Assessment of Ventricular Function in Tetralogy of Fallot Patients Using Tissue Doppler
N Abdelrazik, A Abdelgawad, M Hamed

Citation

Abstract
Background: Echocardiographic findings of Tetralogy of Fallot (TOF) are diagnostic in infants and young children, and echocardiography may be the only examination required prior to surgery. Global left ventricular function determined by conventional Doppler may be normal in these patients; but regional myocardial function assessment by tissue Doppler if abnormal in these patients may affect outcome later on.

Aim of the Work: to evaluate ventricular functions in Fallot's tetralogy using conventional and tissue Doppler echocardiography (DTI).

Patients and Methods: Thirty patients with TOF were included. They included 19 (63.3 %) males and 11 (36.7 %) females, age 37.8 ± 19.31 months. Twenty age-matched healthy subjects (36.3 ± 14.88 months) were included as a control group. Conventional and Doppler tissue Imaging (DTI) were used in the evaluation of both groups.

Results: Analysis of the obtained results showed significantly lower ME, ME/A, TE, TE/A and TS but higher TA in TOF group than in healthy controls by DTI. In addition, there was direct correlation between age and ME/A in TOF patients. Comparison of conventional Doppler parameters in the studied groups shows significantly lower ME, ME/A and TE/A but higher TA in TOF patients than controls. Correlation among Doppler Tissue Imaging and conventional Doppler parameters in the TOF cases showed direct correlation between DTI TA and both Doppler TE and TA. In addition, there was inverse correlation between DTI TE/A and Doppler TE and TA.

Conclusions: DTI is a reliable utility in the diagnosis of ventricular function in TOF cases with many advantages over conventional echocardiography.

ABBREVIATIONS
TOF: Tetralogy of Fallot
DTI: Doppler tissue imaging
RV: right ventricle
ME: early diastolic velocity at mitral valve
MA: late diastolic velocity
ME/A: ratio
MS: peak systolic velocity
TE: early diastolic velocity at tricuspid valve
TA: late diastolic velocity
TE/A: ratio
TS: peak systolic velocity

INTRODUCTION
Echocardiographic findings of tetralogy of Fallot (TOF) are diagnostic in infants and young children, and echocardiography may be the only examination required prior to surgery. Conventional radiography, MRI, and angiography also are helpful for complete preoperative evaluation in some cases. Angiography has been used for preoperative evaluation of the coronary arteries and peripheral pulmonary circulation. However, intracardiac catheterization may stimulate pulmonary outflow tract spasm. Noninvasive peripheral pulmonary arterial evaluation is possible with MRI [1]. Echocardiography proved to be effective in evaluation of left ventricular volumes in patients with Fallot's tetralogy [2]. Right ventricular morphology in tetralogy of Fallot had a great impact in the surgical decision and outcome after total repair. Small ventricular size or impaired function will have a poor prognosis than normal.
ventricle size and function [4]. Left ventricular morphology in tetralogy of Fallot may have a great brunt in surgical decision and outcome after total repair. Small left ventricular size or impaired function may have a poor prognosis than normal left ventricle size and function [5]. Global left ventricular function determined by conventional Doppler may be normal in these patients; but regional myocardial function assessment by tissue Doppler if abnormal in these patients may affect outcome later on [6]. The aim of this study is to evaluate ventricular functions in Fallot's tetralogy using conventional and tissue Doppler echocardiography.

PATIENTS AND METHODS
The present study was conducted in the period from April, 2005 through April, 2006 at Cardiology Unit, Mansoura University Children's Hospital, Mansoura, Egypt. Thirty patients with TOF were enrolled in the study. They included 19 (63.3 %) males and 11 (36.7 %) females, age 37.8 ± 19.31 months. Twenty age-matched healthy subjects (36.3 ± 14.88 months) were included as a control group with approval of the study by the Institutional Ethics Committee and after informed consent was given by the parents.

SELECTION OF PATIENTS
INCLUSION CRITERIA
Tetralogy of Fallot with typical anatomy.

