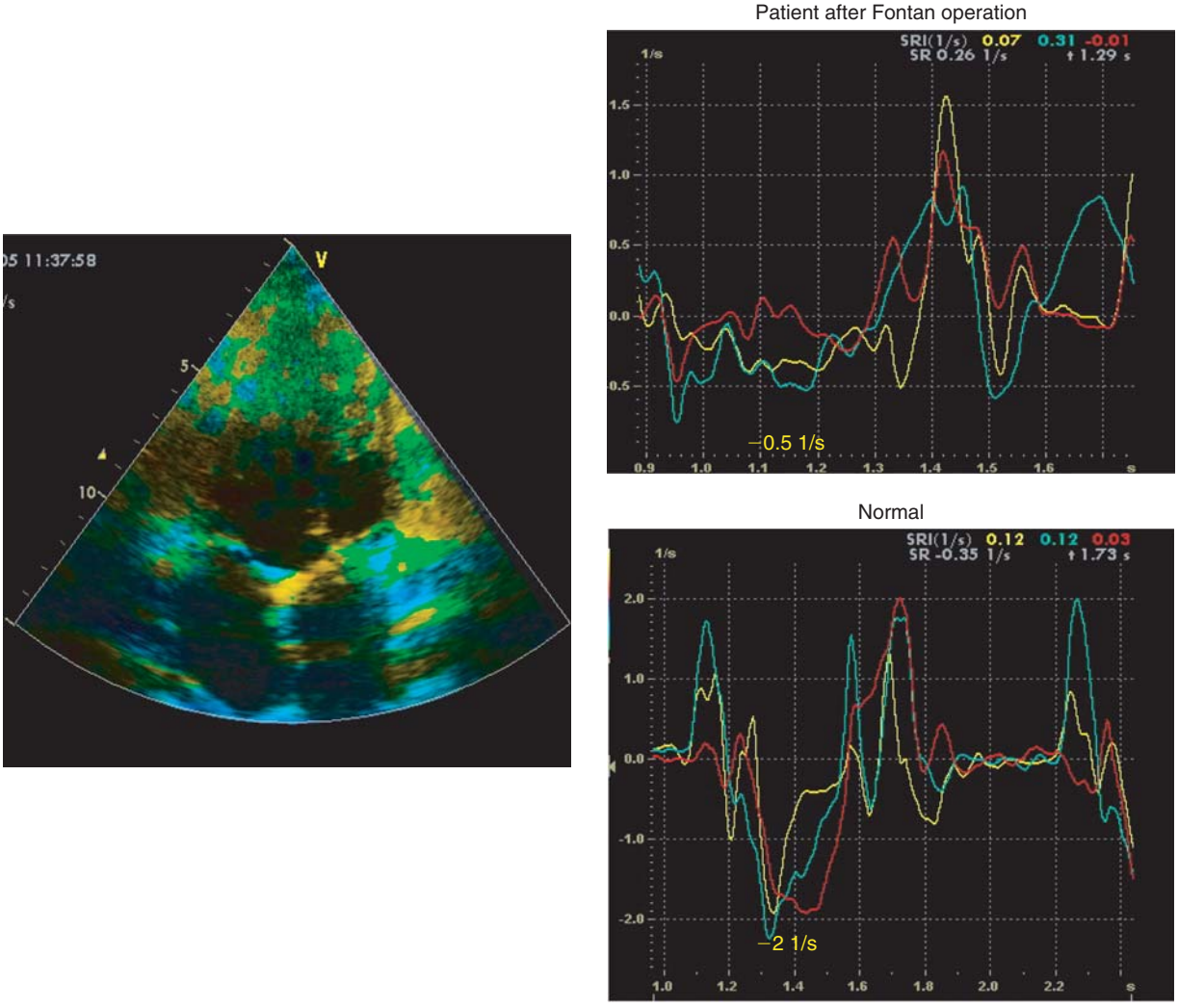


Figure 1.
Comparison of values for strain rate in a patient after the Fontan operation compared to a normal healthy subject. Note that the values for strain rate are homogeneous in the normal subject, but there is a gradient from base to apex after the Fontan operation.

https://doi.org/10.1017/S1047951105001630 Published online by Cambridge University Press

resolve cardiac mechanical events, and to average out the influence of any random noise in the Doppler velocity signal. An appropriate velocity scale was chosen in order to avoid aliasing. The narrowest sector angle, usually 30°, was used to achieve the maximum colour Doppler frame rate possible. For apical views, care was taken to maintain each wall in the centre of the ultrasonic sector in an attempt to align at as near as possible to the direction of longitudinal motion. For the parasternal long-axis view, care was paid to keeping the posterior left ventricular wall perpendicular to the ultrasonic beam in order to be aligned as near as possible to radial motion. Data from three consecutive cardiac cycles were recorded during normal quiet respiration for use in subsequent analysis.

