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ORIGINAL ARTICLE

Regional Analysis of Longitudinal Systolic Function of the Right Ventricle After Corrective Surgery of Tetralogy of Fallot Using Myocardial Isovolumetric Acceleration Index

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Abstract To assess regional longitudinal systolic function of the right ventricle in patients with repaired tetralogy of Fallot (TOF) by tissue Doppler imaging-derived isovolumetric acceleration (IVA) index and determine the effect of right-ventricular (RV) enlargement on regional systolic function. In 30 consecutive TOF patients and 30 age-matched controls, myocardial velocity of the RV ventricular free wall in the basal and middle regions were examined in the apical four-chamber view. Peak myocardial velocity during IVA was recorded on the free RV wall. IVA index was calculated as the difference between baseline and peak velocity divided by their time interval. In 23 of the studied TOF patients, magnetic resonance imaging was performed on the same day to determine global RV volume and ejection fraction. IVA index of the RV lateral free wall was significantly lower in the basal (8.31 ± 6.00 vs. 19.00 ± 10.85 m/s^2, $p = 0.0001$) and middle segments (6.56 ± 5.22 vs. 16.17 ± 7.44 m/s^2, $p = 0.0001$) in patients than in controls. Among TOF patients, a negative correlation was found between IVA index in the middle segment and RV end-diastolic volume/body surface area ($r = -0.549$, $p < 0.01$). Similar to other longitudinal RV wall parameters, the IVA index showed a decreased value in the RV free wall, which is related to the impaired regional and global longitudinal RV systolic dysfunction. RV enlargement adversely affects regional longitudinal systolic function.

Keywords Tetralogy of Fallot · Right-ventricular function · Tissue Doppler imaging · Isovolumetric acceleration index · Magnetic resonance imaging

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Introduction

Tetralogy of Fallot (TOF) is the most common congenital cyanotic heart disease occurring beyond infancy and accounts for approximately 10 % of all congenital cardiac defects [2]. Since the first successful surgical correction of TOF by Lillehei et al. [11] in 1955, there has been tremendous improvement in surgical techniques and methods of myocardial protection. Several follow-up studies have shown persistent right-ventricular (RV) systolic and diastolic dysfunction [12, 14]. Quantitative postoperative analysis of RV function is challenging due to distorted ventricular geometry [3]. Although RV ejection fraction can now be derived from volumetric data obtained by magnetic resonance imaging (MRI) or three-dimensional echocardiography [14, 16], the load dependency of ejection fraction limits its utility to determine postoperative RV systolic function [5, 17]. Tissue Doppler imaging (TDI) has the potential to quantify regional longitudinal wall motions [18] and thereby provide information on RV longitudinal function. However, the magnitude of systolic myocardial velocity has also been shown to be both preload and afterload dependent [13]. Vogel et al. [19] described in an experimental animal setting a novel TDI-derived isovolumetric acceleration (IVA) index to estimate RV contractile function that is unaffected by preload and afterload changes. The aim of the present study was to evaluate systolic regional function of the RV free wall using the IVA index and compare it with the “gold standard” of noninvasive assessment of the global contractile function, ejection fraction derived from MRI.

Materials and Methods

Subject Population

Sixty subjects were included in this study. Subject characteristics are listed in Table 1. The TOF group consisted of 30 patients who had corrective surgery of TOF. These 30 patients were selected on the basis that they had no obvious cardiac symptoms and had a good transthoracic window for echocardiography. Mean age at the time of the study was 19.40 ± 9.54 years (range 6–50). Age at complete repair was 5.09 ± 5.32 years (range 5 months–21 years). Follow-up duration was 12.57 ± 6.47 years (range 3–32). During surgical repair, the RV outflow tract was reconstructed by valved homograft in 14 patients (46.7 %) and by RV outflow patch in 16 patients (53.3 %). In 17 patients (56.7 %) a second surgery was performed because of severe RV outflow tract obstruction ($n = 10$), severe pulmonary regurgitation ($n = 5$), or residual ventricular septal defect ($n = 2$). Tissue Doppler data from the TOF group were compared with those from 30 age-matched healthy children who were examined to exclude cardiac abnormalities. Their mean age was 20.52 ± 11.32 years (range 2–47). Informed written consent was obtained from the patients or their parents.