EXCLUSION CRITERIA
Patients associated with another congenital heart disease.
Fallot's tetralogy with atypical anatomy.

METHODS
All patients were subjected to the following: Clinical assessment & evaluation. This included: Careful history taking, with special attention to symptoms of cyanotic heart disease, growth retardation and heart failure. Thorough general and cardiac examination with particular emphasis on signs of cyanotic heart disease, RVH, VSD, pulmonary hypertension and heart failure. ECG recording, X-ray, conventional (two dimensional) doppler. Tissue Doppler Imaging: Pulsed wave DTI velocities were obtained at the cardiac base in the apical 4-chamber view from 3 locations: the lateral mitral annulus; the interventricular septum; and the lateral tricuspid annulus. DTI measurements from each of these myocardial wall segments included peak systolic annular velocity, peak early diastolic annular velocity, and peak late diastolic annular velocity. Each DTI velocity or time interval was measured on 3 consecutive cardiac cycles and subsequently averaged. DTI signal quality was optimized in several ways. Doppler signal quality was enhanced by lowering the Nyquist limit to 10 to 30 cm/s, using the lowest wall filter settings with minimal optimal gain, decreasing Doppler sample volume size to less than 5 mm, and optimizing the sweep speed to at least 100 mm/s. Care was taken to align the Doppler beam as parallel as possible to the corresponding myocardial wall segment.

STATISTICAL ANALYSIS
The reported data were processed using SPSS ver. 10 under Microsoft Windows XP. Continuous data were expressed in the form of mean ± SD. Student t test was used to compare numerical data, while categorical data were compared using chi-square test. Pearson's correlation coefficient was used to correlate variables. P value < 0.05 was considered significant.

RESULTS
Thirty-patients with TOF, and 20 healthy age-matched controls were included in the present work. There was no significant difference as regard age (months), sex, and weight between patients and controls (P = 0.76, 0.9, 0.66 respectively). There was no significant difference between males (n = 19) and females (n = 11) regarding Doppler Tissues Imaging (DTI) parameters. Comparison of Doppler Tissues Imaging (DTI) parameters between TOF group (n = 30) and control (n = 20) showed significantly lower ME (10.77±3.73 v 14.53±2.64 cm/s, P < 0.0001), ME/A (1.08±0.56 v 1.88±0.41 cm/s, P < 0.0001), TE (11.57±3.89 v 15.86±1.88 cm/s, P < 0.0001), TE/A (1.13±0.59 v 1.55±0.19, P < 0.001), and TS (10.94±2.01 v 12.35±1.60 cm/s, P < 0.012), but higher TA in TOF group than in healthy controls (11.56±3.16 v 10.25±0.96 cm/s, P < 0.041) (Table 1). Using conventional Doppler in both groups (TOF, controls) showed significantly low ME, ME/A, and TE/A (P < 0.0001, 0.0001, 0.004 respectively), but higher TA in TOF group than in healthy controls (11.56±3.16 v 10.25±0.96 cm/s, P < 0.041) (Table 2). Correlation of demographic and clinical parameters with Doppler Tissue Imaging (DTI) parameters in TOF patients showed direct correlation between age and ME/A (r = 0.41, P < 0.02) (Table 3). Correlation between demographic characteristics and Doppler Tissue Imaging parameters in healthy control showed direct correlation between DTI parameters (ME, MS, TS, Septum E, Septum EA, and Septum S) with age and weight (Table 4). Correlation between Doppler Tissue Imaging and Conventional Doppler parameters in the TOF cases showed direct correlation between DTI (TA) and conventional Doppler parameters TE (r = 0.38, P < 0.034),
and TA (r = 0.52, P < 0.003). In addition, there was inverse correlation between DTI (TE/A) and conventional doppler TE (r = –0.36, P < 0.047), TA (r = –0.50, P < 0.004) (Table 5).

