**ORIGINAL**

# Assessment of right ventricular function by isovolumic acceleration of pulmonary and tricuspid annulus in surgically repaired tetralogy of Fallot

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**Abstract : Assessment of right ventricular (RV) function is quite important in patients with surgically corrected tetralogy of Fallot (TOF). However, quantitative assessment of RV function remains challenging, mainly because of the complex RV geometry. This prospective study investigated isovolumic acceleration (IVA), a parameter of myocardial systolic function not influenced by either preload or afterload, using tissue Doppler imaging. We evaluated IVA measured on pulmonary annulus (PA-IVA) and tricuspid annulus (TA-IVA), because we considered that PA-IVA and TA-IVA correspond with systolic function of the RV outflow tract (RVOT) and RV basal function, respectively. Thirty-nine patients with surgically repaired TOF (TOF group) and 40 age-matched healthy children (control group) were enrolled in this study. No significant difference was seen between TA-IVA (2.5 ± 0.8 m/s$^2$) and PA-IVA (2.4 ± 0.8 m/s$^2$) in the control group. In the TOF group, PA-IVA (1.0 ± 0.5 m/s$^2$) was significantly lower than TA-IVA (1.3 ± 0.6 m/s$^2$, $p < 0.05$). Both TA-IVA and PA-IVA were significantly lower in the TOF group than in the control group ($p < 0.05$ each). We concluded that PA-IVA offers a useful index to assess RVOT function in TOF patients. J. Med. Invest. 67 : 145-150, February, 2020**

***Keywords*** **:** *isovolumic acceleration, right ventriclar function, pulmonary annulus, tetralogy of Fallot*

## INTRODUCTION

Right ventricular (RV) function is generally evaluated using parameters such as tricuspid annular plane systolic excursion (TAPSE), fractional area change (FAC), and tricuspid annular systolic velocity (s') by tissue Doppler imaging (TDI) (1). These indexes indicate the systolic motion of the tricuspid annulus towards the cardiac apex, i.e., RV longitudinal systolic function. However, RV morphology is complex, and some regions are not evaluable by analyses in only one direction. The shape of the right ventricle is triangular when viewed from the front. Tricuspid annular motion velocity corresponds to only one of the three sides of the triangle. We hypothesized that pulmonary annular motion velocity would correspond to another side of the triangle and would reflect RV outflow tract (RVOT) function. We have previously reported that motion of the pulmonary annulus differs from that of the tricuspid annulus (2). The present study investigated isovolumic acceleration (IVA), an index that is not influenced by preload or afterload. IVA from TDI has been proposed as a relatively novel index of contractile function for both left and right ventricles (3).

Assessment of RV function is extremely important in congenital heart disease (4). In particular, measurement in the direction from the pulmonary annulus towards the cardiac apex is important in patients with tetralogy of Fallot (TOF) after RVOT reconstruction, because cardiac performance after RVOT reconstruction is thought to have a substantial impact on global RV function in patients with postoperative TOF.

In this study, we hypothesized that measurement of the IVA using pulmonary annular motion velocity would provide useful information regarding RV performance that is not obtainable by measurement of the tricuspid annulus alone.

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## PATIENTS AND METHODS

### *Patients*

The study group comprised 39 consecutive postoperative TOF patients with RVOT reconstruction (TOF group) and 40 healthy subjects (Control group). A total of 79 children were thus enrolled in the present study.

This study were approved by research ethics committees of all the involved institutions, and that written informed consent was obtained from all subjects. This study complied with the Declaration of Helsinki.

### *Echocardiography*

The echocardiographic equipment used was a Preirus digital ultrasound system (Hitachi-Aloka Medical, Tokyo, Japan) equipped with a 3- to 7-Hz transducer. Examination was performed with the patient in the left lateral decubitus position under resting, awake conditions. TDI was recorded during breath-hold at end expiration.

In TDI, the Doppler cursor was placed as close to parallel to the direction of the annular motion as possible, and the sample volume was set at 5 mm to obtain clear Doppler waves. TDI of the tricuspid annulus was obtained from the four apical chamber view, and a sample volume was placed on the tricuspid annulus. TDI of the pulmonary annulus was obtained from the long axis view of the RVOT, and a sample volume was placed on the pulmonary annulus at the RV free wall (Figure 1). Three consecutive heart beats were recorded under both conditions.