Colour Doppler myocardial imaging data was stored in digital format, and transferred to a computer workstation for the off-line analysis of regional strain rate curves. This was carried out using the dedicated software supplied by General Electrics in their Workstation. Longitudinal strain rates were estimated

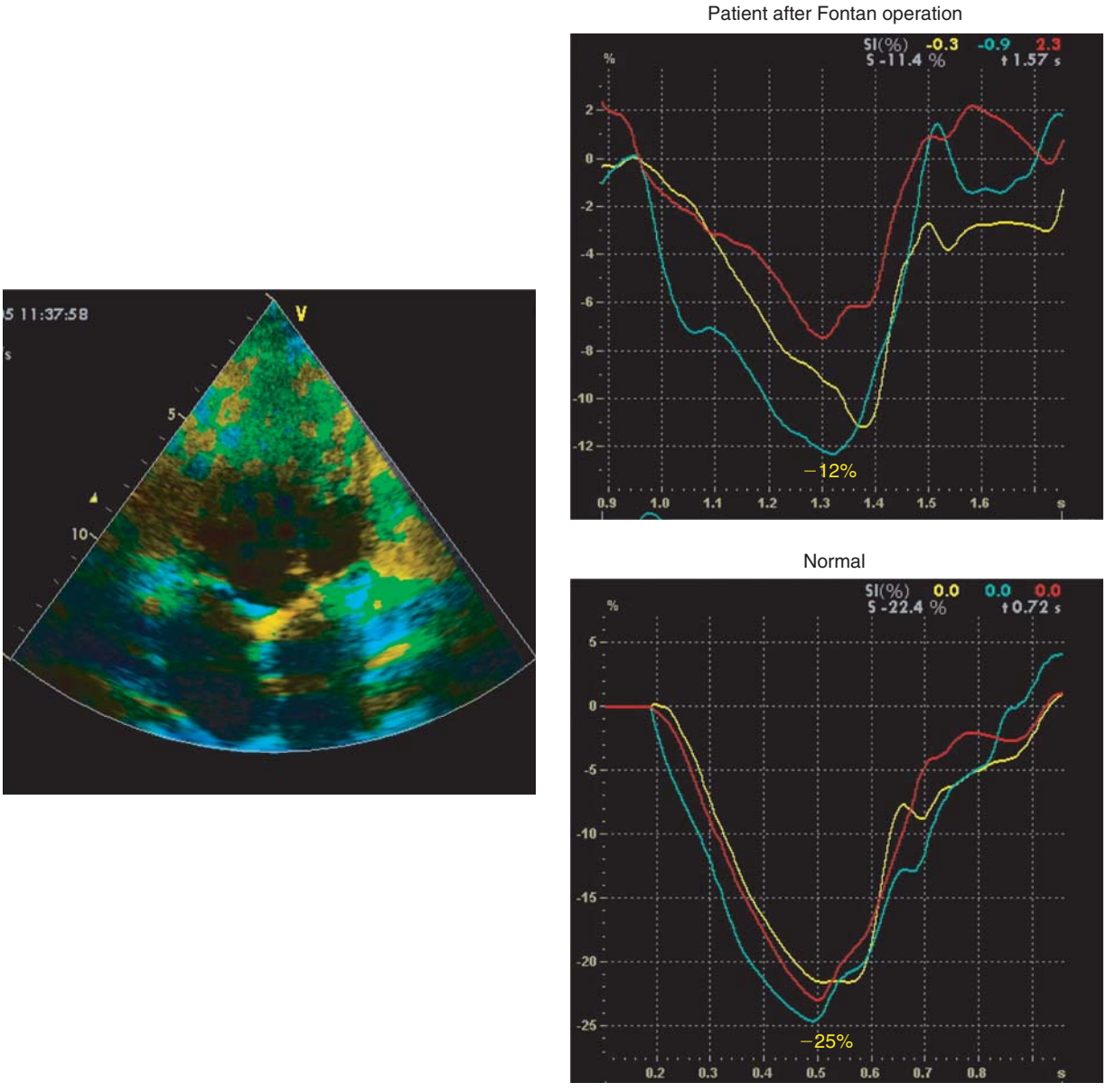


Figure 2.
Comparison of values of strain in a patient with the Fontan circulation compared to a normal healthy subject. Note that, although the analysis of strain rate analysis and values for strain are homogeneous in the normal subject, they show a gradient from base to apex after conversion to the Fontan circulation.

