CASE PRESENTATION

Challenging Management of Pulmonary Regurgitation in an Adult Patient With Tetralogy of Fallot and Pulmonary Arterial Hypertension

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ABSTRACT

Pulmonary regurgitation following correction of tetralogy of Fallot (ToF) is a common postoperative complication associated with progressive right ventricular (RV) enlargement and dysfunction, and is an important determinant of late morbidity and mortality. Usually, pulmonary regurgitation is well tolerated for many years following surgery, but it can lead to progressive exercise intolerance, heart failure, tachyarrhythmias, late sudden death requiring often re-intervention. The appropriate timing of such intervention can be a challenging topic given the risk of prosthetic valve degeneration, the increased risk of reoperation and the decision depends on assessment of right ventricle size and function. Pulmonary hypertension (PH) is not an usual finding in ToF patient and it can be caused by pulmonary agenesis, hypoplasia and/or thrombosis, residual ventricular septal defect, or a large prior systemic-to-pulmonary shunt. Association of pulmonary arterial hypertension in a patient with ToF and pulmonary regurgitation who needs valve correction involves higher surgical risks and the management must be taken in a multidisciplinary team.

Keywords: pulmonary regurgitation, tetralogy of Fallot.

REZUMAT

Regurgitarea pulmonară apărută după corecția tetralogiei Fallot este o complicație frecventă post-operatorie, fiind asociată cu dilatare și disfuncție progresivă a ventriculului drept și este un indicator important pentru morbi-mortalitate. De obicei, regurgitarea pulmonară este bine tolerată mulți ani după intervenția chirurgicală de corecție, dar poate duce la scăderea progresivă a toleranței la efort, insuficiență cardiacă, tahiaritmii, moarte subită și frecvent necesită reintervenție. Momentul oportun pentru reintervenție este un subiect controversat având în vedere riscul de degenerare al protezei valvulare, riscul crescut al unei reintervenții, iar decizia depinde de evaluarea dimensiunii și funcției ventriculului drept. Hipertensiunea pulmonară nu se asociază frecvent la pacienții cu tetralogie Fallot și poate fi cauzată de agenezie de ram pulmonar, hipoplazie și/sau tromboză, defect septal ventricular rezidual sau un șunt sistemico-pulmonar anterior de mari dimensiuni. Asocierea hipertensiunii pulmonare la un pacient cu tetralogie Fallot și hipertensiune arterială pulmonară care necesită corecție valvulară implică riscuri chirurgicale crescute, iar managementul trebuie efectuat în echipă multidisciplinară.

Cuvinte cheie: regurgitare pulmonară, tetralogie Fallot.

CASE PRESENTATION

A 49-year-old woman with a history of tetralogy of Fallot status post-Waterston palliation (1973) followed by complete repair 10 years later (1983) – Waterston ligation, pulmonary valvotomy and transannular patch insertion, ventricular septal defect closure - presented in our clinic with fatigue and exertional dyspnea. Physical exam revealed good overall status, normal blood pressure and heart rate but with low oxygen saturation – 90%, mild cyanosis, systolic murmur at the left sternal border area and mild leg oedema. Resting ECG showed sinus rhythm and complete right

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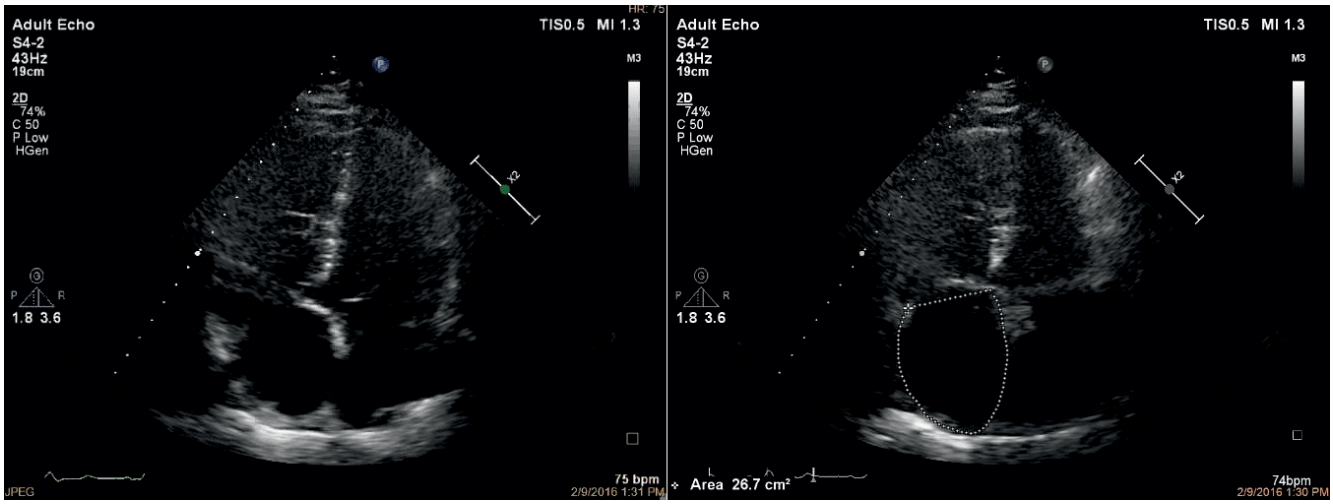