### *Measurement of IVA*

After obtaining tissue Doppler images, peak velocities and

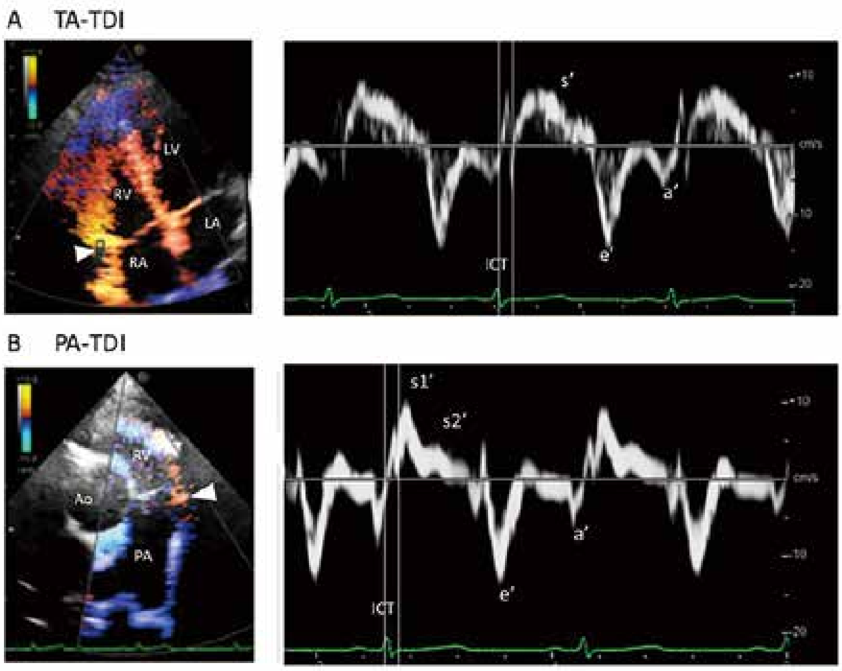


Figure 1 : Representative recording of tissue Doppler imaging
A) Tissue Doppler-derived tricuspid annular velocity.
B) Tissue Doppler-derived pulmonary annular velocity.
Arrowhead shows sample volume position for measurement of tissue velocity.
Ao, aorta ; LA, left atrium ; LV, left ventricle ; PA, pulmonary artery ; AR, right atrium ; RV, right ventricle.

durations of the systolic (s') wave, early diastolic (e') wave, and late diastolic (a') wave were measured. Isovolumic contraction time (ICT) and isovolumic relaxation time (IRT) were also assessed.

IVA indicates acceleration of the wave at the beginning of the isovolumic ventricular contraction phase. IVA index was calculated by dividing peak velocity during the isovolumic contraction phase by the time to reach peak velocity from the start of isovolumic contraction (5). The normal value of IVA in children is reported to be 2-3 cm/m$^2$ (6).

In this study, IVA index was calculated using TDI, and IVAs of the tricuspid annulus (TA-IVA) and pulmonary annulus (PA-IVA) were assessed in healthy individuals and patients with postoperative TOF.

*IVA and postoperative condition in TOF group*

This study also examined the relationship between methods of RVOT reconstruction and IVA in the postoperative TOF group. Patients were divided into three groups according to the method of RVOT reconstruction : an annulus preservation group ; a transannular patch (patch with monocusp) repair group ; and a Rastelli operation with conduit group. The number of patients was 9 (23.1%) in the annulus preservation group, 14 (35.9%) in the transannular patch group, and 14 (35.9%) in the Rastelli group. Two patients (5.1%) were excluded from analysis because of unknown surgical procedure or difficulty in classification. Surgical methods had been selected based on the size of the pulmonary annulus and course of the coronary artery (7) (Table 1). 3-15 years (mean 7 years) have passed since patients of TOF underwent the operation. We also examined the relationship between severity of pulmonary regurgitation (PR) by echocardiography and IVA index. PR can be evaluated by measuring expansion of the color Doppler jet in the right ventricle, but can be influenced by the pressure gradient between the pulmonary artery and right ventricle during diastole (8). Another evaluation method observes the site at which regurgitation of blood was recorded by color Doppler imaging (regurgitation restricted to the vicinity of the pulmonary valve was defined as mild ; regurgitation from the main pulmonary artery as moderate ; and regurgitation from a distal branch of the pulmonary artery as severe) (9). In this study, severity of PR was classified as trivial, mild, moderate, or severe based on the echocardiographic findings in a comprehensive manner. The number of patients was 5 (12.8%) in the trivial PR group, 12 (30.8%) in the mild PR group, 15 (38.5%) in the moderate PR group, and 3 (7.7%) in the severe PR group. Four patients (10.2%) had unknown results. Correlations between PR severity and IVA index were analyzed (Table 1). In addition, tricuspid regurgitation (TR) was observed in all patients in the postoperative TOF group, and the correlation between RV pressure (as estimated from TR) and IVA index was analyzed. RV pressure had been measured in only 28 of the 39 patients. We therefore performed statistical analysis for these 28 patients.

