Indonesian Journal of Cardiology
Indonesian J Cardiol 2024:45:150-158
pISSN: 2830-3105 / eISSN: 2964-7304
doi: 10.30701/ijc.1451

Case Report

Non–surgical Intervention for Palliative Treatment in Late–presentation Tetralogy of Fallot (TOF): Is There Any Hope?

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Abstract

Background: Late congenital heart disease (CHD) in patients with tetralogy of Fallot (TOF). Due to the variable severity of defects in patients with TOF, late presentation of CHD may only be discovered beyond the neonatal period. Chronic polycythemia from TOF may increase the risk of hemorrhaging during surgery and patients with untreated TOF risk developing CHD-related pulmonary hypertension. Non-surgical transcatheter palliation in patients with TOF may be applied; however, studies regarding the efficacy and safety of the method remained very scarce. Therefore, we report two cases of late-presenting TOF treated with non-surgical transcatheter palliation due to high perioperative risks for surgical repair of the defects.

Case Illustration: A 41-year-old (Case 1) and 19-year-old man (Case 2) were admitted to the emergency room due to a chief complaint of dyspnea and severe headache with a previous history of hypoxic spells, respectively. Physical findings showed signs of cardiomegaly and right ventricular hypertrophy. Echocardiography confirmed TOF for both cases. Due to high perioperative risks for surgical repair, non-surgical palliation for both cases was performed, with Right Ventricular Outflow Tract (RVOT) stenting for case 1 and Balloon Pulmonary Valvuloplasty (BPV) for case 2. Both cases showed systolic function and functional capacity improvement after both interventions.

Conclusion: Non-surgical transcatheter palliation is the preferred treatment approach for late-presentation TOF that pose major comorbidities such as hypercyanotic spell and myocardial dysfunction which are not amenable to surgery. Although PA size after palliation had not been evaluated further yet, Improvement of systolic function and functional capacity denoted the benefit of initial palliation. Thus, non-surgical transcatheter palliation as a bridging procedure before complete surgical repair in late-presentation TOF might be a promising option.

(Indonesian J Cardiol. 2024;45:150-158)

Keywords: *Complications, congenital heart disease, palliative, Tetralogy of Fallot.*

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Introduction

Late Congenital Heart Disease (CHD) refers to late presentation in the natural history of the specific cardiac defect, with consequent transient or irreversible hemodynamic and pathologic alterations that would impact the medical and surgical approach, risk, and outcome.[1,2]

Tetralogy of Fallot (TOF) is one of the most common late cyanotic CHD. TOF occurs in approximately 1 in 3600 live births and accounts for 3.5% of infants born with congenital heart disease.[2] Chronic cyanosis in the setting of unoperated tetralogy of Fallot can lead to polycythemia with or without disseminated intravascular coagulopathy, hepatic or renal dysfunction, or stroke. In low- and middle-income countries, however, patients with tetralogy of Fallot commonly present for the first time during childhood, adolescence, or even late adulthood. Some would be natural survivors of the so-called "good anatomy tetralogy of Fallot" with minimal cyanosis and therefore manifest limited consequences of chronic cyanosis. Most patients, however, are markedly cyanotic and may manifest the deleterious sequelae of chronic polycythemia with hyper-viscosity and varying degrees of consumptive coagulopathy.[3] Furthermore, Chronic polycythemia increases the risk of postoperative bleeding from surgical sites, as well as internal organs. CHD-related pulmonary hypertension has been extensively reviewed elsewhere. The incidence of postoperative pulmonary hypertension is much higher in late-presenting CHD.[1,2,4–6]

Uncorrected Tetralogy of Fallot with major comorbidities is significantly limited for definitive complete repair since it could lead to polycythemia with or without disseminated intravascular coagulopathy, hepatic or renal dysfunction, or stroke.[3,7] Traditionally, palliative options such as a surgical systemic to pulmonary shunt (Blalock-Taussig or BT shunt) are frequently employed as bridging procedures before definitive complete repair. Late-presentation Tetralogy of Fallot (TOF) poses major comorbidities that increase the risk of surgery.[1,2] Procedure due to high risk for surgery.