Table 1 Characteristics of the studied TOF patients (mean ± SD)

Age (years)	19.4 ± 9.54
Age at surgery (years)	5.09 ± 5.32
Follow-up period (years)	12.57 ± 6.47
Type of RV outflow	
Reconstruction	
Homograft (%)	14 (46.7)
Enlargement of RVOT with patch (%)	16 (54.3)
Gradient across the RVOT (mmHg)	28.13 ± 14.42
RV systolic pressure (mmHg)	37.7 ± 14.36
Pulmonary insufficiency	
Mild to moderate (%)	$n = 22$ (73.3)
Severe (%)	$n = 8$ (26.7)

RVOT right-ventricular outflow tract, *RV* right ventricle

Echocardiography and TDI Studies

All patients were examined using a 2.5-MHz transducer interfaced with a Vingmed system VII ultrasound system (VII ultrasound scanner; GE Vingmed System, Horten, Norway). Transthoracic imaging was performed with the patient in the left lateral decubitus position. Initially, routine diagnostic imaging was performed, including color flow mapping and continuous wave Doppler. Pulsed Doppler flow across the tricuspid and pulmonary valve was assessed with simultaneous echocardiogram recording in each patient. The degree of pulmonary regurgitation (mild to moderate, severe) was judged by two experienced investigators by the width of the color jet at the valve level and by the extent of the regurgitation jet in the RV on color flow mapping [4].

Afterward, the subject collective underwent color Doppler myocardial imaging (CDMI) study during which the regional basal and middle segments of the lateral RV free wall was analyzed using standard apical four-chamber view [20]. All data were acquired at a high frame rate of >150 frames/s. To achieve such high frame rate, the RV free wall was separately imaged using a small two-dimensional angle. The lateral RV free wall was kept in the center of the ultrasound sector in an attempt to align as near zero degree with the ultrasound beam. An appropriate velocity scale was chosen to avoid CDMI data aliasing. At least three consecutive cardiac cycles (to be used for subsequent analysis) were recorded during normal quit respiration. CDMI data were stored in digital format and transferred to a computer workstation for off-line analysis of regional myocardial velocity curves. This was performed using dedicated software (Echopack, GE Vingmed System). From the myocardial velocity curve, the systolic (S-wave), early diastolic (E-wave), atrial contraction myocardial motion (A-wave), and peak myocardial velocity during isovolumic acceleration (Q-wave or ascending limb of the R-wave to onset of systolic ejection) was recorded (Fig. 1). The IVA index was calculated as the difference between baseline and peak velocity divided by their time interval. Measurements of myocardial acceleration and velocities were calculated from three consecutive cardiac cycles with an average of three measurements recorded. The recordings of 10 patients and 10 normal subjects were randomly selected and analyzed by two

