

## Case Report

# Multidisciplinary Management of Massive Pulmonary Arterial Thrombosis after Early Complete Repair of Tetralogy of Fallot

Matteo Ponzoni, MD<sup>1), #</sup>, Giulio Folino, MD<sup>1), #</sup>, Massimo Padalino, MD, PhD<sup>1)</sup>,  
Fabio Scattolin, MD<sup>1)</sup>, Biagio Castaldi, MD<sup>2)</sup>,  
Giovanni Di Salvo, MD, PhD<sup>2)</sup>, and Vladimiro Vida, MD, PhD<sup>1)</sup>

<sup>1)</sup>Department of Cardiac, Thoracic and Vascular Sciences, Pediatric and Congenital Cardiac Surgery Unit, University of Padua, Padua, Italy

<sup>2)</sup>Pediatric Cardiology, Department of Woman's and Child's Health, University of Padua, Padua, Italy

<sup>#</sup>These authors share co-first authorship.

We present a case of massive pulmonary arterial thrombosis that occurred in an infant, during the early post-operative period after complete surgical repair of a severe form of Tetralogy of Fallot. The patient required emergent circulatory support with veno-arterial extracorporeal membrane oxygenation immediately followed by percutaneous thrombus fragmentation and local thrombolysis, which enabled partial thrombus removal and hemodynamic stabilization. Subsequently, the patient was scheduled for urgent surgical thrombectomy and central pulmonary arterial enlargement plasty, with successive circulatory and clinical improvement. The etiology of this complication was suspected to be multifactorial; multiple surgeries, systemic inflammatory state, hypoplastic pulmonary arteries, and moderate prothrombotic state. A multidisciplinary collaboration between intensivists, cardiologists, and cardiac surgeons and a rationale and step-by-step clinical approach were paramount to face this rare life-threatening complication.

Keywords: pulmonary thrombosis, ECMO, thrombectomy, Tetralogy of Fallot

## Case Presentation

A 4-month-old infant (weight 5.2 kg, BSA 0.29 m<sup>2</sup>, oxygen saturation 84%) suffering from Tetralogy of Fallot (TOF), was referred for complete surgical repair at our institution. Diagnosis was made postnatally for development of cyanosis after birth. No comorbidities were present. Echocardiography showed a severe form of TOF with hypoplastic and dysplastic pulmonary valve of 3.5 mm of diameter with minimal anterograde blood flow and hypoplastic pulmonary branches of 2 mm of caliber. Continuous infusion of prostaglandin E was started, but urgent catheterization was needed because of progressive worsening of hypoxemia. A 6 mm stent was inserted in the right ventricular outflow tract (RVOT) (Fig. 1), with subsequent improvement of blood

oxygenation, which allowed extubation and home discharge. At the age of 4 months, the child underwent preoperative catheterization, which demonstrated good positioning of the previous stent, the pulmonary trunk of adequate caliber (10 mm), the right pulmonary artery (PA) of 4.6 mm, the left PA of 5 mm, and absence of severe stenoses in distal pulmonary branches (Fig. 2). Nakata index was 151 mm<sup>2</sup>/m<sup>2</sup>. After multidisciplinary evaluation, the patient was scheduled for complete surgical correction. Surgery was carried out on cardiopulmonary bypass (CPB). For RVOT reconstruction, a transannular homograft monocusped valve extended to the main pulmonary artery (MPA) was adopted (due to pulmonary valve entrapment in RVOT stent), the malaligned ventricular septal defect (VSD) was patch closed through a right atrial incision, the foramen ovale

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Corresponding author: Vladimiro Vida, MD, PhD, Department of Pediatric and Congenital Cardiac Surgery, University of Padua, Via Giustiniani 2, 35121 Padua, Italy

E-mail: vladimiro.vida@unipd.it

ORCID: Vladimiro Vida (<https://orcid.org/0000-0002-1829-0259>)