Table 1. Classification of patients with TOF by operative procedure and pulmonary regurgitation

| Operative procedure | n = 39 |
|---|---|
| Pulmonary valve preservation | 9 (23.1%) |
| Transannular patch | 14 (35.9%) |
| Rastelli operation | 14 (35.9%) |
| Unclassifiable | 2 (5.1%) |
| **Pulmonary regurgitation** | **n = 39** |
| Trivial | 5 (12.8%) |
| Mild | 12 (30.8%) |
| Moderate | 15 (38.5%) |
| Severe | 3 (7.7%) |
| Unclassifiable | 4 (10.2%) |

*Statistical analysis*

All data are expressed as mean ± standard deviation (SD) or as median with 5th – 95th percentiles and 95% confidence interval. Statistical significance was determined using Student's t-test, the Mann-Whitney U-test, or analysis of variance followed by the Tukey multiple comparison test, as appropriate. Linear regression analyses were performed to assess correlations between IVA and hemodynamic parameters. All statistical data were calculated using IBM SPSS Statistics version 22. Values of $p < 0.05$ (two-sided) were considered significant.

## RESULTS

A summary of subject characteristics is shown in Table 2. Mean age at the time of the study was 10.8 ± 2.8 years in the control group and 13.2 ± 9.2 years in the TOF group. The percentage of males was 65.0% in the control group and 67.5% in the TOF group. With regard to physique, body surface area (BSA) was 0.79 ± 0.28 $m^2$ in the control group and 1.01 ± 0.49 $m^2$ in the TOF group. Heart rate (HR) was 69.6 ± 10.5 beats/min in the control group and 79. ± 13.0 beats/min in the TOF group. BSA and HR are significantly lower value in the control group. No significant differences in other background characteristics were apparent between groups (Table 2).

Table 2. Clinical characteristics of subjects

| | Control (n = 40) | TOF (n = 39) | P value |
|---|---|---|---|
| Sex (male, %) | 65 | 67.5 | NS |
| Age (y) | 10.8 ± 2.8 | 13.2 ± 9.2 | NS |
| Weight (kg) | 37.7 ± 13.7 | 33.0 ± 19.5 | NS |
| Height (cm) | 140.7 ± 18.2 | 129.3 ± 30.7 | NS |
| Body surface area ($m^2$) | 0.79 ± 0.28 | 1.01 ± 0.49 | < 0.05 |
| Heart rate (beats/min) | 69.6 ± 10.5 | 79.1 ± 13.0 | < 0.05 |

TOF, tetralogy of Fallot ; NS, not significant

*TDI of the tricuspid annulus*

TDI of the tricuspid annulus was compared between the control and TOF groups. Systolic velocity (s') was significantly lower in the TOF group ($p < 0.05$). Early diastolic velocity (e') and end-diastolic velocity during atrial contraction (a') were also significantly lower in the TOF group ($p < 0.05$). Duration of isovolumic contraction had no significant difference between the TOF and the control groups ($p = 0.06$).

TA-IVA (calculated by dividing peak velocity during the isovolumic contraction phase by the time to reach peak velocity from the start of isovolumic contraction) was 2.5 ± 0.8 $m/s^2$ in the control group and 1.3 ± 0.6 $m/s^2$ in the TOF group, showing a significantly lower value in the TOF group ($p < 0.05$).