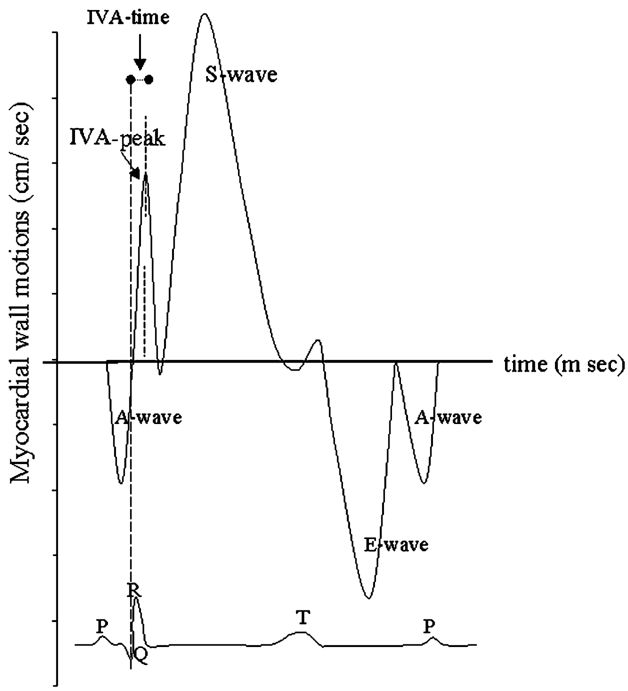

Fig. 1 Diagram of TDI illustrating systolic and diastolic wall motions and calculation of IVA index

independent examiners to assess interobserver variability of the TDI parameters related to ventricular delay.

RV Volume Measurement

Thirty-three patients in the TOF group underwent MTI study in the same day. MRI examination in the same day was not possible to perform in the remaining nine patients, so their data were not included. For MRI imaging, a 1.5-Tesla instrument (Philips, Eindhoven, The Netherlands) was used. Using previously published techniques [5, 17], end-diastolic and -systolic volumes were measured by a third independent observer who was blind to the results of the TDI-derived data analysis. The calculated end-diastolic and -systolic volumes were corrected to the BSA.

Statistical Analysis

Data are expressed as mean ± SD. Assessment of the difference in the means of the measured variables between both groups was generally performed by applying nonparametric Mann–Whitney test for two unpaired samples and Wilcoxon test for two paired samples. For analysis of correlation, nonparametric Spearman rank correlation was performed. Interobserver variability was calculated according to the following formula: (observer 1 − observer 2)/[(observer 1 + observer 2)/2] × 100 %.

Results

Standard Echocardiographic Results

Among the TOF group, none of the examined patients had a residual ventricular or atrial septal defect. Eight patients (26.7 %) had severe pulmonary regurgitation, whereas 22 patients (73.3 %) had mild to moderate pulmonary regurgitation. The gradient across the RV outflow tract was 28.13 ± 14.42 mmHg. Mean RV pressure as assessed from the tricuspid regurgitant jet was 37.70 ± 14.36 mmHg (Table 1).

Regional Longitudinal RV Free Wall Function as Assessed by Ordinary TDI-Derived Parameter

All control subjects (group I) and the TOF patients (group II) had the characteristic pattern of myocardial velocities with an apically directed systolic velocity (S-wave) and an early (E-wave) and late (A-wave) diastolic velocity directed toward the base of the heart, with a gradual velocity decrease from base to middle segment. The decrease in systolic wave velocity from basal to middle segment reaches a significant difference among the two groups. The decrease in E- ($p = 0.028$) and A-wave ($p = 0.014$) velocity from basal to middle segments reached a significant difference among TOF patients but not among the controls. None of the examined normal subjects or patients had reversed systolic or diastolic myocardial velocities in the evaluated regions. Regional peak systolic, early diastolic, and late diastolic velocities were significantly decreased in the basal and middle segments in patients with TOF compared with normal controls (Table 2).

Regional Longitudinal RV Free Wall Function as Assessed by Novel IVA Index

Interobserver variability for RV IVA index in the basal and middle regions was 7 ± 3 and 8 ± 4 %, respectively. In the TOF group, mean IVA index in the basal and middle segments was 8.31 ± 6.00 and 6.56 ± 5.22 m/s^2, respectively. The decrease in the IVA index from basal to middle reached a significant difference among TOF patients ($p < 0.01$) and controls ($p < 0.01$). The IVA index was significantly lower in the basal and middle segments in TOF patients compared with controls (Fig. 2a, b). No influence of surgical technique or incidence of reoperation on IVA index was found. In both groups, IVA index in the basal as well as in the middle segments was heart rate and age independent. No significant correlation was observed in TOF patients between IVA index and gradient across the RV outflow tract. In addition, the IVA index did not significantly correlate with the severity of pulmonary regurgitation as assessed semiquantitatively by echocardiography.