Case Presentation

Case 1

A 41-year-old man was admitted to our hospital with a complaint of breathlessness at rest three days ago accompanied by bilateral leg edema. He had a history of having phlebotomy about 3 times. He knew that he had cardiac disease in the last 6 months. He was also visibly fatigued and experiencing dyspnea without any loss of consciousness or seizure. He denied having a history of breathlessness or bluish-lips discoloration since birth, he also did not have a history of stunted growth and difficulty in feeding. He was born spontaneously, at term, with a birth weight of 3300 g. No family history with the same symptoms were reported.

On physical examination, the patient was lethargic and looked very ill. Body weight of 55 kilograms, body height of 160 cm, blood pressure was 131/84 mmHg, heart rate 96 bpm, respiratory rate 20 x/min, and body temperature was 36.7 C. Peripheral oxygen saturation was 65%. Jugular Venous Pressure (JVP) was distended (5+4 cm H2O). An auscultatory examination showed normal first heart sound, single not attenuated second heart sound was found with ejection systolic murmur grade 3/6 in the upper left sternal border. Hepatic enlargement palpated 2 cm below arcus costae. Both extremities showed clubbing fingers and cyanotic. Electrocardiography showed sinus rhythm and right axis deviation (RAD) with Right Ventricular Hypertrophy (RVH).

Electrocardiography examination at admission showed sinus rhythm, QRS rate 75 x/m, QRS axis +124, QRS duration 80 ms, Abrupt R V1-V2, Right Axis Deviation (RAD), Right Ventricular Hypertrophy (RVH). Chest Xray (C-XR) 3 months before admission showed heart enlargement with cardiothoracic ratio of 66%, reduced pulmonary segment, flatten cardiac waist, upward apex, which showed a boot shaped heart and oligemic pulmonary vascular pattern without pulmonary infiltrates A 2D echocardiography examination was performed to evaluate the LV and RV function. It showed normal LV size with good LV systolic function (LVEF 71%), dilated and right ventricular hypertrophy with normal RV systolic function (TAPSE 18 mm), and moderate to severe tricuspid regurgitation (TR V max 5,3 m/s) (Figure 4. A-D). On the 2D echocardiography,

50% overriding aorta accompanied with antero-cephalad deviated septum which caused infundibular and valvar pulmonary stenosis, subaortic VSD with diameter 22 mm, L to R shunt with good LV systolic function (LVEF 71%), dilated and right ventricular hypertrophy with normal RV systolic function (TAPSE 18 mm).

A 3D echocardiography examination was performed. It showed that LVEF was 59% and RVEF was 49% Laboratory examination showed polycythemia with elevated. Hemoglobin and Hematocrit level Hemoglobin 20.2 g/dl, Hematocrit 69%). He was then diagnosed with TOF.

Cardiac multi-slice computed tomography (MSCT) was performed to measure pulmonary artery size. The scan showed a McGoon Ratio of 1.7, PA half size 14 mm, Bilateral SVCs, Collaterals from the Descending Aorta, and Normal coronary artery. The patient was planned for RVOT stenting with no. 10 mm x 56 mm with balloon pre-dilatation using no. 7,0 mm x 80 mm. The stent was placed in RVOT with a good result. Angiography was performed to visualize the RVOT obstruction due to Infundibular Pulmonary Stenosis. Before RVOT stenting, Pre- dilatation with Balloon no. 7,0 mm x 80 mm was performed followed by stent placement no. 10 mm x 56 mm at RVOT. After RVOT stenting, we performed 3D TTE to evaluate the LV function and RV function. It showed LV systolic function LVEF 67% by 3D echocardiography, dilated and hypertrophy right ventricle, RVEF 42%, RV FAC 36%, RV free wall GLS -11,3%. There is a stent attached to RVOT with a proximal stent protruding to the RV inflow area without disturbing tricuspid closure. RV-PA gradient 70 mmHg, mild tricuspid regurgitation, TVG 100 mmHg.