**Figure 1**
Table 1: Comparison of Doppler Tissue Imaging (DTI) parameters in the studied groups

<table>
<thead>
<tr>
<th></th>
<th>TOF (n=30) mean ± SD</th>
<th>Control (n=20) mean ± SD</th>
<th>Student’s t test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MF</td>
<td>10.8 ± 3.7</td>
<td>14.5 ± 2.6</td>
<td>-3.89</td>
<td>0.0001***</td>
</tr>
<tr>
<td>MA</td>
<td>13.6 ± 14.3</td>
<td>7.95 ± 2.1</td>
<td>2.12</td>
<td>0.087</td>
</tr>
<tr>
<td>MF/A</td>
<td>1.1 ± 0.6</td>
<td>1.9 ± 0.4</td>
<td>-5.49</td>
<td>0.0001***</td>
</tr>
<tr>
<td>MS</td>
<td>14.5 ± 20.8</td>
<td>7.97 ± 1.3</td>
<td>1.72</td>
<td>0.096</td>
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<tr>
<td>TE</td>
<td>11.6 ± 3.9</td>
<td>15.9 ± 1.9</td>
<td>-5.18</td>
<td>0.0001***</td>
</tr>
<tr>
<td>TA</td>
<td>11.6 ± 3.2</td>
<td>10.3 ± 0.96</td>
<td>2.12</td>
<td>0.041*</td>
</tr>
<tr>
<td>TE/A</td>
<td>1.1 ± 0.6</td>
<td>1.6 ± 0.2</td>
<td>-3.59</td>
<td>0.001**</td>
</tr>
<tr>
<td>TN</td>
<td>10.9 ± 2.0</td>
<td>12.4 ± 1.6</td>
<td>-2.61</td>
<td>0.012*</td>
</tr>
<tr>
<td>Septum E</td>
<td>9.95 ± 13.1</td>
<td>11.2 ± 1.6</td>
<td>-0.42</td>
<td>0.68</td>
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<tr>
<td>Septum A</td>
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<td>6.5 ± 1.2</td>
<td>0.41</td>
<td>0.68</td>
</tr>
<tr>
<td>Septum E/A</td>
<td>17.1 ± 1.6</td>
<td>18.4 ± 0.4</td>
<td>-0.25</td>
<td>0.79</td>
</tr>
<tr>
<td>Septum S</td>
<td>10.5 ± 15.7</td>
<td>7.1 ± 0.8</td>
<td>1.19</td>
<td>0.24</td>
</tr>
</tbody>
</table>