Table 2 TDE values (mean ± SD) in patients with repaired TOF compared with normal subjects

Parameters	Normal ($n = 30$) Group I	TOF ($n = 30$) Group II	*p*
Age (years)	20.52 ± 11.32	19.41 ± 9.54	NS
RV basal S-wave velocity (cm/s)	8.79 ± 4.51	5.64 ± 1.53	0.0001
RV basal E-wave velocity (cm/s)	9.82 ± 1.59	7.38 ± 2.40	0.0001
RV basal A-wave velocity (cm/s)	7.21 ± 1.87	2.53 ± 3.32	0.0001
RV basal IVA peak velocity (cm/s)	6.67 ± 2.66	2.70 ± 1.57	0.0001
RV basal IVA time (ms)	42.21 ± 18.48	33.84 ± 20.11	NS
RV basal IVA index (m/s^2)	19.00 ± 10.85	8.31 ± 6.00	0.0001
RV middle S-wave velocity (cm/s)	7.59 ± 2.56	4.00 ± 1.80	0.0001
RV middle E-wave velocity (cm/s)	9.58 ± 2.76	6.12 ± 1.82	0.0001
RV middle A-wave velocity (cm/s)	6.85 ± 3.02	1.96 ± 1.59	0.0001
RV middle IVA peak velocity (cm/s)	4.73 ± 2.13	2.22 ± 1.77	0.0001
RV middle IVA time (ms)	32.21 ± 11.10	35.00 ± 16.17	NS
RV middle IVA index (m/s^2)	16.17 ± 7.44	6.56 ± 5.22	0.0001

Correlation Between RV Regional Longitudinal Systolic Function Assessed by IVA Index and RV Global Function assessed by MRI

Among TOF patients, a negative correlation existed between the IVA index in the middle segment and RV end-diastolic volume (RVEDV)/BSA ($r = -0.53$, $p = 0.009$) as well as RV end-systolic volume (RVESV)/BSA ($r = -0.46$, $p = 0.029$) (Figs. 3, 4). No correlation was found between IVA index and ejection fraction as well as RV muscle mass.

Discussion

Our data show that the regional longitudinal systolic function of the RV lateral free wall, particularly in the middle segment, as assessed by longitudinal wall velocities and TDI IVA index is decreased late after corrective surgery of TOF even in patients who are clinically asymptomatic. Regional RV systolic function analyzed by IVA index is adversely affected by global RV enlargement but not by the pressure load secondary to RV outflow tract obstruction.

Decreased Regional RV Systolic Function Late After Repair of TOF

The present data show that late after repair of TOF without significant residual hemodynamic lesions other than varying degree of pulmonary regurgitation, longitudinal myocardial systolic wave velocity (S-wave) is markedly decreased in the basal and middle segments of the RV free wall. The same alteration in the longitudinal systolic function was previously reported by others [18, 21]. The significant decrease in the magnitude of longitudinal diastolic wall motions from the basal to the middle segment of the RV lateral free wall in TOF patients, but not in the normal controls, may reflect additional alteration in RV diastolic function. Reversed myocardial systolic and diastolic velocities indicating paradoxical wall motions were not identified in our patients as has been reported in previous study [18]. Different in age at surgery and follow-up duration may explain the discrepancy between the results of our study and those of Vogel et al. [18].

