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# Thrombosis of a biological pulmonary valve in a young patient on anticoagulant therapy with rivaroxaban: a case report

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## Background

Patients with repaired tetralogy Fallot often develop severe pulmonary regurgitation (PR) and need surgical or catheter valve replacement/implantation. Early valve failure is not expected and thrombosis of a biological valve in a mid-term period after surgery on pulmonary position is rare.

## Case summary

We report a 33-year-old female patient, who presented with heart failure, 18 months after surgical implantation of a biological valve on pulmonary position for severe PR, after previous complete repair. The patient was on anti-coagulant therapy with novel oral anticoagulants (NOACs) for paroxysmal atrial fibrillation. After revealing a big pulmonary valve (PV) thrombus as a cause of severe valve stenosis and right heart failure, patient was re-operated without complication. After surgery a long-term warfarin therapy was introduced. The patient had an uneventful 9-month follow-up.

## Discussion

Thrombotic events after rivaroxaban therapy are rare in non-valvular disease and there is paucity of data for NOAC therapy related to valve thrombosis. In our case, severe heart failure 1 year and a half after PV replacement, in a patient taking anticoagulant therapy, was unexpected. The diagnosis of valve thrombosis was revealed by echocardiography, and confirmed by computed tomography. We did not find any sign of thrombophilia, or any mechanical reason for valve thrombosis.

## Keywords

Pulmonary valve • Thrombosis • Anticoagulant therapy • Rivaroxaban • Heart failure • Case report

## Learning points

- Pulmonary valve (PV) prosthesis failure, in patients after tetralogy of Fallot (TOF) repair and later PV replacement in majority of cases is the result of degeneration, rather than thrombosis.
- Thrombosis of a tissue PV is rare in absence of thrombophilia, especially in patients treated with anticoagulant therapy.
- Heart failure in early to mid-term period after PV replacement can be a result of tissue valve thrombosis.
- Therapy with novel oral anticoagulant rivaroxaban, might not prevent valve thrombosis.

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## Introduction

Pulmonary regurgitation (PR) is common after tetralogy of Fallot (TOF) surgical repair. It is increasingly recognized that right-sided valve disease is not a benign lesion and that it has a significant and an independent impact on morbidity and mortality.<sup>1</sup> Surgical procedure often involves pulmonary valvulotomy, a transannular patch, or incision in the right ventricular (RV) infundibulum, which can all contribute to long-term PR.<sup>2</sup> Despite being well tolerated for a long time, there is evidence that PR leads to progressive RV dilatation and eccentric hypertrophy. With time, it can be conducive to RV dysfunction, exercise intolerance, ventricular arrhythmias, and, rarely, a sudden cardiac death.<sup>3</sup> Dilatation and failure of the RV can be prevented by valve replacement.<sup>4</sup> Surgical bioprosthetic valves will eventually degenerate. In pulmonary position, this can be expected to occur 5–10 years after implantation.<sup>5</sup>

Apart from valve degeneration, endocarditis can also be the cause of pulmonary valve (PV) failure. Valve thrombosis is considered rare.<sup>6</sup> Long-term anticoagulant therapy for tissue valves is not indicated.<sup>7</sup> There is, however, a positive effect on biological valve thrombosis, when there is a suspicion of it.<sup>8</sup> There is so far no evidence of any positive influence of novel oral anticoagulants (NOACs) on valvular thrombus formation.

We present a case of surgical tissue PV obstruction caused by a big thrombus in a patient on anticoagulation therapy with rivaroxaban.

## Timeline

Date	Events
1989	Total repair of tetralogy of Fallot
6 April 2016	Emergency admittance for atrial flutter. Successful ablation was performed. For paroxysmal atrial fibrillation (AF), anticoagulation therapy with rivaroxaban was started
30 May 2016	Pulmonary tissue valve implantation for severe regurgitation with excellent postoperative recovery. Warfarin therapy for 3 months followed by rivaroxaban for AF
20 December 2017	Admitted to our department for severe heart failure (clinical deterioration 4 weeks before admission). Biological pulmonary valve (PV) thrombosis was diagnosed, and fractionated heparin was introduced
28 December 2017	Reoperation: replacement of a thrombosed tissue valve. Uneventful postoperative course. Warfarin for long-term therapy introduced (target INR 2.5–3)
9 October 2018	Clinically without events, on transthoracic echocardiogram normal PV function without thrombus formation

## Case presentation

A 33-year-old female patient was admitted to our Clinic with severe heart failure. She was referred for the first time 2 years earlier, as an emergency, for atrial flutter, frequency 215/min. An immediate cardioversion was performed, followed by electrophysiology and radiofrequency ablation and anticoagulant therapy with NOACs was introduced for paroxysmal atrial fibrillation (AF).