https://doi.org/10.1017/S1047951105001630 Published online by Cambridge University Press

by measuring the spatial velocity gradient over an area of computation of 10 millimetres. Left ventricular regional longitudinal function was evaluated on the apical, mid, and basal segments of the anterior and posterior left ventricle walls. Left ventricular radial strain rates were estimated using a computational area of 5 millimetres chosen from the mid segment of the left ventricular posterior wall. To derive strain rate profiles from the different segments, the region of interest was maintained in a constant position using a semi-automatic tracking algorithm within the segment under interrogation. The timing of ventricular ejection and relaxation was obtained using the traces for mitral and aortic flow obtained with pulsed wave Doppler. Natural strain profiles were obtained by integrating the mean values for strain rate over time, using end-diastole as the reference point. Using the data for averaged strain rate and strain, we measured peak systolic strain rate and systolic strain. Our intra and inter observer variability has been presented elsewhere.[16] Statistical analysis was carried out by Stat View software, marketed by the SAS Institute, Cary, North Carolina. Values are presented as mean plus or minus standard deviations. Multiple comparisons were performed using repeated analysis of variance measurements with post hoc Bonferroni's test. Qualitative data were compared using the two-tailed Fisher's exact test. The null hypothesis was rejected for p-values of less than 0.01.

Results

The patients with the Fontan circulation presented significantly higher left ventricular dimensions than their controls, with end-diastolic dimensions of 6.4 plus or minus 0.8 centimetres compared to 3.8 plus or minus 0.7 centimetres (p less than 0.001). Ejection fraction was significantly reduced in the patients, at 52 plus or minus 5%, compared to their controls, at 65 plus or minus 8% (p-value less than 0.001), but ejection fraction was in the normal range, at greater than 55%, for eight of the patients. The eight patients in whom the Fontan circuit had been established before the age of 10 years had significantly smaller left ventricular dimensions than those undergoing surgery at later ages (p-value less than 0.01). Indeed, all the indexes of left ventricular function for all our patients were strongly correlated in an inverse fashion with age at surgery (p-value less than 0.01, regression coefficient equal to minus 0.45).

Colour Doppler myocardial imaging study

After conversion to the Fontan circulation, the values for radial strain, at 30 plus or minus 8% as opposed to 55 plus or minus 6% for controls, and strain rate, at 1.6 plus or minus 0.6 versus 3 plus or minus 0.5 for controls, both of these significant at p-values less than 0.0001, along with the properties of longitudinal myocardial deformation were significantly reduced (Table 1). The properties for myocardial deformation were reduced in non-homogeneous fashion along the walls studied (Table 1), showing a gradient from base to apex in both walls, and a more severe reduction in the peak values for systolic strain rate along the posterior wall. When analysing these properties within our cohort, those patients undergoing surgery at earlier ages showed values for both strain and strain rate greater than those undergoing later surgical procedures for both radial and longitudinal function, these all being significant with p-values of less than 0.05. The parameters for both strain and strain rate also correlated significantly with the age at the surgical repair, the p-value being less than 0.01, and the regression coefficient equal to 0.53. We also noted that both

Table 1. Properties of myocardial deformation of patients with the Fontan circulation compared to their controls.

	After Fontan operation (20 patients)		Controls (20 subjects)	
	Strain (%)	Strain rate (1/s)	Strain (%)	Strain rate (1/s)
Parasternal long-axis view				
Posterior wall	30 ± 8*	1.6 ± 0.6*	55 ± 6	3 ± 0.5
Apical view				
Anterior wall				
Basal	−14 ± 6*	−1.1 ± 0.6*	−21 ± 3	−2 ± 0.6
Mid	−14 ± 5*	−1.2 ± 0.5*¶	−19 ± 4	−1.7 ± 0.4
Apical	−8 ± 5*	−0.7 ± 0.4*¶	−24 ± 4	−2.1 ± 0.7
Posterior wall				
Basal	−15 ± 6^	−0.9 ± 0.3*	−20 ± 3	−2 ± 0.6
Mid	−12 ± 5^	−0.8 ± 0.2*	−21 ± 4	−2.1 ± 0.4
Apical	−6 ± 5*	−0.4 ± 0.3*	−24 ± 4	−2.1 ± 0.7

*$p < 0.0001$ versus controls; ^$p < 0.001$ versus controls; ¶$p < 0.01$ versus posterior wall

https://doi.org/10.1017/S1047951105001630 Published online by Cambridge University Press

radial and strain rate were significantly reduced in our patients with normal ejection fractions.