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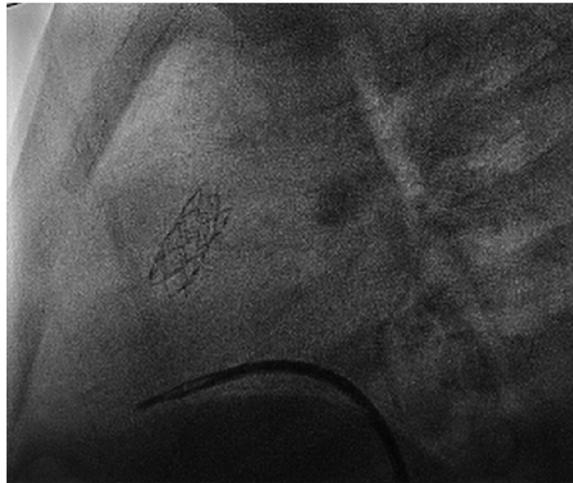


Fig. 1 Right ventricular outflow tract stenting at birth

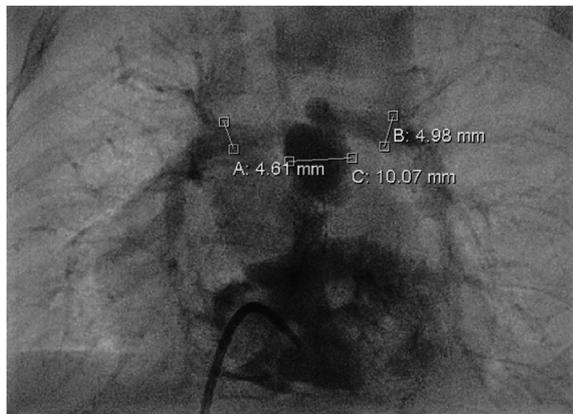


Fig. 2 Preoperative catheterization demonstrating the pulmonary trunk of 10mm, the right pulmonary artery of 4.6mm, the left pulmonary artery of 5mm, and absence of stenoses in distal pulmonary branches

was left open. Pulmonary arteries (PAs) were probed and accepted a 5 mm Hegar. No intervention on PAs was performed. Extubation was possible on day 10th after resolution of transient right ventricular (RV) dysfunction due to junctional ectopic tachycardia and acute kidney injury requiring peritoneal dialysis. Postoperative echocardiography showed good reconstruction of MPA, but severe pulmonary regurgitation, and mild hypoplastic distal pulmonary branches. The patient was transferred to the ward on day 13th and maintained on prophylactic unfractionated heparin (UFH) 10 U/kg/h until right jugular central venous line removal on day 15th. The subsequent postoperative course was regular, with improving clinical status and nearly complete nor-

Table 1 Complete coagulation parameters and prothrombotic genetic polymorphisms screening on postoperative day 41st

	Patient's value	Normal range
Protrombin time (%)	55.8	70.0–100.0
International normalized ratio	1.40	0.88–1.13
Activated partial thromboplastin time (s)	98	22–32
D-dimer (ng/mL)	571	0–500
Fibrinogen (g/L)	2.07	1.50–4.50
Factor II activity (%)	115.7	80.0–120.0
Factor VIII activity (%)	255.1	60.0–160.0
Factor IX activity (%)	49.2	80.0–120.0
Factor X activity (%)	90.3	80.0–120.0
Factor XI activity (%)	46.8	80.0–120.0
Antithrombin III activity (%)	96.3	80.0–120.0
Protein C activity (%)	72.1	80.0–120.0
Protein S activity (%)	122.9	70.0–130.0
Protein C antigen (%)	130	80.0–120.0
Protein S free antigen (%)	114	80.0–120.0
Leiden V factor mutation	Absent	Absent
G20210A prothrombin gene mutation	Absent	Absent