Case Illustration 2

A 19-year-old boy came to the National Cardiovascular Centre Harapan Kita with a chief complaint of severe headache lasting for a day. Severe headache accompanied by a history of three times episodes of hypoxic spell in the last 1 year. The patient also felt easily fatigued and breathless after doing mild activities. The patient also had a history of bluish discoloration on lips and tip of nails fingers and toes in the last 2 years. Patients had a history of repeated phlebotomy about 7 times a year. No prior history of repeated cough or fever, his parents mentioned a history of cyanotic spell at 8 months of age. He was born spontaneously, assisted by a midwife, with no history of blue appearance after birth, birthweight of 4200 grams, and no history of familial congenital heart disease.

On physical examination, the patient was fully conscious but looked severely ill. Body weight of 59 kilograms, body height of 170 cm, blood pressure was 178/112 mmHg, heart rate 96 bpm, respiratory rate 20 x/min, and body temperature was 36.7 C. Peripheral oxygen saturation was 60%. Jugular Venous Pressure (JVP) was not distended, Auscultatory examination found normal first heart sound, the single not attenuated second heart sound with ejection systolic murmur grade 3/6 in the upper left sternal border. Both extremities showed clubbing fingers and cyanotic. Electrocardiography examination showed sinus rhythm with Right axis deviation (RAD) and Right Ventricular Hypertrophy (RVH).

The ECG 1 year before BPV showed sinus rhythm, QRS rate 113 x/m, Abrupt R V1-V2 with Right axis deviation (RAD) and Right Ventricular Hypertrophy (RVH). Chest x-ray 4 days before BPV showed heart enlargement with cardiothoracic ratio 60%, flatten cardiac waist, slightly upward apex and oligemic pulmonary vascular pattern and no pulmonary infiltrates seen. The 2D echocardiography showed normal LV size with reduced LV systolic function (LVEF 49%) and reduced RV systolic function (TAPSE 11 mm) with 50% Overriding aorta accompanied with antero-cephalad deviated septum which caused severe valvar pulmonary stenosis (PS), subaortic VSD with diameter 21 mm, L to R shunt. The patient was planned to have a right heart catheterization and was scheduled for 22nd October 2021. However, before RHC was performed, it was found that peripheral saturation was 53% and TEE evaluation pre-RHC found Tetralogy of Fallot, subaortic VSD with valvar severe Pulmonary Stenosis then it was decided to do Balloon Pulmonary Valvuloplasty (BPV). The balloon was successfully dilated with an improvement of RV-PA gradient from 77 mmHg to 50 mmHg and peripheral saturation was significantly improved from 53% to 90% while aortic saturation was significantly improved from 76% to 94%.