The young woman is an adult congenital heart disease patient, after surgical correction of TOF at the age of 4 years. She underwent ventricular septal defect (VSD) closure, right ventricle outflow tract resection, and PV repair with a Dacron annular patch. She has regularly been followed by an adult cardiologist without expertise in congenital heart disease.

At her first presentation in our hospital, echocardiographic (ECHO) examination revealed a dilated RV with already reduced systolic function and volume overload, dilated tricuspid annulus, and intermediate tricuspid regurgitation, with no evidence of residual VSD, obstruction of PV and pulmonary hypertension. A significant PR was observed, confirmed by cardiac magnetic resonance imaging, with regurgitation fraction of 41% and diastolic volume of the RV of 233 mL (116 mL/m<sup>2</sup>), with RV ejection fraction of 48%.

A surgical procedure was proposed. Pulmonary valve prosthesis implantation (SJM Biocor A 25 mm), tricuspid anuloplasty (Edwards MC 3 Tricuspid Ring 34 mm) and patch reconstruction of pulmonary artery (BioIntergral Surgical Patch) was successfully performed. Clinical recovery was fast, and postoperative ECHO indicated good function of biological prosthesis on PV position, and reduction of RV volume.

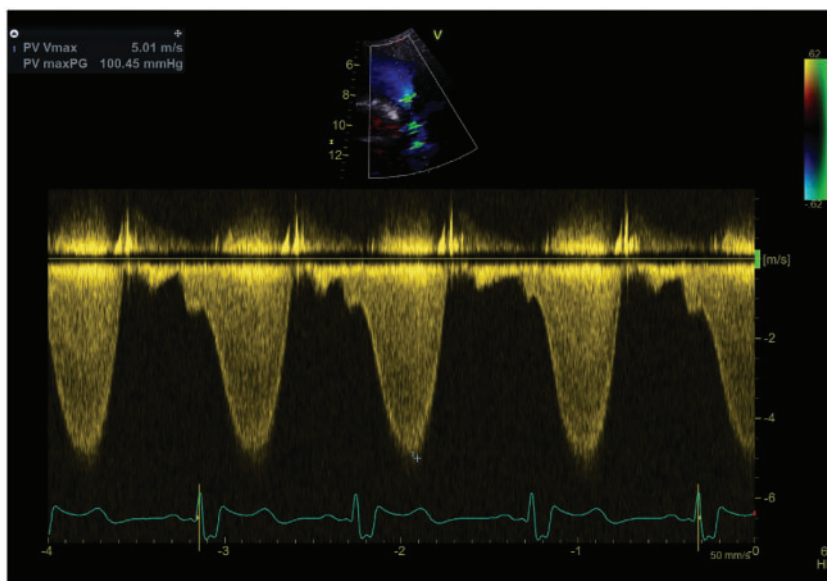
One year and a half after the surgery, the clinical course was uneventful. The patient was treated by anticoagulation therapy with warfarin 3 months after surgery, followed by rivaroxaban 20 mg daily, for paroxysmal AF.

She arrived again 18 months later, with right heart failure, after a month of progressive effort intolerance. The ECHO revealed again the dilatation of RV, this time with signs of pressure overload, and pulmonary pressure gradient of 110 mmHg (*Figure 1*). Transoesophageal ECHO (TOE) established an organized thrombus formation on the prosthesis, measuring 25 × 10 mm with an additional floating formation of 8 × 5 mm and a residual valve ‘tunnel’ of ~8 mm (*Figure 2*). The findings of electrocardiogram-triggered pulmonary computed tomography (CT) angiography were similar (*Figure 3A and B*). We did not find thrombophilia, or a mechanical reason for valve thrombosis.