The TDI derived S-wave is a load-dependent parameter [13]; thus, interpretation of regional longitudinal systolic function of the right ventricle after corrective TOF surgery using this parameter may not reflect the actual systolic state. In contrast, IVA index has been shown to be unaffected by preload or afterload hemodynamic changes [19]. In the present study, we were able to demonstrate that the regional longitudinal systolic function of the right ventricle as assessed by IVA index is also decreased. The combined effects of preoperative hypertrophy and hypoxia [1], possible intraoperative myocardial damage [8], change in myocardial architecture [15], and myocardial fibrosis [9] may all contribute to altered longitudinal RV systolic and diastolic function. Regional longitudinal systolic function seems not to be affected by the moderate RV pressure overload secondary to residual RV outflow tract obstruction because no correlation between Doppler gradient across the RV outflow tract and IVA index was found in our study. Accordingly, we can support the results of previous studies signifying that mild to moderate RV outflow tract obstruction after corrective surgery of Fallot may be well tolerated [6].

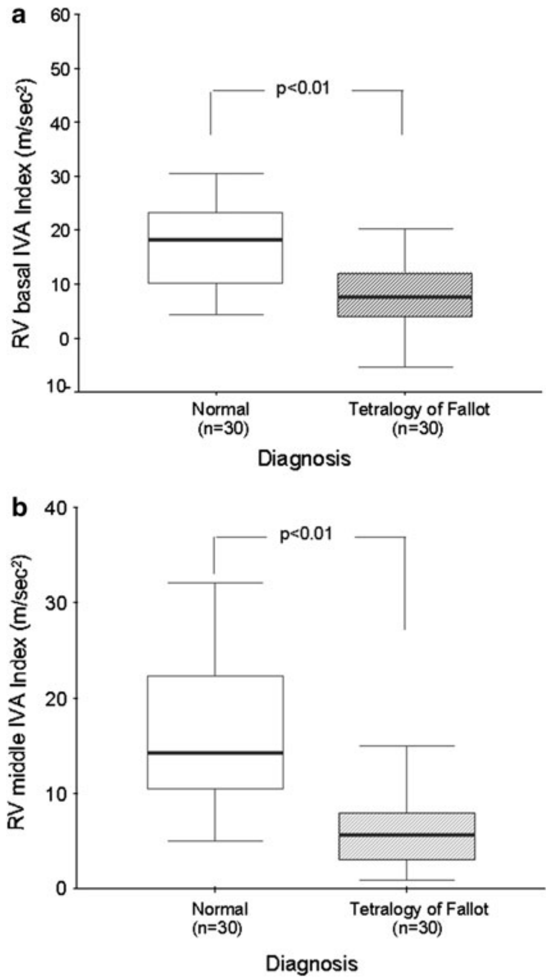

Fig. 2 **a** *Box plot* comparing regional longitudinal systolic function in the basal segment of the RV lateral free wall as assessed by IVA index in TOF patients and normal subject. **b** *Box plot* comparing regional longitudinal systolic function in the middle segment of the RV lateral free wall as assessed by IVA index in TOF patients and normal subjects

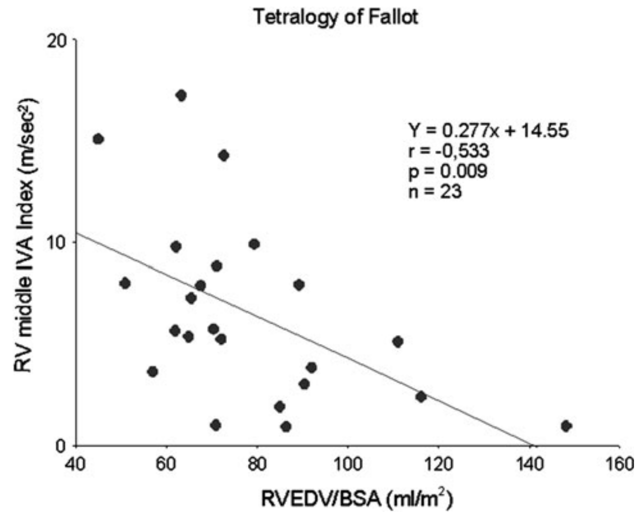

Fig. 3 Correlation among TOF patients between longitudinal systolic function in the middle segment of the RV lateral free wall as assessed by IVA index and RVEDV corrected to BSA as assessed by MRI