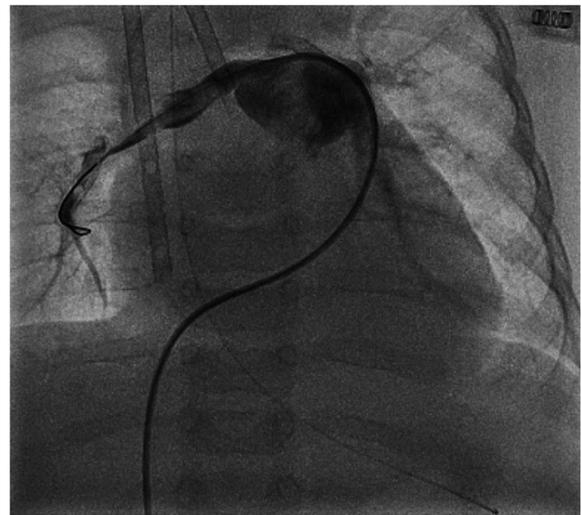


Fig. 3 Urgent diagnostic catheterization showing lack of contrast staining of the right pulmonary artery suggestive of thrombosis

malization of blood exams (see Table 1). On day 24th the patient presented sudden circulatory collapse requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Echocardiography showed severe RV dysfunction and absent blood flow through the right PA. Urgent diagnostic cardiac catheterization showed lack of contrast staining of the right PA suggestive of thrombosis (Fig. 3). Percutaneous thrombus fragmentation with multiple balloon dilations, local thrombolysis (Urokinase 4000 U/kg over 20 min), and aspiration were performed with partial thrombus removal and hemo-

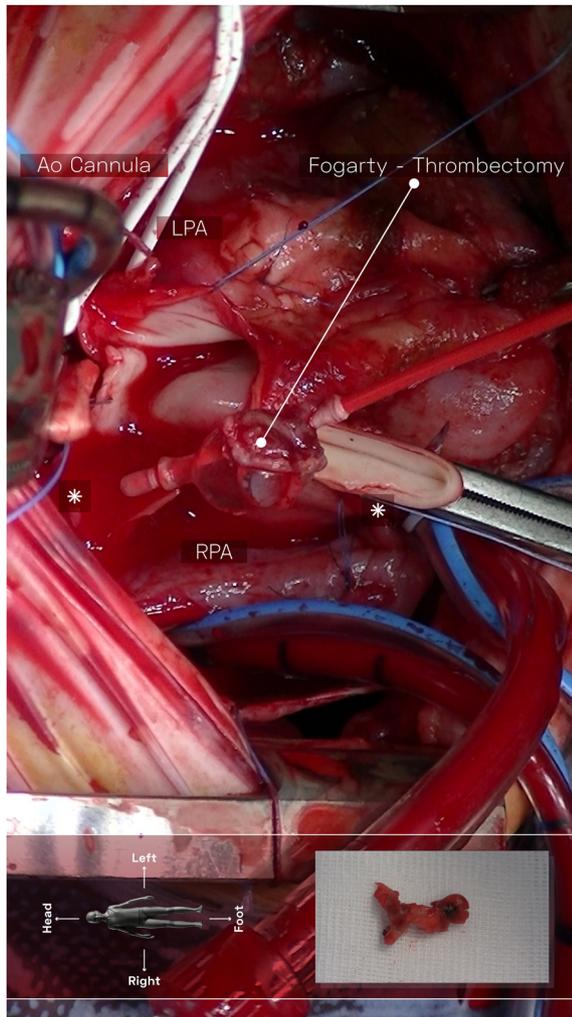


Fig. 4 Thrombus removal with Fogarty technique  
 Insert: gross specimen of thrombus; RPA and LPA=right and left pulmonary artery; Ao cannula=aortic cannula; \*transected aorta.