Figure 1. Transthoracic echocardiography, apical view, 2D, dilated RV, RA.

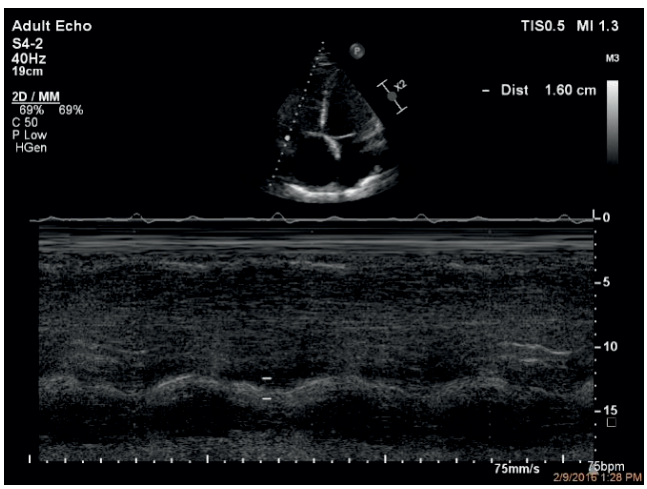

Figure 2. Transthoracic echocardiography, apical view, M mode, TAPSE 16 mm.

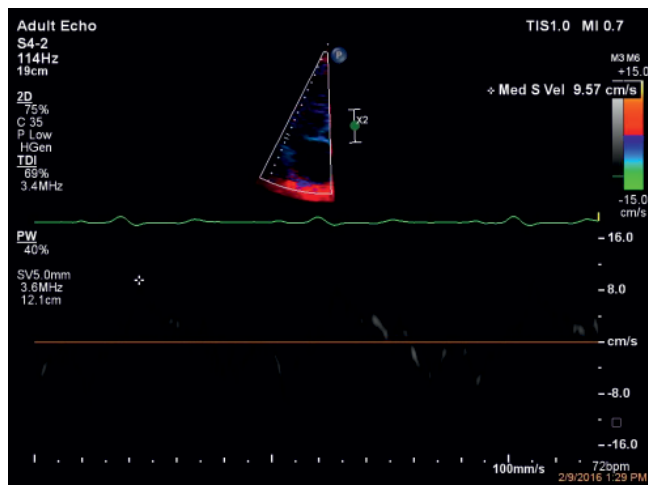

Figure 3. Transthoracic echocardiography, apical view, TDI, S velocity 9.5 cm/s.

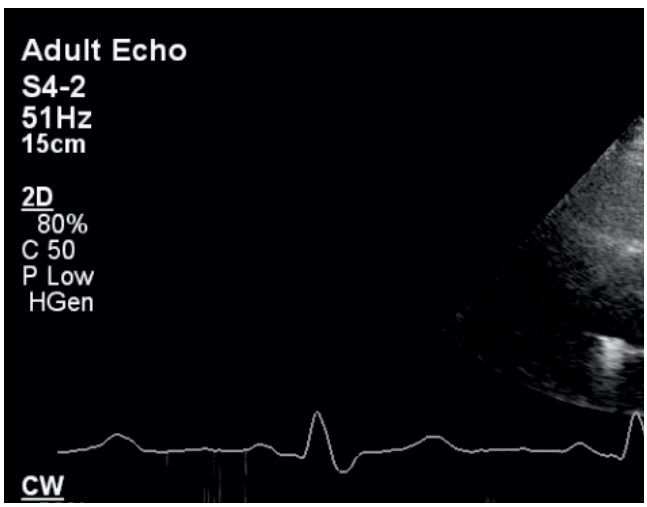

Figure 4. Transthoracic echocardiography, parasternal short axis view, continuous wave Doppler, mPAP 36 mmHg.