Discussion

To the best of our knowledge, ours is the first attempt to image strain and strain rate in order to assess the properties of regional myocardial deformation in the dominant left ventricle of patients converted to the Fontan circulation. This type of imaging is able to detect myocardial abnormalities even in the presence of normal ejection fractions. Indeed, in eight patients in our cohort, ejection fraction was in the normal range, but the parameters for strain and strain rate were reduced compared to values obtained in our control population. This finding could be explained by the fact that strain rate imaging has been shown to be less dependent on load.[10–14,16,17] Our data also showed that the properties of regional myocardial deformation properties are significantly reduced for both radial and longitudinal myocardial function. The properties for longitudinal regional deformation were reduced in dishomogenous fashion within the walls we were able to study. Indeed, peak values for systolic strain rate along the posterior wall showed a more severe reduction compared to those obtained for the anterior wall. Moreover, the lowest values of strain and strain rate were found in the apical segments of both anterior and posterior walls (Table 1). Compared to the indexes for radial deformation, the values of longitudinal strain and strain rate were more significantly impaired. The degree of myocardial impairment was also correlated significantly with the age at the time of surgery.

Although myocardial fibres oriented in longitudinal direction make up only a small portion of the myocardial mass, several studies have shown that the contraction along the longitudinal plane is an important component of the systolic performance of the left ventricle.[18,19] The chronic volume overload increases the wall stress leading to hypertrophy without adequate neoangiogenesis, which in turn leads to increased consumption of oxygen and reduced coronary arterial perfusion, especially to the longitudinal fibres in the subendocardial layer.[20] We found a significant correlation between the age of the patients at the time of their conversion to the Fontan circulation and longitudinal strain and strain rate. This demonstrates a strong relationship between subendocardial ischaemia and the duration of overload. Thus, our findings confirm previous suggestions that left ventricular dysfunction appears to result at least in part from volume overload, and worsens with its duration.[16]

Moreover, the dominant left ventricle responds to volume overload by evolving from ellipsoidal to spherical shape, increasing the end-diastolic ratio between the minor and long axes.[3] The reason for this change is not yet known. The ability of the pericardium to expand only laterally, nonetheless, along with the failure to maintain normal ventricular configuration in presence of inadequate hypertrophy, may play crucial roles.[3] According to Reynertson et al.,[21] who studied the impact of overload on the right ventricle in patients with acute tricuspid regurgitation, the systolic shortening along the minor axis is comparable to that of normal subjects. The changes in ventricular shape with significant increase of the minor axis might explain the apparently normal systolic function on the radial plane assessed by load-dependent indexes such as fractional shortening.[1–3] In our patients, however, the parameters for strain and strain rate were also significantly reduced in the radial plane, even in patients with normal ejection fractions. Use of analysis of strain and strain rate in the radial plane, therefore, rather than mere assessment of the extent of myocardial shortening as evaluated in fractional shortening, is necessary so as adequately to evaluate ventricular function. As did others,[7,22] we found dishomogenous compromise in the properties of regional systolic deformation, suggesting that such regional abnormalities of mural motion are not rare in patients with the Fontan circulation, and may be related to excessive hypertrophy contributing to cardiac dysfunction.[3]

Our study has its limitations. The usual ones inherent in the angle dependency of all echocardiographic Doppler techniques also apply to ultrasonically derived values for strain and strain rate. We always took care, however, to align the ultrasonic beam with the direction of movement of the myocardial region to be interrogated.

In conclusion, our study has demonstrated the presence of abnormal properties of radial and longitudinal deformation in patients after conversion to the Fontan circulation despite the presence, in some, of an apparent normal ejection fraction. Moreover, longitudinal function is dishomogeneously reduced. The degree of impairment was found to be correlated significantly with the age at surgical repair. Our findings suggest that imaging of strain rate will permit us better to monitor myocardial function in patients after they have been converted to the Fontan circulation.