*TDI of pulmonary annulus*

TDI of the pulmonary annulus was compared between the control and TOF groups. Tissue Doppler measurement of the pulmonary annulus was recorded. Two peaks were seen in systole ($s_1$', $s_2$') in all patients. Systolic velocity ($s_1$') was significantly lower in the TOF group. Systolic velocity ($s_2$') had no significant difference between the two groups. Early diastolic velocity (e') and End-diastolic velocity during atrial contraction (a') were significantly lower in the TOF group ($p < 0.05$). PA-IVA was 2.4 ± 0.8 $m/s^2$ in the control group and 1.0 ± 0.5 $m/s^2$ in the TOF group, showing a significantly lower value in the TOF group ($p < 0.05$) (Table 3).

*Comparison between TA-IVA and PA-IVA*

We compared TA-IVA and PA-IVA obtained from the above-mentioned measurements in the control and TOF groups. In the control group, no significant difference was seen between TA-IVA (2.5 ± 0.8 $m/s^2$) and PA-IVA (2.4 ± 0.8 $m/s^2$) (Figure 2A). On the other hand, PA-IVA (1.0 ± 0.5 $m/s^2$) was significantly lower than TA-IVA (1.3 ± 0.6 $m/s^2$ ; $p < 0.05$) (Figure 2B) in the TOF group. The results showed that systolic performance of the pulmonary annulus towards the cardiac apex was inferior to that of the tricuspid annulus towards the apex in the post-

Table 3. Measured values from tissue Doppler imaging

| | | Control (n = 40) | TOF (n = 39) | P value |
|---|---|---|---|---|
| Tricuspid annular | IVA ($m/s^2$) | 2.5 ± 0.8 | 1.3 ± 0.6 | < 0.05 |
| motion (cm/s) | ICT (ms) | 59.7 ± 12.2 | 58.30 ± 15.40 | NS |
| | s' (cm/s) | 12.6 ± 2.8 | 7.9 ± 2.1 | < 0.05 |
| | e' (cm/s) | 15.0 ± 2.6 | 11.7 ± 3.5 | < 0.05 |
| | a' (cm/s) | 8.0 ± 2.2 | 6.1 ± 2.0 | < 0.05 |
| | s' duration (ms) | 272.9 ± 26.2 | 258.0 ± 46.0 | NS |
| | e' duration (ms) | 200.9 ± 39.3 | 152.9 ± 38.8 | < 0.05 |
| | a' duration (ms) | 131.6 ± 18.6 | 118.2 ± 26.5 | < 0.05 |
| Pulmonary annular | IVA ($m/s^2$) | 2.4 ± 0.8 | 1.0 ± 0.5 | < 0.05 |
| motion (cm/s) | ICT (ms) | 49.21 ± 10.26 | 55.76 ± 15.78 | < 0.05 |
| | $s_1$' (cm/s) | 12.0 ± 2.5 | 6.7 ± 2.0 | < 0.05 |
| | $s_2$' (cm/s) | 4.0 ± 1.1 | 3.6 ± 1.2 | NS |
| | e' (cm/s) | 13.7 ± 3.0 | 10.0 ± 3.9 | < 0.05 |
| | a' (cm/s) | 5.4 ± 1.4 | 3.8 ± 1.9 | < 0.05 |
| | $s_1$' duration (ms) | 108.2 ± 15.8 | 121.5 ± 56.0 | NS |
| | $s_2$' duration (ms) | 179.3 ± 23.4 | 182.9 ± 53.6 | NS |
| | e' duration (ms) | 135.5 ± 19.3 | 136.0 ± 37.1 | NS |
| | a' duration (ms) | 98.5 ± 25.8 | 107.2 ± 31.0 | NS |

IVA, isovolumic acceleration ; ICT, isovolumic contraction time ; IRT, isovolumic relaxation time ; TOF, tetralogy of Fallot ; NS, not significant operative TOF group. Subsequently, TA-IVA and PA-IVA were compared between the control and TOF groups.

TA-IVA was significantly lower in the TOF group ($1.3 \pm 0.6$ m/s$^2$) than in the control group ($2.5 \pm 0.8$ m/s$^2$ ; $p < 0.05$). Furthermore, PA-IVA was also significantly lower in the TOF group than in the control group (control, $2.4 \pm 0.8$ m/s$^2$ ; TOF, $1.0 \pm 0.5$ m/s$^2$ vs. $2.4 \pm 0.8$ m/s$^2$ ; $p < 0.05$) (Figure 2C, D). These results showed decreased RV function in the postoperative TOF group, suggesting that pulmonary annular velocity may represent a useful index, like tricuspid annular velocity, which has been traditionally used for assessing RV function.