bundle branch block. Laboratory studies highlighted a high value of BNP (320 pg/ml). 6 minutes walking test was performed and a reduced exercise tolerance was observed – 350 m in 6 minutes. The patient underwent transthoracic echocardiography which revealed dilated right chambers - basal RV dimension – 56 mm, RA area - 26.7 cm2 (Figure 1), moderate right ventricle dysfunction – fractional area change (FAC) 30%, tricuspid annular plane systolic excursion (TAPSE) 16 millimeters (Figure 2), tricuspid lateral annular peak systolic velocity (S') 9.5 cm/s (Figure 3), severe pulmonary regurgitation (PR) with an estimated mean pulmonary pressure (mPAP) of 36 mmHg (Figure 4), moderate tricuspid regurgitation with an estimated systolic pulmonary pressure (sPAP) of 80 mmHg (Figure 5), short pulmonary velocity acceleration time

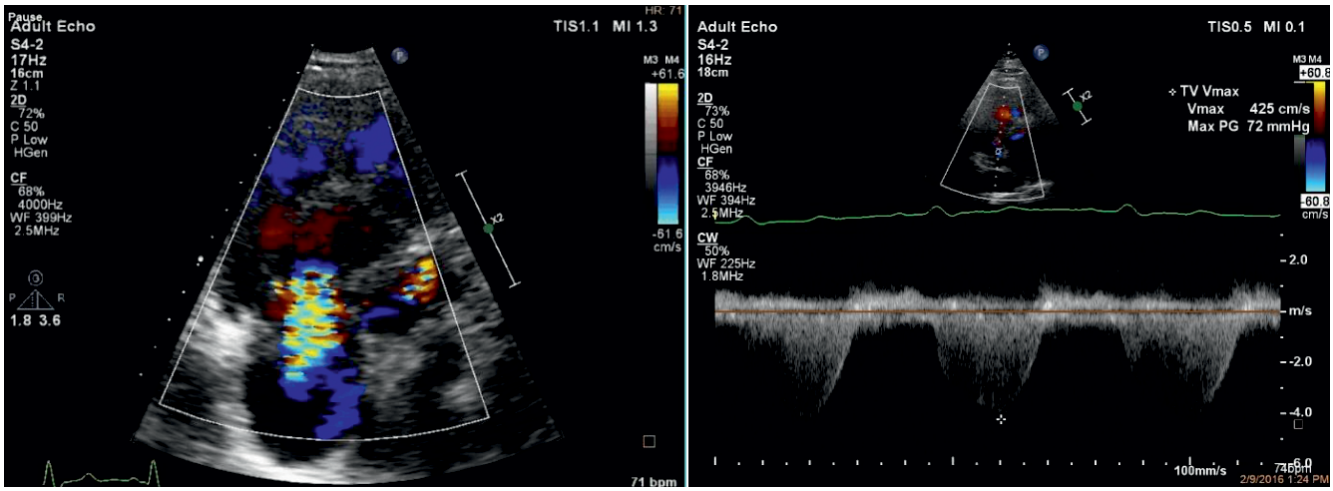

Figure 5. Transthoracic echocardiography apical view, color Doppler, continuous wave Doppler, sPAP 80 mmHg.

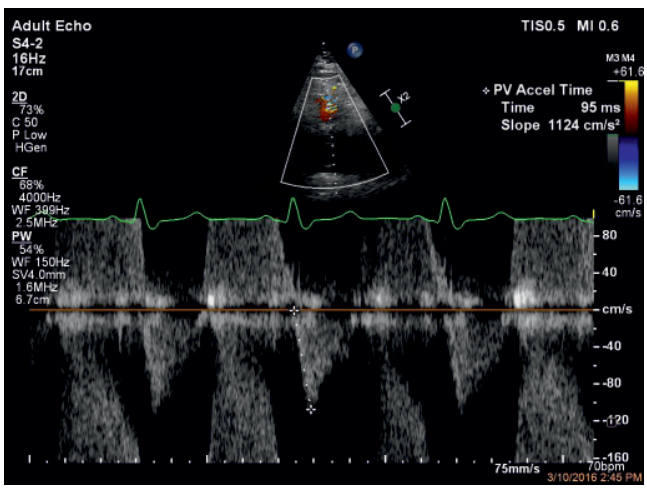

Figure 6. Transthoracic echocardiography parasternal short axis view, pulsed wave Doppler, PVAT 95 msec.