Angiography was performed to visualize the

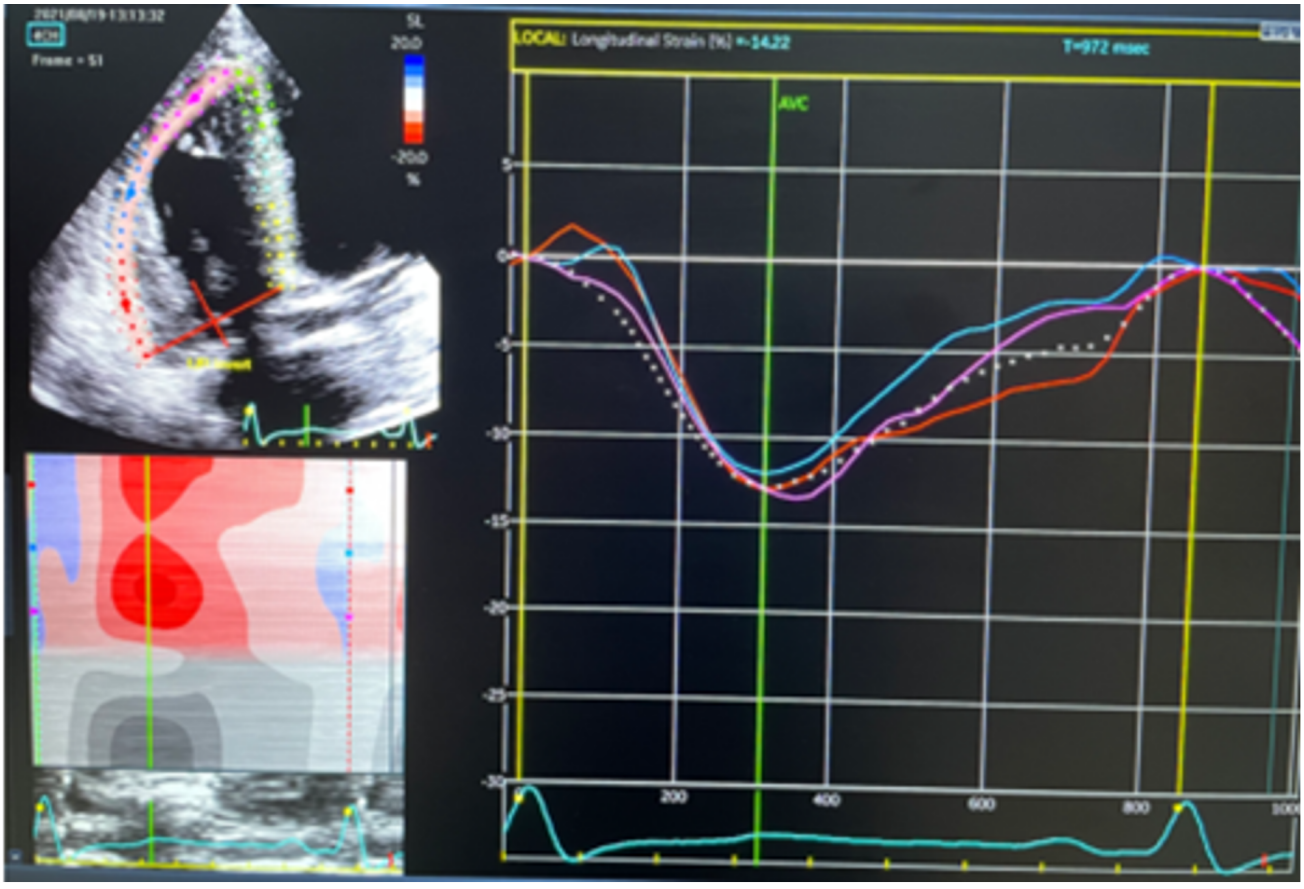

Figure 1. Speckle tracking echocardiography to assess RV-free wall GLS after RVOT stenting.

RVOT obstruction due to severe valvar Pulmonary Stenosis. BPV was performed by dilating the Balloon 18 mm x 3.0 mm x 110 cm RV-PA until the balloon waist disappeared. After BPV, we performed 3D TTE and speckle tracking echocardiography to evaluate LV function and RV function. It showed RV Free Wall GLS -17,8% and LV GLS -14,7% after BPV.

Discussion

Non-surgical palliation approach in late presentation TOF

Twenty-five percent of infants with severe obstruction not treated surgically will die within the first year.[1] If Left untreated, about 40% of TOF patients will die by age 3 years, 70% by age 10 years, and 95% by age 40 years. After the first year, the risk is constant until age 25 years, but then it increases.[1] The severity of RVOTO dominates clinical presentation. Moderate RVOTO gives rise to a systolic murmur in an asymptomatic child. Cyanosis may develop between 6–8 months as infundibular stenosis increases, producing a right to left shunt. The presentation may also be with a hypercyanotic attack from total obstruction of the infundibular.[6] Major comorbidities found in TOF such as severe cyanotic condition, small pulmonary arteries, atrioventricular Septal Defect (AVSD), or complex defects are considered to be high preoperative risk for surgical repair.[6,7] Chronic hypoxia in late presentation TOF is a strong risk factor for myocardial dysfunction. Traditionally, surgical systemic to pulmonary shunt (Blalock-Taussig or BT shunt) is frequently employed as bridging procedures for patients who are not ideal for complete surgical repair. With the advancement of technology, non-surgical palliation was intended to be a salvage procedure for late presentation that poses high-