*Relationship between IVA and postoperative condition in the TOF group*

We analyzed the relationship between methods of RVOT reconstruction and IVA in the TOF group. Multiple comparisons of TA-IVA and PA-IVA were performed between the three groups.

TA-IVA was $1.9 \pm 0.7$ m/s$^2$ in the annulus preservation group, $1.3 \pm 0.6$ m/s$^2$ in the transannular patch group, and $1.0 \pm 0.4$ m/s$^2$ in the Rastelli group.

Tukey's test for multiple comparisons showed that IVA was significantly lower in the Rastelli group than in the annulus preservation group ($p = 0.006$). No significant statistical differences were seen between the annulus preservation and transannular patch groups, or between the transannular and Rastelli groups (Figure 3A). PA-IVA was $1.3 \pm 0.8$ m/s$^2$ in the annulus preservation group, $1.2 \pm 0.3$ m/s$^2$ in the transannular patch group, and $0.7 \pm 0.3$ m/s$^2$ in the Rastelli group.

Tukey's test for multiple comparisons showed no significant difference between the annulus preservation and transannular patch groups, but a significantly lower result from in the Rastelli group compared with the annulus preservation or transannular patch group ($p = 0.038$ and $0.038$, respectively) (Figure 3B).

Next, the relationship between PR and IVA was examined. In this study, a comparison was made between the trivial-mild group (17 patients, 43.5%) and the moderate-severe group (18

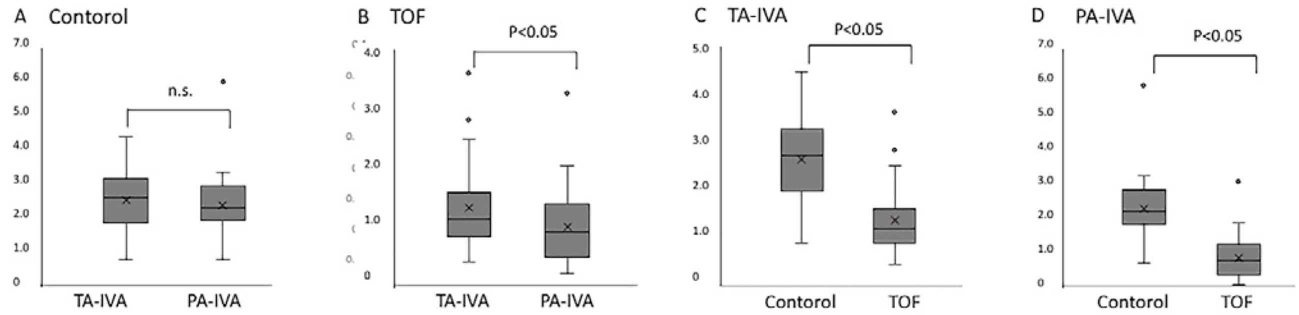


Figure 2 : Measurement of TA-IVA and PA-IVA in each group
Boxes show the distribution of IVA (25th and 75th percentiles ; central line, median). Vertical lines represent range between the 5th and 95th percentiles.
Mean values are shown as "x".
No significant difference in TA-IVA and PA-IVA (A) is seen in the control group, while PA-IVA is significantly lower than TA-IVA in the TOF group (B).
Both TA-IVA and PA-IVA are significantly lower in the TOF group than in the control group (C and D).
TA-IVA, isovolumic acceleration of tricuspid annulus ; PA-IVA, isovolumic acceleration of pulmonary annulus.

