The multidisciplinary management of a mechanical mitral valve thrombosis in pregnancy: a case report and review of the literature

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Background

The management of anticoagulation for mechanical heart valves during pregnancy poses a unique challenge. Mechanical valve thrombosis is a devastating complication for which surgery is often the treatment of choice. However, cardiac surgery for prosthetic valve dysfunction in pregnant patients confers a high risk of maternofetal morbidity and mortality.

Case summary

A 39-year-old woman in her first pregnancy at 30 weeks gestation presented to hospital with a mechanical mitral valve thrombosis despite therapeutic anticoagulation with low-molecular-weight heparin. She underwent an emergent caesarean section followed immediately by a bioprosthetic mitral valve replacement. This occurred after careful planning and organization on the part of a large multidisciplinary team.

Discussion

A proactive, rather than reactive, approach to the surgical management of a mechanical valve thrombosis in pregnancy will maximize the chances of successful maternal and fetal outcomes.

Keywords

Case report • Pregnancy • Mechanical heart valve • Thrombosis • Warfarin • Low-molecular-weight heparin • Surgery

ESC Curriculum

2.2 Echocardiography • 4.10 Prosthetic valves • 7.3 Critically ill cardiac patient • 7.5 Cardiac surgery • 9.8 Pregnancy with cardiac symptoms or disease

Learning points

• Mechanical valve thrombosis in pregnancy can occur despite appropriate therapeutic anticoagulation with low-molecular-weight heparin.
• For pregnant patients with mechanical valve thrombosis who require surgery, the chances of a successful outcome are maximized using a multidisciplinary approach, as well as careful logistical planning to deal with potential perioperative complications.

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Primary specialties involved other than cardiology
Maternal-Fetal Medicine, Obstetric Medicine, Cardiac Surgery, Cardiac Anaesthesia, Obstetric Anaesthesia, Intensive Care, Pediatric Intensive Care, Haematology.

Introduction
Pregnant women with mechanical heart valves (MHVs) are at significant risk of morbidity and mortality, due to both thrombotic and haemorrhagic complications. Managing anticoagulation in this context is challenging, given the pregnancy-induced physiological prothrombotic state, and the varying maternal and fetal risks associated with the different options for anticoagulation. Thus, the anticoagulation strategy in pregnant women with MHVs should be selected on a case-by-case basis through a process of shared decision-making.

Mechanical valve thrombosis in pregnancy complicates 4.7% of pregnancies with MHVs and is associated with a 20% risk of maternal mortality. Surgery is often the treatment modality of choice and poses substantial risks to both the mother and fetus. Here, we describe the clinical course and management of a pregnant woman with a MHV thrombosis at 30 weeks of gestation.

Timeline

Case presentation
A 39-year-old primigravid woman was referred to our tertiary care centre for management of her MHV in pregnancy. She had a history of rheumatic heart disease with symptomatic severe mitral stenosis, severe tricuspid regurgitation, severe left atrial enlargement (LA indexed volume of 92 mL/m²), Type II pulmonary hypertension, and chronic atrial fibrillation. One year prior to pregnancy, she underwent a 33 mm St-Jude bi-leaflet metallic mitral valve replacement, tricuspid valve annuloplasty, and an amputation of the left atrial appendage containing a large thrombus discovered intraoperatively. A mechanical valve was chosen because of its longer durability in light of the patient’s young age, and the presence of another indication for anticoagulation (i.e. atrial fibrillation). At the time, the patient had no future pregnancy plans. Her surgery was well tolerated and without complications. She was adherent to her antithrombotic regimen, which consisted of daily oral warfarin 5 mg (targeting an International Normalized Ratio [INR] of 2.5–3.5) since her surgery.

At four weeks of gestation, her warfarin was discontinued due to teratogenicity concerns, and she was switched to low-molecular-weight heparin (LMWH). Aspirin 81 mg orally daily was added at 10 weeks as an adjunct antithrombotic therapy to LMWH in pregnancy, and for preeclampsia prophylaxis given the presence of some risk factors (i.e. nulliparity and maternal age ≥35 years). She was referred for multidisciplinary high-risk pregnancy care at our tertiary healthcare centre at 12 weeks of gestation. The potential anticoagulation strategies for the remainder of the pregnancy were reviewed, along with an in-depth discussion regarding their associated risks and benefits. After shared decision-making, and despite detailed explanations on the risks and benefits of each anticoagulation modality on multiple occasions, it was decided that LMWH was to be continued (i.e. enoxaparin 1 mg/kg SC BID) due to its better fetal safety profile. The importance of strong adherence to therapy was reinforced, as well as the need for meticulous monitoring of anti-Xa levels throughout pregnancy. Her anti-Xa levels were measured every 1–2 weeks, targeting peak levels of 1.0–1.2 IU/mL and trough levels >0.6 IU/mL. Anticoagulation modalities were revisited at each follow-up appointment. A transthoracic echocardiogram (TTE) at 17 weeks of gestation demonstrated the mechanical mitral valve in situ with a mean transvalvular gradient of 4 mmHg, mild-moderate mitral regurgitation, severe left atrial dilatation, and normal biventricular systolic function and pulmonary artery pressure.