**Figure 2**
Table 2: Comparison of Conventional Doppler parameters in the studied groups

<table>
<thead>
<tr>
<th></th>
<th>TOF (n=30) mean±SD</th>
<th>Control (n=20) mean±SD</th>
<th>Student’s t test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MF</td>
<td>0.7 ± 0.2</td>
<td>0.9 ± 0.2</td>
<td>-5.05</td>
<td>0.0001***</td>
</tr>
<tr>
<td>MA</td>
<td>0.6 ± 0.2</td>
<td>0.6 ± 0.1</td>
<td>-0.57</td>
<td>0.56</td>
</tr>
<tr>
<td>MF/A</td>
<td>1.2 ± 0.3</td>
<td>1.7 ± 0.5</td>
<td>-3.90</td>
<td>0.0001***</td>
</tr>
<tr>
<td>TE</td>
<td>0.6 ± 0.2</td>
<td>0.6 ± 0.1</td>
<td>0.35</td>
<td>0.72</td>
</tr>
<tr>
<td>TA</td>
<td>0.7 ± 0.2</td>
<td>0.5 ± 0.1</td>
<td>3.66</td>
<td>0.001**</td>
</tr>
<tr>
<td>TE/A</td>
<td>1.03 ± 0.4</td>
<td>1.3 ± 0.2</td>
<td>-3.01</td>
<td>0.004**</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Doppler Tissue Imaging (DTI) is an echocardiographic technique that measures myocardial velocities and has been demonstrated to be an indicator of global left ventricular (LV) function [6] and right ventricular (RV) function [7]. The majority of noninvasive measures of systolic and diastolic...
ventricular performance are significantly impacted by changes in loading conditions. Traditional echocardiographic measures of systolic function including shortening fraction and ejection fraction and Doppler measures of left ventricular (LV) diastolic function, namely mitral and pulmonary venous inflow Doppler, are significantly affected by altered LV preload and afterload [9]. DTI has been reported to be a sensitive measure of longitudinal systolic and diastolic LV function that is relatively independent of changes in ventricular loading [10]. Recent studies in children, however, have demonstrated that DTI velocities are not only influenced by aging but also more significantly by changes in LV growth parameters, most notably LV end-diastolic dimension and LV mass [11]. Compared with studies of the left ventricle, determining RV function has proved to be challenging using echocardiographic methods because of the unique, eccentric, and complicated morphology of the chamber [12]. Reliable, rapid non-invasive evaluation of right ventricular function, especially in congenital heart disease lesions affecting primarily the right ventricle (RV) such as Tetralogy of Fallot (TOF), is desirable but presents many methodological issues. Standard two-dimensional echocardiographic evaluation of RV volumes and ejection fraction is inaccurate due to the difficulty in defining the RV endocardial surfaces as well as the complexity of its shape. Pulsed Doppler Tissue Imaging (DTI) is a unique tool of measuring systolic and diastolic motion velocities of the tricuspid annulus with high spatial and temporal resolution, that appears to be associated with RV function [13] and RV performance during exercise [14]. DTI evaluation of the lateral tricuspid annular motion has been correlated with RV ejection fraction in adult patients with heart failure [15], while DTI velocities have been associated with RV performance in various congenital heart lesions affecting the RV, whether it supports the systemic [16] or the pulmonary circulation [17]. In the current study, we aimed to evaluate the utility of DTI in comparison with conventional Doppler in assessment of ventricular function in cases of TOF prior to surgical repair. Our study included 19 males (63.3 %) and 11 females (36.7 %) with mean age of 37.8 ± 19.31 months. This sex distribution of cases is in agreement with Eiriksson et al., [15] who reported a higher incidence of TOF in males (male to female ratio 1.2:1). Comparison of tissue Doppler parameters between males and females didn't reveal any significant differences. This is supported by the findings of Ayabakan and Ozkutlu, [16] who noted that tissue Doppler velocities didn't differ between both sexes. Comparing DTI velocities between TOF cases and controls revealed variable results. DTI detected significantly lower velocity at the mitral orifice during early diastole (ME) in TOF than controls (10.77 ± 3.77 versus 14.5 ± 2.6, P < 0.0001). As regards the mitral E/A ratio, control subjects had significantly higher values (1.08 ± 0.56 versus 1.88 ± 0.41, P < 0.0001). For late diastolic velocity (MA), TOF cases had lower values; in spite these didn't reach significant levels (13.61 ± 14.32 versus 7.95 ± 2.12, P = 0.087). This is in partial agreement with Wierzbowska-Drabik et al., [17] who reported that pulsed DTI offers good accuracy for the diagnosis of pseudo-normalization with increased ratio of peak early mitral wave velocity to peak velocity of mitral annulus being the optimal predictor of advanced diastolic dysfunction. It should be noted that Eidem et al., [18] concluded that increases in chronic LV preload do not significantly affect the majority of DTI velocities in children with ventricular septal defects. At the tricuspid orifice, significantly lower TE (11.57 ± 3.89 versus 15.86 ± 1.88, P < 0.0001), TE/A (1.13 ± 0.59 versus 1.55 ± 0.19, P < 0.001) and TS (10.94 ± 2.01 versus 12.35 ± 1.60, P < 0.012) but higher TA (11.56 ± 3.16 versus 10.25 ± 0.96, P < 0.041) were detected in TOF cases than in controls. These results are in agreement with the conclusions obtained by Pegas et al., [19] who noted that in TOF, there is a spectrum of obstruction in the right ventricular outflow tract, which characteristically progresses with age. Using conventional Doppler to evaluate ventricular function demonstrated that flow velocity at the mitral orifice was significantly different between TOF cases and healthy controls regarding ME (P < 0.0001) and subsequently ME/A (P < 0.0001) but not for MA (P = 0.56). At the tricuspid orifice, significant differences were detected for TA (P < 0.001) and TE/A (P < 0.004) but not for TE (P = 0.72). Comparison of tissue Doppler and conventional Doppler parameters in the studied cases shows that both correlates well with more sensitivity for tissue Doppler results. These results are supported by findings of Saygili et al., [20] who concluded that DTI findings correlate well with conventional Doppler echocardiography findings. Moreover, other authors reported that DTI measurements have been correlated with invasively measured haemodynamic parameters, both in heart transplant recipients [11] and in children with various congenital heart defects [21]. Further, Abd El Rahman et al., [22] showed that the DTI-derived Tei index correlated strongly with the conventional pulsed Doppler Tei index within the statistical limits of agreement. This indicates that the Tei index can be accurately measured by DTI. Assessment of the global left ventricular function using the
Assessment of Ventricular Function in Tetralogy of Fallot Patients Using Tissue Doppler