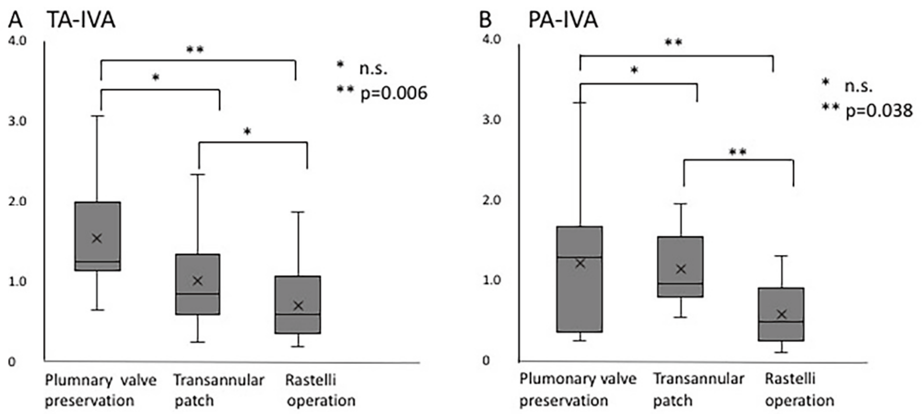


Figure 3 : TA-IVA and PA-IVA in each operative method
Boxes show the distribution of IVA (25th and 75th percentiles; central line, median). Vertical lines represent the range between the 5th and 95th percentiles.
Mean values are shown as "x".
IVA is significantly lower in the Rastelli group than in the annulus preservation group. No significant differences are seen between the annulus preservation and transannular patch groups, or between the transannular and Rastelli groups (A). PA-IVA is significantly lower in the Rastelli group than in the annulus preservation or transannular patch groups (B).

patients, 46.1%).

TA-IVA was $1.2 \pm 0.5$ m/s$^2$ in the trivial-mild group and $1.3 \pm 0.7$ m/s$^2$ in the moderate-severe group, with no significant difference ($p = 0.07$). The PA-IVA was $1.2 \pm 0.7$ m/s$^2$ in the trivial-mild group and $0.9 \pm 0.4$ m/s$^2$ in the moderate-severe group, and there was also no significant difference between the two groups ($p = 0.26$) (Figure 4A, B). Both TA-IVA and PA-IVA tended to be lower in patients with severe PR, but the differences were not significant. Although decreased right ventricular function is suggested in certain patients with severe PR, there was no significant difference between the two groups. This may be due to the fact that IVA indicates myocardial acceleration during isovolumic contraction and that it is not influenced by preload or afterload (i.e., volume overload by PR). Furthermore, the relationship between RV systolic pressure and IVA was examined. RV systolic pressure was estimated by tricuspid regurgitation pressure gradient (TRPG) on echocardiography. The measurements were available only in 28 of 39 patients. Although we had expected that IVA would decrease due to increase in right ventricular pressure, there were no correlations between right ventricular pressure and TA-IVA or PA-IVA (the Pearson correlation coefficient was -0.16 for TA-IVA and 0.21 for PA-IVA, with a slightly higher value for PA-IVA) (Figure 5A, B).

## DISCUSSION

There are few reports that evaluated right ventricle in the direction from the pulmonary annulus towards the cardiac apex, i.e., the right ventricular outflow tract direction. We considered about a difference of the movement in the longitudinal direction from the tricuspid annulus towards the cardiac apex and that in the right ventricular outflow tract direction using IVA, and we report that measurement in the right ventricular outflow tract direction is useful of evaluating RV function.

Traditionally, RV systolic function has been evaluated using parameters such as TAPSE, FAC, and tricuspid annular systolic velocity (s') by TDI in the apical four-chamber view. However, these indexes are used to assess the systolic motion of the tricuspid annulus towards the cardiac apex, i.e., systolic function only in longitudinal direction.

We have previously shown that the motion of the pulmonary annulus towards the cardiac apex, which indicates RVOT function, was different from the tricuspid annulus motion towards the cardiac apex in the RV, and reported that TDI could assess the two different motions (2).

In this study, we analyzed patients with postoperative TOF who were expected to have decreased systolic function after