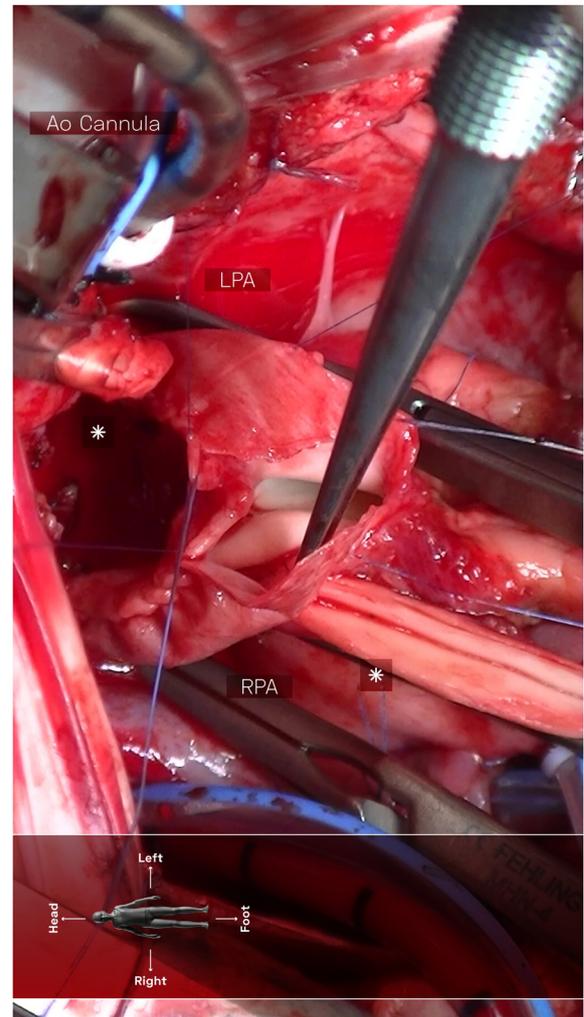


Fig. 5 Pulmonary arterial augmentation plasty with heterologous pericardial patches  
 RPA and LPA=right and left pulmonary artery; Ao cannula=aortic cannula; \*transected aorta.

dynamic improvement. Continuous Urokinase infusion was not performed due to recent VA-ECMO cannulation. Following heart-team discussion, the patient was referred for surgical thrombus removal and concomitant central PAs enlargement plasty (Video 1): on CPB, MPA was transected and two thrombi were removed adopting the Fogarty technique (Fig. 4). Neither signs of intimal damage nor macroscopic focal arterial stenoses were noticed. Proximal right and left PAs enlargement plasty with heterologous pericardial patches was carried out (Fig. 5). An additional 3.5 mm opening was performed at the VSD patch. The patient was weaned from VA-ECMO easily in the operating room. Right ventricular function recovered gradually, with left-to-right shunting at the calibrated VSD, and estimated RV pressure equal to

half of the systemic. Blood exams showed an isolated moderate increase in factor VIII activity and a slight decrease in factor IX and XI activity (see Table 1). Most frequent prothrombotic genetic polymorphisms were excluded (Leiden V factor and G20210A prothrombin gene mutation) and common inherited severe thrombophilia was ruled out (see Table 1). During hospital stay he was maintained on UFH increased to 20 U/kg/h and discharged home one month later on Warfarin (target INR 2-3) for six months, after hematological consultation. One-month control cardiac magnetic resonance revealed satisfactory PAs reconstruction and no thrombi were detected. Currently, the patient is in good clinical status and he had no relapse of thrombosis after discontinuation of anticoagulation therapy.

## Discussion

Thrombosis in the pediatric population is rare. However, among children undergoing cardiac surgery, the incidence of postoperative thrombosis has been reported between 3.6 and 11%,<sup>1)</sup> with a significant impact on morbidity and mortality. Tetralogy of Fallot, as a cyanotic congenital heart disease (CHD), might be at an increased risk of developing thrombosis.<sup>1,2)</sup> Cases of life-threatening pulmonary arterial thrombosis after complete early surgical repair of TOF are anecdotal and they are always linked to patient-specific risk factors; malignancy, sepsis, and thrombophilia.<sup>3)</sup>

In our case, besides the CHD, no preoperative adjunct risk factors were identified. Subsequent hematologic exams revealed a moderate prothrombotic state of uncertain meaning, because of recent multiple major surgeries, extracorporeal circulations, thrombolytic drugs, and transfusions. Since the presence of a central venous line represents the first cause of thrombosis in children,<sup>4)</sup> prophylactic UFH was used to minimize the risk of central venous catheter (CVC)-driven thrombosis. Furthermore, due to the demanding postoperative course and the prolonged need for intubation, the infusion of UFH served also as prophylaxis against the immobilization of the patient. Although a meta-analysis by Vidal et al. suggested the inefficacy of any prophylactic medical option to prevent CVC-driven thrombosis,<sup>5)</sup> in our case, because of the relatively long time (10 days) between CVC removal (which could represent a possible source of thrombus embolization) and pulmonary thrombosis, we speculate that this mechanism may not be involved. Thus, the etiology of thrombosis remains unclear. We speculate that the combination of diffuse PAs hypoplasia, the potential endothelial injuries due to PAs manipulation, the systemic inflammatory response, and the potential prothrombotic predisposition may have led to thrombus apposition in the right PA.