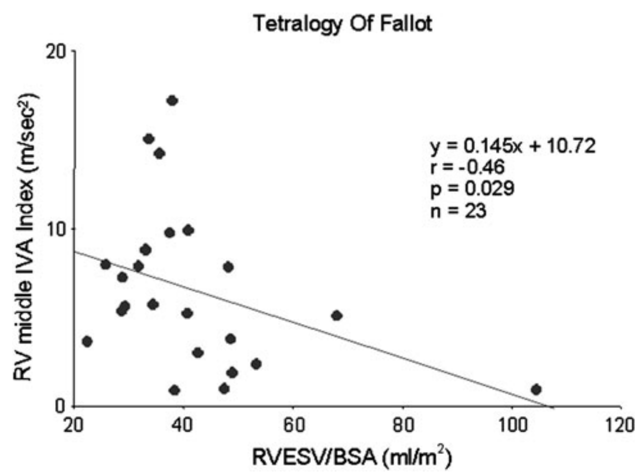

Fig. 4 Correlation among TOF patients between longitudinal systolic function in the middle segment of the RV lateral free wall as assessed by IVA index and RVESV corrected to BSA as assessed by MRI

Effect of RV Enlargement on Regional Longitudinal Systolic Function

A possible deleterious effect of RV enlargement secondary to pulmonary regurgitation has been suggested by previous studies [7, 10]. In the present study, we were able to demonstrate a negative correlation between regional longitudinal systolic RV function as quantified by IVA index and RVEDV/BSA derived from the gold-standard MRI. However, the correlation between both parameters is rather weak, suggesting that RV enlargement may not be the only culprit for regional longitudinal systolic dysfunction.

Optimal timing for reintervention in TOF patients is debatable especially among asymptomatic patients with pulmonary insufficiency. One of the reasons for such debate is the difficulty in quantitative evaluation of RV function among such a cohort. In addition, most of the parameters obtained noninvasively are load dependent. Serial estimation of RV IVA index, a relative load-independent parameter, will provide the treating physician with more reliable information regarding RV contractile status and might therefore improve the proper timing for intervention before irreversible myocardial damage develops. Further studies are needed to prove our hypothesis.

Correlation Between RV Regional Longitudinal Systolic Function Assessed by IVA Index and RV Ejection Fraction Assessed by MRI

In the present study, we did not found a significant correlation between global RV ejection fraction and longitudinal systolic function as assessed by TDI-derived IVA index. This may appear initially as not expected. However, one should remember that the RV lateral free wall may be less affected compared with the outflow tract, in which repaired TOF patients have a ventriculotomy scar or insertion of on contractile materials or a transannular patch. To clarify this hypothesis, one should visualize the RV outflow tract in other views, such as parasternal short-axis view or modified parasternal long-axis view. However, obtaining such views after corrective surgery is difficult in all patients especially among adults. Other possible explanation for the absence of significant correlation between global RV ejection fraction and IVA index is the afterload dependency of the ejection fraction. The IVA index as shown by Vogel et al. [19] is comparatively after-load independent.

Limitations of the Study

One of the major limitations of this study is its cross-sectional and nonlongitudinal nature. Lack of imaging of the RV outflow tract segments in other views and determination of IVA index in additional regions may be another limitation of this study. Although short or modified long-axis views can visualize such segments, delineation of the patch from the myocardium would be difficult.

Conclusion

Using the load-independent IVA index, we were able to quantify regional longitudinal RV systolic and diastolic dysfunction. RV enlargement adversely affects regional longitudinal systolic function, particularly in the middle region. Regional longitudinal RV systolic function as determined by IVA index may not necessarily reflect global RV function.

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