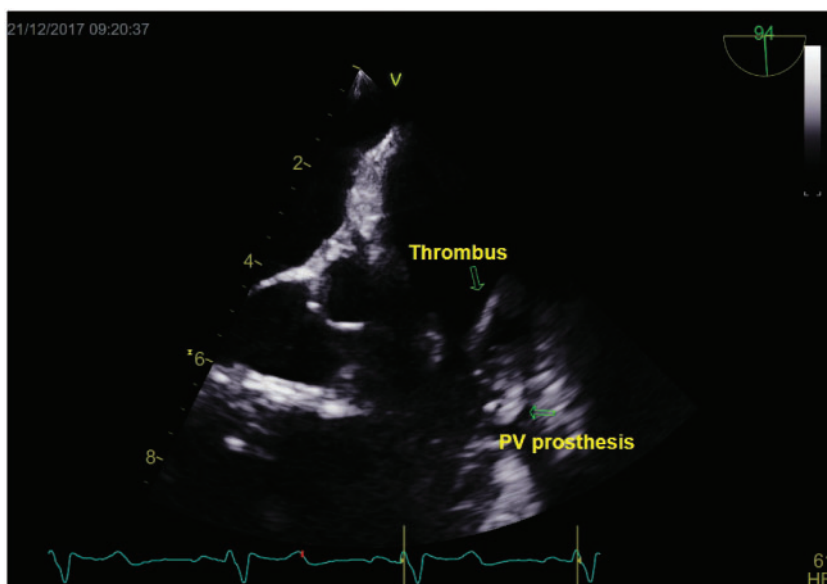
Reoperation was proposed and performed: excision of a thrombosed tissue valve and re-implantation of St. Jude Biocor valve A 25 mm, in pulmonary position. The patient made a good postoperative recovery. A long-term anticoagulation therapy with warfarin was induced. Postoperative ECHO showed reduction of RV volume and an improvement in systolic function. The PV gradient was 25 mmHg. The 9-month follow-up was uneventful.

## Discussion

Pulmonary valve replacement after repair of TOF is recommended before the occurrence of RV dysfunction, but the timing is still



**Figure 1** Continuous-wave Doppler tracing indicating severe pulmonary stenosis with maximum pressure gradient of 100 mmHg.



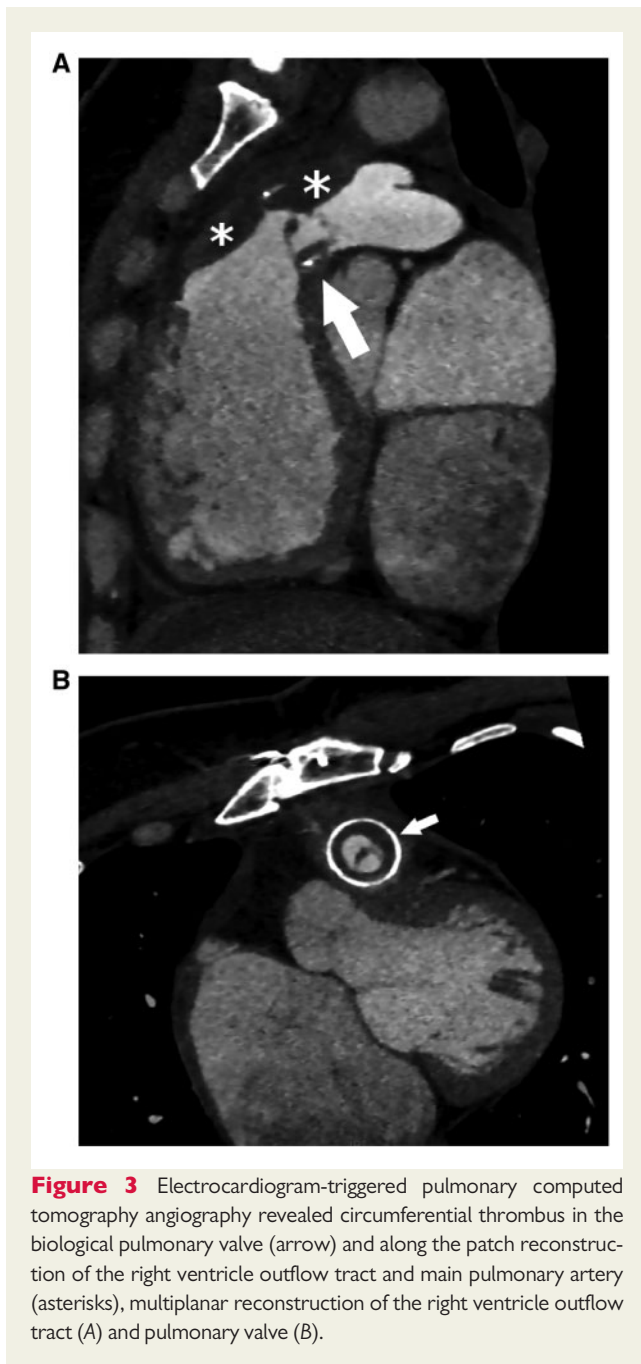
**Figure 2** Transoesophageal echocardiogram showing thrombotic mass extending across prosthetic pulmonary valve into the pulmonary trunk (arrows).