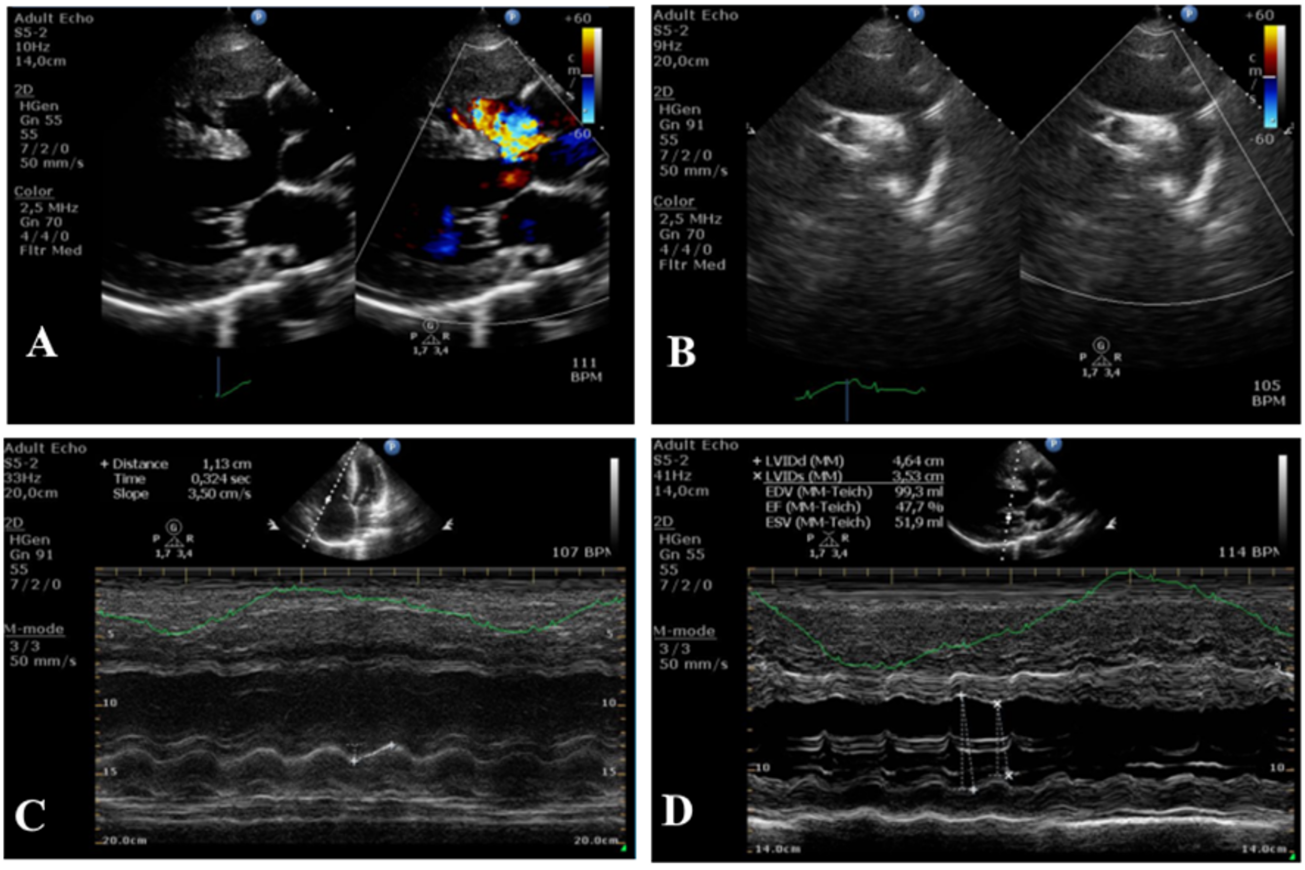

Figure 2. (A). Echocardiography 2D before BPV showed 50% Overriding aorta accompanied by anterocephalad deviated septum which caused (B) severe valvar pulmonary stenosis (PS), subaortic VSD with diameter 21 mm, L to R shunt (C) reduced LV systolic function (LVEF 71%), (D). dilated and right ventricular hypertrophy with reduced RV systolic function (TAPSE 18 mm).