DTI derived Tei index may enhance the utility of DTI for providing quantitative data regarding global ventricular function. In addition, pulsed DTI offers good accuracy for the diagnosis of pseudo-normalization with increased ratio of peak early mitral wave velocity to peak velocity of mitral annulus being the optimal predictor of advanced diastolic dysfunction \cite{9}. Notable, (Rodriguez et al., \cite{5} and Sohn et al., \cite{8} have reported that tricuspid annular DTI patterns in normal infants and children are similar to the patterns previously described for mitral annular motion Reference values for DTI velocities in the pediatric population have been reported and are affected primarily by age and cardiac growth of the patients \cite{6}. In the current study, we reported that DTI velocities were positively correlated with age in normal healthy controls with variable degrees of significance. In TOF cases age was only positively correlated with ME/A ratio. This may be explained by the variation in the pathological stages of the underlying cardiac disease and the relatively small sample size. Reviewing the literature has shown inconsistent data. Ayabakan and Ozktlu \cite{10} have demonstrated that the longitudinal velocity of the heart in early diastole has a positive correlation with age (p < 0.05; midseptum velocity r = 0.57, left ventricular lateral wall velocity r = 0.56, mitral annulus velocity r = 0.56), and the tissue velocities are not influenced by respiration (p < 0.05). The myocardial velocities of different segments of the left ventricle are not correlated with the transmural or pulmonary venous flows (p < 0.05). When age is controlled for heart rate, age mainly affects the systolic velocity of the mitral annulus and the early diastolic velocity of the midseptum in longitudinal axis, as well as the early diastolic velocity of the midseptum in transverse axis (p < 0.05 for all, r = 0.34, 0.29, 0.30 respectively). It should be noted this study was run on healthy children. In another study by Frommelt et al., \cite{11}, infants had significantly decreased peak early diastolic annular velocities and early diastolic annular velocity-to-diastolic annular velocity at atrial contraction ratios compared with children \cite{12}. 

Conclusively, DTI velocities measurement is a reliable investigation to assess LV and RV systolic and diastolic function in TOF. Our results confirm the previous results obtained by many authors. These include Frommelt et al., \cite{11} who concluded that RV systolic and diastolic function can be assessed noninvasively using DTI analysis of tricuspid annular motion. Other added that DTI offers an easily obtained, quantitative, reproducible echocardiographic measure of LV and RV function \cite{13}. Further, Lytrivi et al., \cite{14} concluded that color DTI indices are superior to traditional echocardiographic techniques given their reproducibility and ability to be obtained even for patients with poor acoustic windows. The use of color DTI derived systolic indices can be proposed as an adjunctive tool in the comprehensive evaluation of the RV function in patients with CHD who frequently have alterations in RV loading conditions.

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