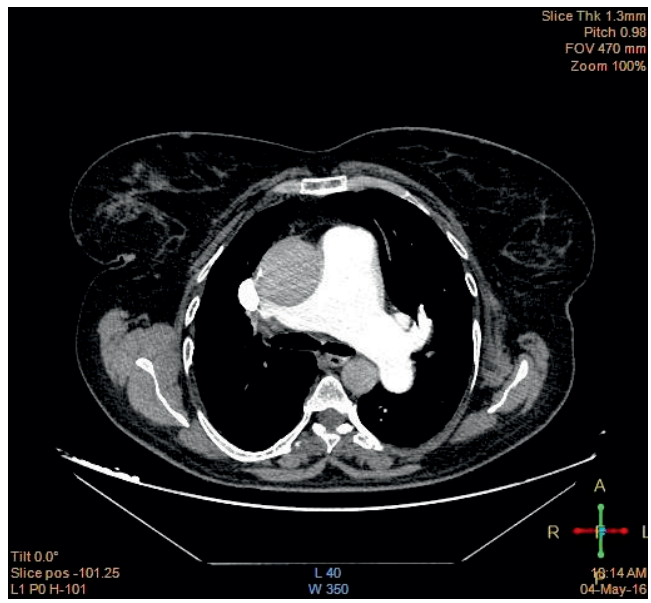

Figure 7. CTA, right superior lobe artery 5 mm, left superior lobe artery 10 mm.

(PVAT) - 95 milliseconds (Figure 6). There was no signs of right ventricle outflow tract (RVOT) obstruction or residual ventricular septal defect. The left ventricle (LV) was normal in size and function – ejection fraction (EF) – 50% with flattened interventricular septum and mild mitral regurgitation.

Considering that the pulmonary hypertension (PH) is not an usual finding in TOF patient, a computed tomography angiography (CTA) was performed to exclude a thromboembolic disease and it revealed stenosis of right superior lobe artery (Figure 7). Also, no aortopulmonary collateral arteries were found.

In order to establish the PH etiology, the patient underwent subsequent right heart catheterization (RHC) that demonstrated precapillary PH: mPAP in the left pulmonary artery (LPA) of 35 mmHg, mPAP in the right pulmonary artery (RPA) of 36 mmHg, pulmonary vascular resistances (PVR) of 6.35 Wood Units, pulmonary wedge capillary (PW) of 11 mmHg, with a cardiac output (CO) of 3.5 l/min. Also, a pulmonary arteriography was performed showing dilated bilateral pulmonary arteries and stenosis of right superior lobe artery (Figure 8), but without a hemodynamic impact: prestenotic pressure - 69/18 mmHg, poststenotic pressure - 68/20 mmHg.

Given the results of the investigation, most likely, the PH was secondary to systemic-pulmonary shunt, the stenosis of right superior lobe artery was not he-

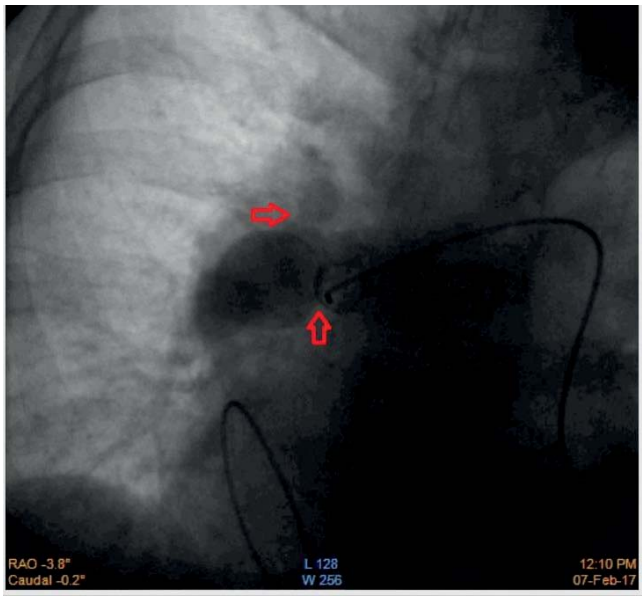

Figure 8. Pulmonary arteriography: stenosis of right superior lobe artery.