risk conditions for surgery.[8,9] Recent options such as Right Ventricular Outflow Tract (RVOT) stenting and Balloon Pulmonary Valvulotomy (BPV) had already been known as non-surgical palliation.

In our case, RVOT stenting was performed in case 1 due to a hypercyanotic spell with myocardial dysfunction due to chronic hypoxia. Due to infundibular pulmonary stenosis, RVOT stenting is preferred over other approaches. BPV was performed in case 2 due to a hypercyanotic spell since it had pulmonary valvular stenosis. BPV is preferred over other approach in pulmonary valvular stenosis cases.[1,6]

Surgical Primary Repair following Initial Palliation

Trend had been increasingly toward primary repair ever since Castaneda and Jonas demonstrated in the 1980s that excellent outcomes could be achieved in early infancy. Numerous studies demonstrated that primary repair of ToF between the ages of 3-9 months has become the standard of care. However, higher-risk patients in whom staged repair may still be indicated could be divided into: (i) neonates/small infants with small pulmonary arteries (PAs) and (ii) complex anatomical variants (such as Fallot/Atrioventricular Septal Defect [AVSD] or major non-cardiac conditions) where single-stage repair may carry higher risk or there may be benefit from planned delay.

Concern towards primary surgical repair after RVOT stenting had been increasing. Barron, et al showed low procedural-related mortality in surgical repair following RVOT stenting. RVOT stenting seems a safe alternative to systemic-to-pulmonary shunting to achieve improved

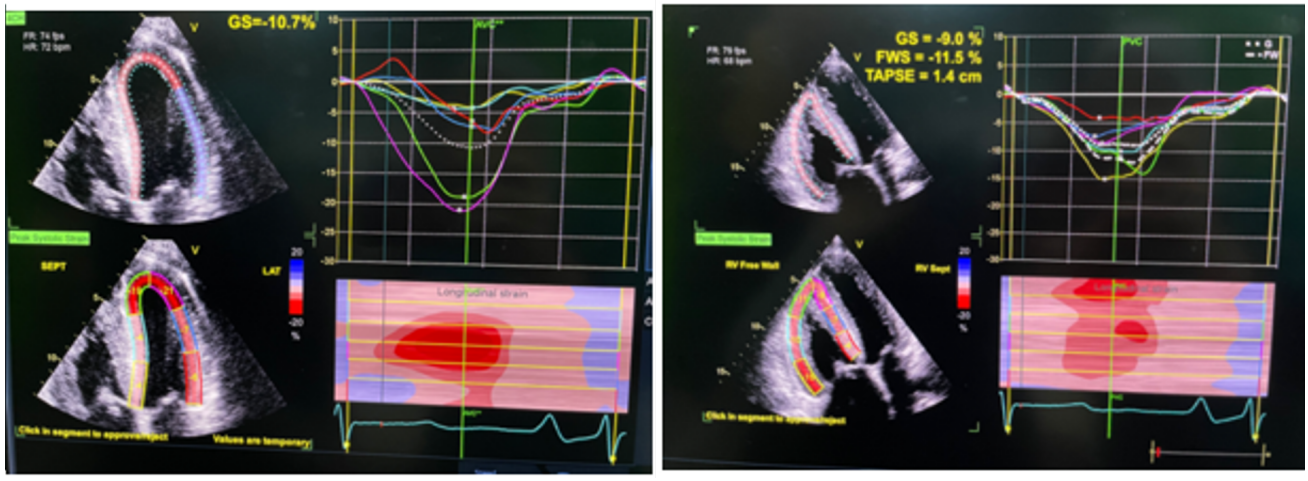

Figure 3. Speckle tracking echocardiography showed RV Free Wall GLS -11,5% (left) and LV GLS -10.7% before BPV (right).