At 30 weeks of gestation, she presented to the emergency room with an acute onset of dyspnoea, orthopnoea, bilateral lower extremity oedema, and a new cough with scant hemoptysis. Blood pressure was 110/71 mmHg, and the heart rate was 100–115 beats per minute (sinus rhythm), and her oxygen saturation ranged between 88 and 91% on room air. She was afebrile. Her chest X-ray showed pulmonary oedema. A TTE was performed emergently and demonstrated a mass of 2.5 cm in diameter on the ventricular lateral aspect of the mitral valve prosthesis with some multi-lobulated mobile projections, and a
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The mass was concerning for MHV thrombosis. The differential diagnosis included infective endocarditis and myxoma, albeit these diagnoses were felt to be less likely in the given clinical context. Nevertheless, empiric antibiotics were started with gentamycin and vancomycin pending blood culture results. The position of the mass and the rapidity with which it developed (i.e. within 1 year of cardiac surgery) made a myxoma highly improbable.

The patient was admitted to the intensive care unit for monitoring, diuresis, and anticoagulation with intravenous (IV) unfractionated heparin. She received betamethasone for fetal lung maturation and magnesium sulfate for foetal neuroprotection in anticipation of an intervention leading to preterm delivery. After 48 h, a repeat TTE and transesophageal echocardiography were performed and redemonstrated the large mass. The mitral valve mean gradient had decreased from 28 mmHg to 20 mmHg (heart rate of 72 bpm), however the mass size remained unchanged.

An urgent multidisciplinary meeting was held. Present at this meeting were specialists in cardiology, cardiac surgery, obstetric medicine, haematology, maternal–fetal medicine, neonatal intensive care, adult intensive care, cardiac anaesthesia, and obstetric anaesthesia. It was decided that the patient would undergo a caesarean section followed immediately by cardiac surgery to replace her mitral valve.

The patient’s IV heparin was held for 4 h in preparation for surgery. However, a repeat TTE revealed an increase in the size and mobility of the mass, and an acute worsening of the diastolic mean gradient to 34 mmHg at 84 bpm. Therefore, anticoagulation was immediately restarted, and the caesarean section was performed while on therapeutic IV heparin. The high-risk nature of the surgical plan necessitated careful logistical organization before proceeding to the operating room. Specifically, the medical and surgical teams that were required to be present or on standby throughout the perioperative course was communicated and confirmed with all team members (see Table 1).

Peripheral cannulation for extracorporeal membrane oxygenation (ECMO) was installed while awake under local anaesthesia in her right femoral vein and artery to be prepared in case of severe haemodynamic instability on induction of general anaesthesia or during surgery. The risk of neonatal respiratory depression using high-dose opioid induction precluded its use for cardiac stability, so induction was achieved with propofol and succinylcholine. The caesarean section was performed by two maternal-fetal medicine specialists. Bleeding was surgically cauterized to optimize haemostasis. A live baby boy weighing 1560 g was delivered. The placenta was delivered manually, and the uterus was closed in one layer. Filshie clips were used bilaterally for tubal ligation, as consented by the patient prior to surgery. An attempt to insert an intrauterine Bakri balloon was unsuccessful, and a Foley catheter was placed into the uterine cavity as an alternative. She lost an estimated 500–600 mL of blood during the caesarean section and an additional 800 mL was measured by the intrauterine Foley catheter during the cardiac surgery. She received 3 units of packed red blood cells before proceeding to cardiac surgery.

**Figure 1** Mechanical heart valve mass on echocardiography. Transthoracic echocardiography [parasternal long axis (PLAX) view] showing the large multilobed thrombus on ventricular surface of the bi-leaflet metallic mitral valve. LV = left ventricle, MV = mitral valve, LA = left atrium, RV = right ventricle.
The patient then underwent a redo sternotomy to replace her MHV prosthesis. Cardiopulmonary bypass was established using femoral artery cannulation and bicaval venous cannulae. A 31 mm St. Jude Epic bioprosthetic valve replaced the previous mechanical mitral valve. The rationale for choosing a bioprosthetic valve instead of a mechanical valve despite her age was in the event of post-operative bleeding requiring interruption of anticoagulation (as occurred in this case), which would pose a particularly high risk of thrombosis in the early post-operative and postpartum periods. She remained stable coming off cardiopulmonary bypass. Intravenous protamine was given to reverse the effect of heparin. A thrombus was confirmed upon pathological examination (Figure 2). Cerebral embolic events were excluded through serial neurologic exams performed pre- and post-operatively.