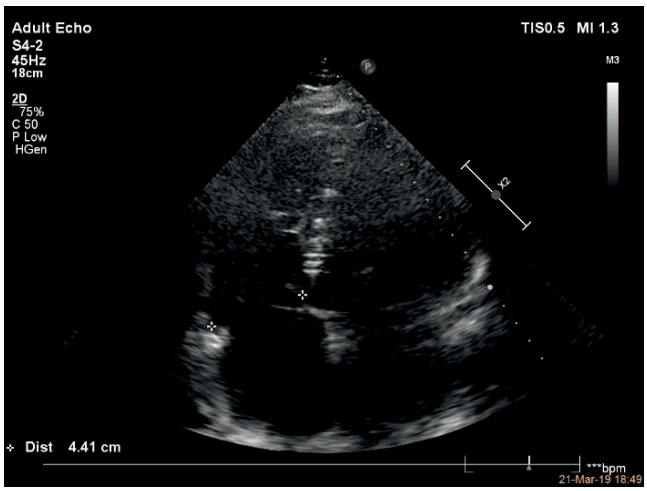

Figure 9. Transthoracic echocardiography, apical view, basal RV dimension 44 mm.

modynamically significant and the aspect of stenosis could have been caused by the palliative anastomosis.

Regarding the severe pulmonary regurgitation associated with a dilated and hypokinetic RV and moderately reduced exercise tolerance, the patient was referred for surgical pulmonary valve replacement (PVRep). Thus, a reintervention was discussed but carrying an increased risk due to PH and the decision was to initiate dual PH therapy with Bosentan and Sildenafil. After three months of PH therapy, the clinical evolution was favorable, her symptoms, which included fatigue, tiredness, and dyspnea, were alleviated by PH therapy and the quality of life appeared to have improved with

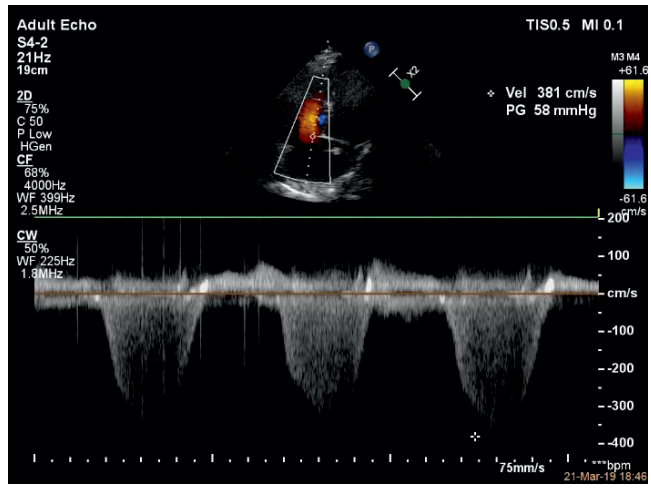

Figure 10. Transthoracic echocardiography, apical view, sPAP 63 mmHg.

a mild improvement of the walking distance (395 m versus 350 m); lab tests showed a reduction of BNP value (148 pg/ml vs 320 pg/ml). The echocardiographic parameters remained relatively stationary. A new RHC was performed and revealed a decrease in mPAP - 30 mmHg (versus 35 mmHg) and RVP - 4 Wood Units (versus 6.35) and an improvement of CO 4.4 l/min (versus 3.5 l/min). Thereby, considering the patient's evolution, the case was referral for surgical valve repair and the patient underwent successful PVRep with Perimount bovine pericardial valve. At six months follow-up, echocardiographic, right ventricle function and dimension had improved – basal RV dimension 44 mm (Figure 9), FAC 35%, while the estimated systolic pulmonary pressure was maintained at 63 mmHg (Figure 10), with mild tricuspid regurgitation.

The patient continued treatment with Sildenafil and Bosentan, but after few months after surgery, she developed hepatic cytolysis related to Bosentan, and the treatment was switched to Macitentan. No adverse effects were observed under this therapy, and the evolution was favorable but with poor prognosis related to the presence of PH.