References

1. Graham TP, Erath HG, Boucek RJ, Boerth RC. Left ventricular function in cyanotic congenital hearth disease. Am J Cardiol 1980; 45: 1231–1236.
2. Gewillig M, Kalis N. Pathophysiological aspects after cavopulmonary anastomosis. Thorac Cardiovasc Surg 2000; 48: 336–341.
3. Sluysmans T, Sanders SP, van der Velde M, et al. Natural history and patterns of recovery of contractile function in single left ventricle after Fontan operation. Circulation 1992; 86: 1753–1761.

https://doi.org/10.1017/S1047951105001630 Published online by Cambridge University Press

4. Parikh SR, Hurwitz RA, Caldwell RL, Girod DA. Ventricular function in the single ventricle before and after Fontan surgery. Am J Cardiol 1991; 67: 1390–1395.
5. Berman NB, Kimball TR. Systemic ventricular size and performance before and after bidirectional cavopulmonary anastomosis. J Paediatr 1993; 122: S63–S67.
6. Chin AJ, Franklin WH, Andrews BAA, Norwood WI. Changes in ventricular geometry early after Fontan operation. Ann Thorac Surg 1993; 56: 1359–1365.
7. Fogel MA, Weinberg PM, Chin AJ, Fellows KE, Hoffman EA. Late ventricular geometry and performance changes of functional single ventricle throughout staged Fontan reconstruction assessed by magnetic resonance imaging. J Am Coll Cardiol 1996; 28: 212–221.
8. Tanoue Y, Sese A, Ueno Y, Joh K, Hijii T. Bidirectional Glenn procedure improves the mechanical efficiency of a total cavopulmonary connection in high-risk Fontan candidates. Circulation 2001; 103: 2176–2180.
9. Hjortdal VE, Stenbog EV, Ravn HB, et al. Neurohormonal activation late after cavopulmonary connection. Heart 2000; 83: 439–443.
10. Sutherland GR, Di Salvo G, Claus P, D'hooge J, Bijnens B. Strain and strain rate imaging: a new clinical approach to quantifying regional myocardial function. J Am Soc Echocardiogr 2004; 17: 788–802.
11. Di Salvo G, Pacileo G, Caso P, et al. A new echocardiographic approach to evaluate myocardial function in congenital cardiopathies: strain and strain rate imaging. Ital Heart J Suppl 2003; 4: 375–382.
12. D'hooge J, Bijnens B, Thoen J, Van de Werf F, Sutherland GR, Suetens P. Echocardiographic strain and strain-rate imaging: a new tool to study regional myocardial function. IEEE Trans Med Imaging 2002; 21: 1022–1030.
13. D'hooge J, Heimdal A, Jamal F, et al. Regional strain and strain rate measurements by cardiac ultrasound: principles, implementation and limitations. Eur J Echocardiogr 2000; 1: 154–170.
14. Greenberg NL, Firstenberg MS, Castro PL, et al. Doppler-derived myocardial systolic strain rate is a strong index of left ventricular contractility. Circulation 2002; 105: 99–105.
15. Sahn DJ, DeMaria A, Kisslo J, Weyman A. The Committee on M-Mode Standardization of the American Society for Echocardiography. Recommendations regarding quantitation in M-mode echocardiography; results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072–1083.
16. Di Salvo G, Pacileo G, Verrengia M, et al. Early myocardial abnormalities in asymptomatic patients with severe isolated congenital aortic regurgitation: an ultrasound tissue characterization and strain rate study. J Am Soc Echocardiogr 2005; 18: 122–127.
17. Jamal F, Bergerot C, Argaud L, Loufouat J, Ovize M. Longitudinal strain quantitates regional right ventricular contractile function. Am J Physiol Heart Circ Physiol 2003; 285: H2842–H2847.
18. Arce OX, Knudson OA, Ellison MC, et al. Longitudinal motion of the atrioventricular annuli in children: reference values, growth related changes, and effects of right ventricular volume and pressure overload. J Am Soc Echocardiogr 2002; 15: 906–916.
19. Wandt B. Long-axis contraction of the ventricles: a modern approach but described already by Leonardo da Vinci. J Am Soc Echocardiogr 2000; 13: 699–706.
20. Claus P, Bijnens B, Weidemann F, Dommke C, et al. Post systolic thickening in ischemic myocardium: a simple mathematical model for simulating regional deformation; functional imaging and modelling of the heart. Lect Notes Comput Sci 2001; 2230: 134–139.
21. Reynertson S, Kundur R, Mullen GM, Costanzo MR, McKiernan TL, Louie EK. Asymmetry of right ventricular enlargement in response to tricuspid regurgitation. Circulation 1999; 100: 465–467.
22. Fogel MA, Gupta KB, Weinberg PM, Hoffman EA. Regional wall motion and strain analysis across stages of Fontan reconstruction by magnetic resonance tagging. Am J Physiol Heart Circ Physiol 1995; 269: H1132–H1152.

https://doi.org/10.1017/S1047951105001630 Published online by Cambridge University Press