pulmonary blood flow while avoiding low diastolic pressures. The study also demonstrated that PA growth following stenting might create a more suitable substrate for subsequent repair, especially for severe cyanosis and very small-branch PA patients. Previous studies also demonstrated that stent can successfully palliate these patients such that elective repair can be performed with better-sized PAs.[10]

Similar with RVOT stenting, BPV is one of the established initial palliation in treating Tetralogy of Fallot mainly with pulmonary valvular stenosis cases. Some studies have shown that BPV may reduce the need for transannular patching (TAP) in patients with TOF. Some patients may require additional surgery before receiving total correction due to valvular pulmonary restenosis and these patients are at risk of pulmonary regurgitation. However, Geena et.al demonstrated that BPV produces outcomes similar to other palliative procedures and allows for a higher rate of PV annulus growth compared with other modalities, which may alleviate the need for TAP in patients with an initially small PV annulus.

As the previous study aforementioned, both cases will undergo primary complete surgical repair with better pulmonary artery size and a higher rate of PV annulus growth after initial palliation. Both cases should be monitored for pulmonary artery size, ventricular function, and valvular pathology to minimize further complications of surgical primary repair.

RVOT stenting vs BPV

RVOT stenting emerged as a good alternative for BT shunt with acceptable early and long-term outcomes and continues to be an important option in the initial management of cyanotic patients with low birth weight, inadequate pulmonary artery size, or complex anatomy.[9,10] RVOT stenting resulted in improving the pulsatile forward flow of systemic venous blood to the pulmonary artery, improving arterial O2 saturation, as well as improving pulmonary arterial growth. RVOT stenting has become one of the preferred transcatheter palliations with better branch pulmonary arterial growth as compared to modified BT shunts.[11]

While BPV was the earlier interventional palliation, it has limited utility in patients with predominantly infundibular obstruction. Studies demonstrated that balloon dilatation clearly resulted in a rise in pulmonary valve dimensions, with a mean gain of 1.74 standard deviations immediately after dilatation and 2.17 SD before surgical correction. The balloon-to-annulus ratio correlated significantly with the change in pulmonary annulus diameter, with the biggest increase observed with a balloon-to-annulus ratio of 1.5. Balloon pulmonary valvotomy would logically work best when there is predominantly valvar pulmonary stenosis in a patient with an adequately sized pulmonary annulus. Often, in newborns and young infants, the degree of infundibular hypertrophy is less, and hence BPV may yield satisfactory results despite this theoretically multilevel obstruction in Tetralogy of Fallot.