The treatment for PAs thrombosis in children is not standardized and current guidelines have low level of evidence.<sup>6,7)</sup> Thrombolysis is recommended as first-line therapy in case of hemodynamic compromise, however, current guidelines do not consider special populations as the ones which recently underwent cardiac surgical procedures or under mechanical circulatory support.<sup>6)</sup> Furthermore, the paucity of studies comparing systemic versus catheter-delivered local administration

of thrombolytic drugs does not allow to demonstrate a safety advantage of the second technique in patients at risk of bleeding complications.<sup>6)</sup> On the other hand, catheter-based mechanical thrombectomy is emerging as an appealing option for PAs thrombosis also in pediatric patients, however, to date, series are very limited<sup>8)</sup> or are isolated reports<sup>9,10)</sup> and often exclude patients with CHDs.<sup>8)</sup> The role of surgical thrombectomy in the pediatric population remains unclear, because it is often discouraging,<sup>7)</sup> due to its high operative risk and technical difficulty in smaller patients,<sup>11)</sup> and reserved mainly for life-threatening thrombosis.<sup>12)</sup>

Our case represents a unique situation, in which a massive thrombosis occurred after a recent cardiac surgical operation, with a concrete potential of bleeding complications, and it required mechanical circulatory support, thus limiting the pharmacological therapeutic options of thrombolysis and increasing the operative risk of a surgical approach. Therefore, we adopted a combined and staged percutaneous and surgical approach, which finally allowed radical thrombus removal. Particularly, we firstly attempted local thrombolysis to minimize the possible bleeding complications which may occur after major surgical procedures and during ECMO support. Catheter-based balloon fragmentation and aspiration allowed partial thrombus aspiration and its softening, facilitating the subsequent surgical removal. After a multidisciplinary evaluation, the patient was scheduled for a reoperation because the persisting hemodynamic instability requiring continuous ECMO support underlined the presence of a still significant pulmonary thrombus, to inspect the pulmonary arteries directly, and to rule out the presence of any local factor contributing to thrombosis. The intraoperative Fogarty technique demonstrated good feasibility and it was free from complications. Furthermore, we opted for a PAs augmentation plasty, combined with the calibrated VSD and the patent foramen ovale, in order to facilitate the RV unloading during the transient RV dysfunction. This strategy might have contributed to RV recovery by lowering the RV pre and after-load, meanwhile preserving the systemic circulation. In conclusion, this case highlights that: 1) although rare, massive PAs thrombosis could occur after early complete repair of TOF even in infants with none or few predisposing factors. 2) The combination of local pharmacological and mechanical thrombolysis and surgical thrombectomy may be a

valuable solution in selected cases. 3) PAs augmentation plasty and surgical calibrated VSD may facilitate RV recovery. More evidence in the pediatric population is needed to establish the optimal treatment options for life-threatening thrombosis.

### Funding

No funding was received for conducting this study.

### Conflicts of Interest

All authors have no conflicts of interest to disclose.

### Ethical Considerations

Since this is a retrospective case report and all the performed procedures were part of the routine care, no ethical approval was needed. Parents' consent to clinical data and images/videos' use for scientific purposes (including publication) was obtained, preserving the anonymity of the patient.

### Abbreviations

CHD, congenital heart disease; CPB, cardiopulmonary bypass; CVC, central venous catheter; MPA, main pulmonary artery; PA, pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract; TOF, Tetralogy of Fallot; UFH, unfractionated heparin; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VSD, ventricular septal defect

### Note

Supplementary movies are provided online for this article.

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