DISCUSSION

Tetralogy of Fallot (ToF) is a rare condition caused by a combination of four heart defects: ventricular septal defect (VSD), right ventricle outflow tract (RVOT) obstruction, right ventricle (RV) hypertrophy and dextroposition of the aorta. ToF represents approximately 7%-10% of congenital heart diseases (CHDs)[2], and it is the most common cyanotic CHD, with 0.23-0.63 cases per 1000 births[3]. Until the development of palliative systemic-to-pulmonary shunts, ToF was a lethal

CHD. First palliative anastomosis was described in 1945[4] by Blalock and Taussig between subclavian artery and pulmonary artery; in 1946 Potts developed a left pulmonary artery-descending aorta shunt[5] and later, in 1962[6], Waterston described the anastomosis of the ascending aorta to the right pulmonary artery and became the procedure of choice in neonates and small infants because the difficulties in performing the Blalock-Taussig shunt in small infants and because of the problems experienced during the takedown of the Potts anastomosis at the time of total surgical correction6; despite extensive use of this palliation shunt in an earlier surgical era, two major complications: kinking of the anastomosis and the development of a pulmonary vascular obstructive disease led to the abandon of this procedure[6].

However, even with success of contemporary approaches with early complete repair, late complications are frequent. More than half of the patients after primary ToF repair (rToF) develop RVOT dysfunction at some point in their lives. Similarly, patients with a RV to pulmonary artery conduit sooner or later experience a deterioration in conduit function leading to stenosis, regurgitation, or both[7]. Thus, regular assessment of the postoperative patient with tetralogy of Fallot, including evaluation of pulmonary regurgitation, right heart structure and function, is crucial to the optimal care of these patients[8].

Pulmonary regurgitation is a common complication following repair of ToF and even if it is well tolerated, in the long term, chronic PR has a considerable impact over the right ventricle[8]. PR is related to the use of a transannular patch – an early technique which has been abandoned in favor of limited RVOT patching with preservation of pulmonary valve function. Several risk factors – as MccGoon ratio and follow-up duration – have been identified as predictors of severe pulmonary regurgitation prior to repair of tetralogy of Fallot[9].

Pulmonary valve replacement is often used to treat right ventricle volume overload from pulmonary regurgitation. The procedure can be performed minimally invasive by a transcatheter technique or surgically, using bioprosthetic valves, but the integrity of all available bioprosthetic valves deteriorates over time, requiring repeat valve replacement - average time to reoperation is around 15 years for most adult rTOF patients[10]. The appropriate timing of such intervention it's challenging, the main indication of a new surgery is the existence of significant pulmonary regurgitation with clinical symptoms[8]. In asymptomatic patients, pulmonary valve replacement is indicated by progressive right ventricle dilatation, or dysfunction and development or progression of tricuspid valve regurgitation – all these indications are summarized in the new European Guidelines of Congenital Heart Disease[8]. Preferably, the intervention should be performed before there is irreversible RV dysfunction. Normalization of RV size after reintervention becomes unlikely as soon as the end systolic index exceeds 80 mL/m^2 and the end diastolic volume index exceeds 160 mL/m^2, but this cut-off for reintervention may not correlate with clinical benefit[8]. A recent meta-analysis demonstrated that PVRep can improve symptoms and reduce RV volume, but a survival benefit still needs to be shown[8].

PAH is a rare complication in patients with ToF, RVOT obstruction is severe enough to keep the pulmonary artery pressure normal or below normal but it might be caused by pulmonary atresia, hypoplasia and/or thrombosis, residual ventricular septal defect, or a large prior systemic-to-pulmonary shunt. The influence of a Waterston shunt on the mortality in complete correction of Fallot's tetralogy varies from series to series[11]. Some authors believe that it has no influence and others, on the contrary, believe it plays an important role to the point of recognizing a particular premonitory syndrome of pulmonary hypertension and a low output state[11].

The presented case illustrates the aspects discussed above. A patient with ToF needs to be closely and carefully evaluated to detect possible complications in timely manner. The management plan of this case was established by a Heart Team including cardiologists, interventional cardiologists, radiologists and cardiac surgeons. Given the association between PH and severe pulmonary regurgitation, PH therapy was chosen in order to improve hemodynamic parameters before surgical valve replacement.

CONCLUSION

ToF is a complex condition, every case requires a personalized management plan. Although the late-term survival after correction of tetralogy of Fallot is good and as the population of patients with repaired ToF ages, a growing number of patients can be expected to develop various complications. Special care should be taken in patients with Waterstone anastomosis due to hemodynamic impact on pulmonary circulation. The development of PH increases the surgical risk for PVRep and the decision to reintervene must be

taken in a multidisciplinary team. Moreover, PH show similar hemodynamic and clinical features to patients with Eisenmenger syndrome and initiation of pulmonary vasodilator therapy to improve the preoperative parameters might be considered.

Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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