Challenges of managing patients with mechanical heart valve thrombosis in pregnancy: A case series

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ABSTRACT

Mechanical valve thrombosis is a feared complication in pregnant women with mechanical heart valves (MHV). It is associated with a high maternal and foetal morbidity and mortality. Optimal anticoagulation strategies for pregnant women with MHV remain controversial. Vitamin K antagonists (VKA) are the most effective treatment regimen to prevent valve thrombosis and are therefore considered the safest treatment for the mother. However, VKAs increase the risk of embryopathy, foetopathy, foetal haemorrhage and foetal loss. A particular challenge is to balance the need for adequate anticoagulation for MHV during pregnancy against the risk of bleeding, teratogenicity and fetotoxicity. In this case series, we describe complexity of the management of anticoagulation in pregnant patients with MHV, and describe 2 treatment approaches in patients with MHV thrombosis. Our case series high-lights that anticoagulation strategy should be individualised, and that best management is provided by a multidisciplinary cardio-obstetric team.

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INTRODUCTION

Rheumatic heart disease (RHD) affects large populations in low- and middle- income countries (LMICs) such as sub-Saharan Africa. RHD is associated with progressive valvular disease, which commonly develops years after an episode of acute rheumatic fever (ARV). RHD is a common indication for prosthetic valve implantation in young adults in Africa.[1]

In clinical practice, mechanical valves are often preferred over bioprosthetic valves in young patients as they combine good haemodynamic performance with long-term durability. This includes women of child-bearing age. However, mechanical valves necessitate life-long anticoagulation with a Vitamin K antagonist (VKA), which increases maternal and foetal morbidity and mortality.[2]

As pregnancy is a hypercoagulable state, mechanical valve thrombosis (MVT) is a feared complication in these patients.[3,4] Data from the ROPAC registry showed that MVT complicated 4.7% out of 212 pregnancies and was associated with 20% maternal mortality.[5] VKAs are the most effective treatment regimen to prevent valve thrombosis and are therefore considered the safest treatment for the mother.[6,7] However, VKAs increase the risk of embryopathy, foetopathy, foetal haemorrhage and foetal loss, especially at higher daily doses.[8] In contrast, low molecular weight heparin (LMWH) has a higher risk of valve thrombosis, however, poses a lower foetal risk.[7] Therefore, the current European Society of Cardiology (ESC) guidelines for the management of cardiovascular diseases during pregnancy suggest to continue with VKAs, if the VKA dose is low (i.e. warfarin <5mg/day). An alternative strategy is an in-hospital change to LMWH from weeks 6 - 12, which reduces the risk of warfarin embryopathy.[3] However, this requires strict monitoring of anti-Xa levels.

In this case series, we describe 2 patients who presented with MVT, highlighting the dangers to the mother and foetus.

CASE SERIES

Case 1

A 30-year-old female underwent aortic and mitral mechanical valve replacement (AVR, MVR) for RHD. Postoperatively, she received a permanent pacemaker due to complete heart block (CHB) and was initiated and discharged on a VKA.

Three years later, she represented to hospital in her 25th week of pregnancy with a short history of dyspnoea and haemoptysis. This was preceded by 10 days of non-adherence to her oral anticoagulation. Clinical examination revealed signs of congested cardiac failure with hypotension and sinus tachycardia. On auscultation mechanical clicks could not be heard. Emergent transthoracic echocardiogram (TTE) found a non-dilated left ventricle (LV) with severely impaired LV systolic function (LV ejection fraction of 28%). There was evidence of aortic valve prosthetic obstruction with flow acceleration across the prosthetic aortic valve with a mean gradient of 38mmHg and moderate aortic regurgitation. The mitral valve prosthesis also had severe mitral valve obstruction with an elevated transvalvular gradient (mean gradient of 39mmHg).

She was referred for urgent repeat dual valve replacement for aortic and mitral valve prosthestic valve obstruction. Intraoperatively, a large thrombus and pannus formation on both prosthetic valves was found, resulting in 1 immobile occluder of both valves. Both prostheses were successfully excised and replaced with new mechanical valves. Unfortunately, the foetus did not survive the aorto-pulmonary bypass. The patient, however, had an uneventful postoperative recovery. She was counselled about the importance of adherence and monitoring of warfarin therapy and continues regular outpatient monitoring of her INR.