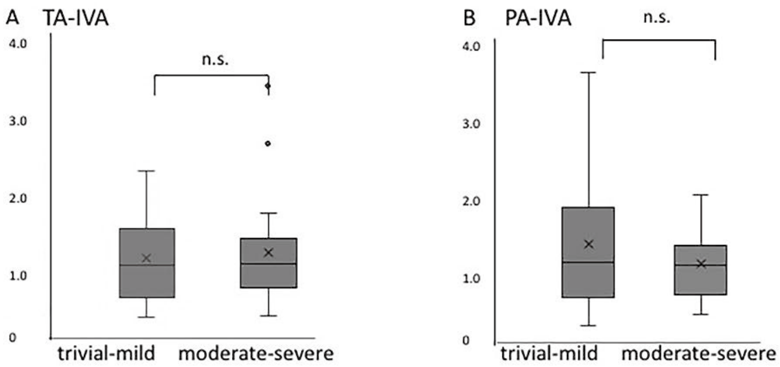


Figure 4 : Relationship between IVA measurement and PR severity
Boxes show the distribution of IVA (25th and 75th percentiles; central line, median). Vertical lines represent the range between the 5th and 95th percentiles.
Mean values are shown as "x".
TA-IVA is $1.2 \pm 0.5$ m/s$^2$ in the trivial-mild group and $1.3 \pm 0.7$ m/s$^2$ in the moderate-severe group, showing no significant difference. PA-IVA is $1.2 \pm 0.7$ m/s$^2$ in the trivial-mild group and $0.9 \pm 0.4$ m/s$^2$ in the moderate-severe group, and no significant difference is evident between groups.

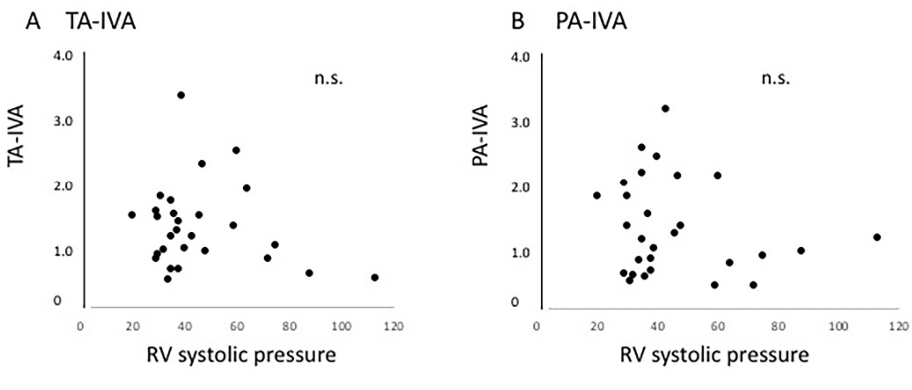


Figure 5 : Relationship between IVA measurement and RV systolic pressure
No correlations are seen between right ventricular systolic pressure and TA-IVA or PA-IVA.

right ventricular outflow tract reconstruction. PA-IVA was lower in patients with postoperative TOF compared with healthy children, and PA-IVA was significantly lower than that TA-IVA in patients with TOF. In addition, there was a significant difference in PA-IVA between the annulus preservation group and the Rastelli group using an artificial conduit.

This indicates that measurement in the right ventricular outflow tract direction can provide information regarding right ventricular function that is not obtainable by measurement in the longitudinal direction in the right ventricle.

The assessment of right ventricular function is difficult because of the complexity of the structure and morphology. Our results suggest that combined measurement of movement in the longitudinal direction from the tricuspid annulus towards the cardiac apex and that in the direction from the pulmonary annulus towards the cardiac apex may contribute to the overall assessment of right ventricular function.

In addition, given that both volume and pressure of the right ventricle are influenced by preload and afterload, IVA is considered useful as a parameter not influenced by these factors.

These findings suggest that IVA in right ventricular outflow tract direction, can be the new parameter of RV systolic function.

Assessment of left ventricular function and RV function are equally important for the management of congenital heart diseases. In the future, we plan to use the parameter for assessing RV function in patients with a wide variety of congenital heart diseases.

## LIMITATIONS

This study compared 39 patients with TOF and 40 healthy individuals. Although age was generally matched between groups, age and body size, etc., varied among postoperative patients with TOF.

Furthermore, there was a possibility that tissue Doppler results were influenced by the restricted movement of the pulmonary annulus due to postoperative adhesions, because the anterior wall of the right ventricle is anatomically close to the chest wall. In this regard, analyses of the timing of surgery and duration from surgery to time of study are also needed. In addition, the relationship between the parameter and RV volume or PR should be examined using imaging modalities other than echocardiography, such as magnetic resonance imaging.

Further accumulation of cases is needed. In future studies, patients with congenital heart diseases other than tetralogy of Fallot need to be investigated.

## CONCLUSION

IVA of the pulmonary annulus offers a useful index of RVOT function in postoperative patients with TOF.

## CONFLICTS OF INTEREST

Akemi Ono declares no conflict of interest.
Yasunobu Hayabuchi declares no conflict of interest.
Shoji Kagami declares no conflict of interest.
Manami Tanaka declares no conflict of interest.

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