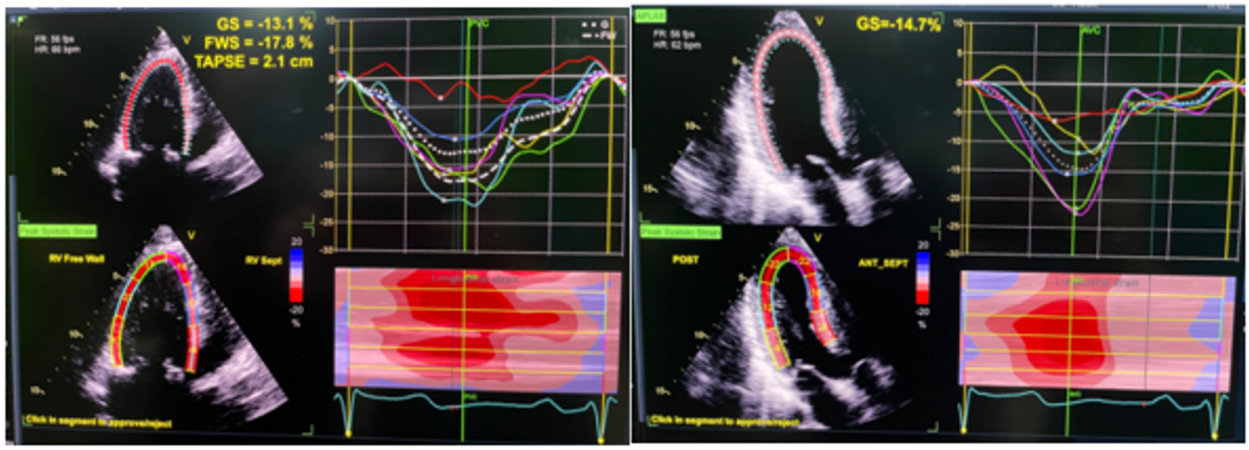

Figure 4. Speckle tracking echocardiography showed RV Free Wall GLS -17,8% after BPV (left) and LV GLS -14,7% after BPV (right).

Unlike BPV, RVOT stenting would address the predominantly infundibular stenosis, and pulmonary annular hypoplasia with higher effectiveness and reliability compared to static balloon dilation.[9] In our case, we did not perform BPV followed by RVOT stenting if echocardiogram and angiograms suggest multilevel RVOT obstruction which would have a suboptimal result with BPV.[13–15] The underlying reasons are highlighted. First, BPV itself may precipitate cyanotic spells and would make the condition become more unstable and higher risk. Second, if we plan to anchor the RVOT stent across the pulmonary annulus, prior BPV could increase the potential risk of stent migration by enlarging the valvar constriction, or forcing the use of an oversized RVOT stent leading to pulmonary overcirculation.

Functional Capacity after non-surgical palliation intervention

The 6-MWT distance predicted cardiovascular events and provided similar prognostic value to treadmill exercise capacity. It was previously reported that decreasing 6-MWT distance was an independent predictor of increasing mortality in patients with left ventricular systolic dysfunction. Although cardiopulmonary exercise testing (CPET) is a gold standard method for assessing exercise capacity, the more commonly used test for assessing LV function is the 6-minute walk test (6-MWT).[18,19]

After palliation, case 1 was able to have the 6-min walk distance in 320 m (3.7 METS) in first trial and 7 days later increasing to 800 m (9.1 METS) meanwhile Case II was able to have the 6-min walk distance in 474 m (5.0 METS) and 7 days later increasing into 1200 m (11.2 METS). Both cases showed improvement in functional capacity in terms of METS after having a non-surgical palliation transcatheter.

Conclusion

Non-surgical transcatheter palliation is the preferred treatment approach for late-presentation TOF that pose major comorbidities such as hypercyanotic spell and myocardial dysfunction which are not amenable to surgery. RVOT stenting is the preferred non-surgical palliation option for predominantly infundibular pulmonary stenosis meanwhile BPV is a safe and effective option for predominantly valvular pulmonary stenosis. Although PA size after initial palliation had not been evaluated further yet, improvement of systolic function and functional capacity denoted the benefit of initial palliation. Thus, non-surgical transcatheter palliation as a bridging procedure before complete surgical repair in late-presentation TOF might be a promising option.

Acknowledgments

The authors would like to extend their gratitude to the National Cardiovascular Center Harapan Kita

and the Department of Radiology for providing the echocardiographic images from the patients.

Conflict of Interest

The case report was self-funded; no conflict of interest was reported for both authors.

List of Abbreviations

6-MWT	6-minute walk test
AVSD	Atrioventricular Septal Defect
BPV	Balloon Pulmonary Valvulotomy
CHD	Congenital Heart Disease
CPET	Cardiopulmonary Exercise Testing
PAs	Pulmonary Arteries
PS	Pulmonary Stenosis
RAD	Right axis deviation
RVH	Right Ventricular Hypertrophy
RVOT	Right Ventricular Outflow Tract
TTE	Transthoracic Ehocardiography
TOF	Tetralogy of Fallot
TAP	Transannular Patching

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