Case 2

A 34-year-old female presented to hospital in her 29th week of her fifth planned pregnancy in 2021. Her obstetric history included 3 previous stillbirths and 1 miscarriage on warfarin therapy. She was known with RHD and previous mechanical MVR in 2000 and AVR in 2017. In view of the previous foetal losses, a decision was made to change her oral anticoagulation LMWH in her first trimester at a peripheral hospital. The prescribed dose was inadequate for her body weight (no factor Xa levels were measured) and was continued into the second trimester. In her second trimester she developed gradually worsening dyspnoea and reduced effort tolerance. Her clinical examination found no overt features of heart failure. She was normotensive and her electrocardiogram showed normal sinus rhythm. Opening and closure of the mechanical prosthetic clicks were still audible on auscultation. Her TTE showed a non-dilated LV with preserved LV systolic function. The AVR had mobile occluders with normal transvalvular gradients and no paravalvular leaks. However, the mitral valve prosthesis had one immobile occluder with a mean gradient of 12.6mmHg across the valve and a pressure half time (PHT) of 233ms. Fluoroscopy confirmed the immobile mitral valve occluder (Figure 1).

Subsequently, the patient was admitted to the intensive cardiac care unit for continuous haemodynamic monitoring. Unfractionated heparin (UFH) was administered intravenously, whilst VKA was recommenced. Obstetric consultation confirmed a viable foetus and corticosteroid administration for lung maturation was given. Following a multi-disciplinary discussion, her management options included an urgent MVR after foetal maturation with a risk of loss of the foetus or an initial in-hospital conservative strategy of intravenous heparinisation with an elective MVR at 34 weeks of gestation with a risk of worsening valve obstruction. The benefits and risks of both strategies were discussed with the patient and jointly we made the decision to continue with the pregnancy. Regular follow-up TTE examination confirmed stable gradients across her MVR. At the onset of the 34th week of pregnancy, the patient was switched back to UFH prior to the induction of labour. An emergency Caesarean section was performed for foetal distress syndrome (FDS) and healthy neonate was delivered. Postnatally, therapeutic UFH was re-started and the patient was referred for redo MVR. Her procedure was performed 3 weeks post-delivery because of postpartum wound-related bleeding complications related to the Caesarean section and heparinisation. The operation showed a thrombosed mitral valve prosthesis, which was excised and replaced with a new mechanical MVR. The AVR had no thrombus/pannus and functioned well. The postoperative recovery was uneventful.

DISCUSSION

Pregnant women with mechanical heart valves (MHV) are at increased risk of complications (WHO risk classification III).[3] Due to the hypercoagulable state of pregnancy, these patients have an elevated risk of valve thrombosis.[4,9] A particular challenge in pregnant patients with MHV is to balance adequate anticoagulation against the risk of bleeding, teratogenicity and foetotoxicity. Optimal anticoagulation strategies for pregnant women with MHV remain controversial.[2]

The anticoagulation regimen in pregnancy is complex and depends on maternal preference. There are 2 main anticoagulation regimens for pregnant women with MHV: VKA or heparin (UFH or LMWH). According to contemporary ESC guidelines,[3,10] the decision to anticoagulation strategy during pregnancy, depends largely on the VKA dose that ensures therapeutic anticoagulation. Continuation of VKA throughout pregnancy should be considered in patients who require a low dose VKA. However, for patients who require higher VKA doses, it is recommended that the VKA is changed to LMWH (with dose adjustments according to strict anti-Xa monitoring) or UFH intravenously (i.v.) (aPTT target ≥2 control) between weeks 6 and 12 of the pregnancy. This strategy is particularly