controversial. Cardiac magnetic resonance imaging has become accepted as the gold standard for the assessment of RV remodelling.<sup>9</sup> Despite RV diastolic volume was less than recommended for PV replacement, considering our patients RV volume overload, along with rhythm disturbances, a decision for PV replacement was made.

The effects of PR on some electrocardiographic predictors of arrhythmia, for example AF, are not clear. Restoration of PV

competence often leads to stabilization or reduction of QRS duration with a corresponding decrease in arrhythmia.<sup>10</sup> In our case, the atrial flutter was the first presentation of hemodynamic deterioration, a long time after TOF repair.

Data concerning the best tissue valve prosthesis for use in the pulmonary position are scarce.<sup>11</sup> Literature describes several factors which influence the time of valve degeneration: the timing of surgery,



**Figure 3** Electrocardiogram-triggered pulmonary computed tomography angiography revealed circumferential thrombus in the biological pulmonary valve (arrow) and along the patch reconstruction of the right ventricle outflow tract and main pulmonary artery (asterisks), multiplanar reconstruction of the right ventricle outflow tract (A) and pulmonary valve (B).

the patient's age, valve size, immunological factors, operative complexity, and also postoperative valve gradients.<sup>12</sup>

Bio-prosthetic valve thrombosis is a rare event, which may occur late after surgery.<sup>13</sup> Patients with tissue heart valve prosthesis still have a risk of developing valve thrombosis and arterial thromboembolism. Antithrombotic therapy with warfarin in the early postoperative period is controversial, but still recommended.<sup>14</sup> Our patient was treated with warfarin for up to three months following surgery, whereupon rivaroxaban was introduced, for long-term thromboembolic protection after paroxysmal AF.

In patients with AF, rivaroxaban was not inferior to warfarin for the prevention of stroke or systemic embolism.<sup>15</sup> Although there is no evidence of NOAC activity in thrombotic events in valve disease, presence of any valvular disease did not influence the comparison of dabigatran with warfarin, and no difference in events was found.<sup>16</sup> A fixed-dose regimen of rivaroxaban alone showed no inferiority to standard therapy for the initial and long-term treatment of pulmonary embolism and had a potentially improved risk benefit profile. Novel oral anticoagulants appear to be safe and effective in adult patients with congenital heart disease.<sup>17</sup> There are no published data about influence of rivaroxaban or other NOACs on thrombotic events related to surgical tissue valves.

Echocardiographic plays an important role to the diagnosis of biological valve thrombosis and CT may be of added value.<sup>18</sup> In our patient, PV thrombosis was first revealed by TOE, and then confirmed by CT.

Bioprosthetic valves are generally considered to carry a low risk of thrombosis and only few reports exist of the valve thrombosis. Majority data refer to left heart mechanical valves thrombosis.<sup>19</sup> For the management, thrombolytic therapy has been suggested as an alternative to surgery. It is associated with lower mortality rate but carries the risk of embolism, bleeding, and re-thrombosis. The optimal treatment of biological valve thrombosis is still a matter of debate. Anticoagulation and operative intervention are the mainstay of treatment. A response to anticoagulation therapy is usually observed 4–12 weeks after initiation.<sup>13</sup> In our case, repeated surgery was performed, expecting complete haemodynamic success in a patient with high functional class, big thrombus burden, severe valve obstruction and low surgical risk.<sup>20</sup>

## Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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