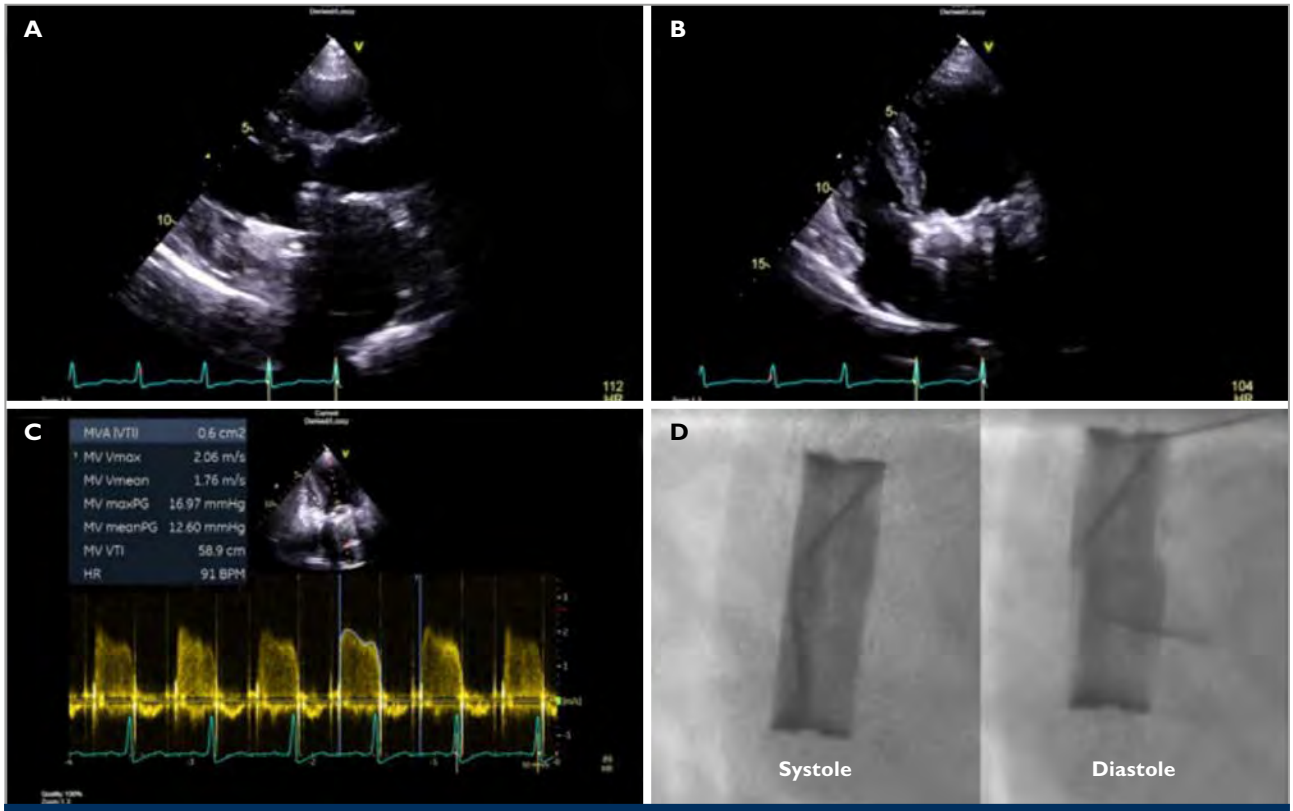

FIGURE 1: Parasternal long axis (PLAX) (A) and 4 chamber view (B) showing mechanical mitral valve (MV) prosthesis. (C) Continuous wave doppler over the prosthetic MV shows elevated transvalvular gradients (MV mean gradient of 12.6mmHg) and (D) fluoroscopy confirmed an immobile MV occluder (white arrow) in a pregnant woman with prosthetic valve thrombosis.

challenging in the South African setting, where monitoring of anti-Xa levels is not readily available and with limitation of hospital resources. At the onset of the second trimester (week 13), the patient should be changed back to VKA with INR monitoring weekly until the 36th week of gestation, at which time the VKA should be changed to i.v. UFH or LMWH. At 36 hours prior to planned delivery, the patient should receive UFH that could be stopped 4 - 6 hours prior to delivery.[3]

Our 2 cases demonstrate the catastrophic sequelae of inadequate anticoagulation during pregnancy. In the first case, the VKA was continued throughout the pregnancy, as she required a low dose VKA. However, the patient failed to adhere regular INR monitoring visits, which resulted in subtherapeutic anticoagulation in the second trimester.

It has to be considered that any therapeutic anticoagulation strategy in pregnancy increases the risk of miscarriage, and haemorrhagic complications such a post-partum haemorrhage (PPH) and retroplacental bleeding.[3] However, data from the ROPAC registry demonstrated, that VKA use in the first trimester compared to heparin was associated with higher rates of miscarriage (28.6% vs. 9.2%).[5] VKA use, particularly in the first trimester of pregnancy, is known to be associated with embryopathy. Foetopathy includes skeletal abnormalities, nasal hypoplasia, ocular and central nervous systems defects and intracranial haemorrhage.[11] However, the risk of embryopathy is dose-dependent.[7,12] On the contrary, LMWH and UFH do not cross the placenta. For these reasons, LMWH or UFH could be considered even in patients that require low dose VKA. For MHV, VKA remains the most effective therapy to prevent valve thrombosis.[7] In the second case, considering the obstetric history of multiple miscarriages on VKA therapy, the managing physicians opted to prescribe LMWH in the first trimester. The patient declined in-hospital change from VKA to LMWH and no anti-Xa level monitoring was performed. Her rural residency made it difficult to adhere to the recommended weekly anti-Xa monitoring. In addition, she continued LMWH far into the second trimester, instead of the change back to VKA after the first trimester, as recommended by contemporary guidelines.[3] This highlights the importance of cardio-obstetric teams managing these high-risk patients jointly.[13]

Valve thrombosis should be suspected in any patient with a MHV, who presents with a new onset of dyspnoea or embolic

phenomena. This should prompt urgent echocardiography to examine the mobility of the prosthetic occluders and assess the transvalvular gradients. In case of elevated transvalvular gradients fluoroscopy can also be performed to further inspect the mobility of the occluders.

MHV thrombosis is complicated by high mortality and morbidity, regardless of the treatment strategy.[5] Generally, pregnant patients with MHV thrombosis have similar treatment strategies than non-pregnant patients.[10] In patients with subtherapeutic anticoagulation who are not critically ill, anticoagulation should be optimised using i.v. UFH or oral anticoagulation should be resumed. Emergency surgery should be considered in unstable patients with obstructive thrombosis, if surgery is readily available. However, there are many regions in sub-Saharan Africa where there is either no or delayed access cardiothoracic surgery.[14] In particular in those circumstances fibrinolysis should be used for critically ill patients, if urgent valve replacement is not immediately possible, or if the risk of surgery is high.[3] In a study on 24 women with prosthetic heart valve thrombosis in pregnancy, a low dose (25mg) slow infusion (over 6 hours) of tissue-type plasminogen activator under transoesophageal echocardiography guidance resulted in excellent thrombolytic success (mean dose 48.7 ± 29.5mg (range, 25 - 100mg).[15] The choice of anti-fibrinolytic should favour an agent with a molecular weight >1 000 Da, which prevents crossing of the placental barrier.[10] For instance, alteplase (a recombinant tissue plasminogen activator) does not cross the placenta, considering its high molecular weight. However, it is associated with embolisation and subplacental bleeding and data on its use in pregnancy are limited. As surgery is associated with a high rate of foetal loss (30%), fibrinolysis should be considered in stable patients in whom anticoagulation has failed.[3,15]

Our cases demonstrate different management approaches in patients with MHV thrombosis. As the first patient was critically ill and surgery was readily available, she was referred for urgent valve replacement. Although this could save her life, the cardiopulmonary bypass led to loss of the foetus. The second patient presented in a haemodynamically stable condition. After discussion with the multi-disciplinary team, the patient decided to continue with her pregnancy under in-hospital management. This allowed for planned delivery of a healthy neonate prior to redo valve surgery.

CONCLUSION

Valve thrombosis in pregnant patients with MHV is a feared complication, which is associated with high morbidity and mortality. Our case series highlights the complexity of management of these high-risk patients. A particular challenge in pregnant patients with MHV is to balance adequate anticoagulation against the risk of bleeding, teratogenicity and foetotoxicity. Optimal anticoagulation strategies for pregnant women with MHV remain controversial. Anticoagulation strategy should be individualised, and requires informed consent of the patient. Best management is provided by multidisciplinary input from the cardio-obstetric team.

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