In the ICU, vasopressor requirements increased post-operatively with a drop in haemoglobin from 94 g/L to 57 g/L. Chest imaging revealed a large loculated right haemothorax causing leftward mass effect, active arterial extravasation in the superior anterior mediastinum, and a displaced chest tube. Thus, the patient was taken back to the operating room on post-operative day one for surgical exploration. No bleeding source was identified, but a large amount of blood and clots were evacuated from the right pleural space. While her haemodynamic status rapidly normalized following surgery, she developed an expanding rectus sheath haematoma measuring up to 11×9×11 cm on post-operative Day 4. It improved with expectant management while receiving prophylactic dose dalteparin. Anticoagulation with warfarin targeting an INR of 2–2.5 was initiated on post-operative Day 12 for valvular atrial fibrillation. She otherwise recovered well and was discharged home after a 28-day hospital stay. Her baby was hospitalized in the NICU for 9 weeks due to prematurity.

**Discussion**

We hereby outline the multidisciplinary planning and execution of a caesarean section followed by bioprosthetic mitral valve replacement after mechanical mitral valve thrombosis in pregnancy. MHVs are classified as a modified World Health Organization pregnancy risk class III due to high risk of maternal mortality and severe morbidity; as such, patients with MHVs require counselling and close follow-up in an expert centre for pregnancy and cardiac diseases.\(^5,9\) Anticoagulation for pregnant women with MHVs poses a significant challenge. First, pregnancy is a prothrombotic state increasing the risk of valve thrombosis.\(^1,11\) Second, other physiologic changes in

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**Table 1** Illustrative example of the multidisciplinary management of mechanical valve thrombosis in pregnancy

| Location | Intervention | Must be present | Must be on standby |
|----------|--------------|-----------------|-------------------|
| ICU      | IV heparin   | ICU team        | -                 |
| OR part 1| ECMO cannulation (under local anaesthesia) | Cardiology | ECMO team |
|          |              | Obstetric anaesthesia | Cardiac surgery |
|          |              | Cardiac anaesthesia | Blood bank/Massive transfusion protocol |
| OR, part 2 | Mitral valve replacement | Obstetric anaesthesia | Obstetrics backup |
|          |              | Cardiac anaesthesia | Blood bank/Massive transfusion protocol |
| ICU      | Immediate post-op | ICU team | Neurology |
|          |              | Obstetrics | Interventional neurology |
|          |              | Obstetric medicine | |

ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; IV = intravenous; NICU = neonatal intensive care unit; OR = operating room

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**Figure 2** Mechanical mitral valve thrombus. Surgical specimen of the mass resected from the patient’s mechanical mitral valve. It measured 3.5×1.5×1.5 cm on the ventricular side and a 2.3×1×1 cm on the atrial side. A thrombus was confirmed upon pathological examination.
pregnancy, such as increased renal clearance and volume of distribution, can affect the pharmacokinetics of anticoagulants, requiring close monitoring and regular dose adjustments. Finally, there is no ideal anticoagulation strategy for MHVs in pregnancy: each option is a trade-off between maternal and fetal risks.

The relatively higher rate of thrombotic complications during pregnancy in patients with MHVs demonstrates the high-risk nature of the peripartum state. In the ROPAC study, 4.4% of patients with a mechanical mitral valve and 2.4% of patients with mechanical aortic valves experienced a valve thrombosis during pregnancy despite an acceptable anticoagulation regimen. This is in contrast to the risk of all thromboembolic complications in patients with MHVs outside of pregnancy (i.e. 0.9%/year for mitral and 0.5%/year for aortic valves). Pregnancy may also accelerate time to prosthetic valve reoperation, with mechanical valves in the mitral position carrying a disproportionately higher risk of reoperation within 1 year of delivery, driven largely by valve thrombosis.

Outside of pregnancy, anticoagulation for MHVs is achieved with vitamin K antagonists (VKAs) targeting a specified INR range. However, VKAs cross the placenta and are associated with a spectrum of adverse fetal outcomes. Teratogenicity is increased when VKAs are taken in the first trimester and when higher doses are required for therapeutic anticoagulation. Fetal risks remain present, even when VKAs are taken at lower doses (i.e. < 5 mg warfarin orally daily) or exclusively taken in the second and third trimesters. Conversely, heparins (either LMWH or unfractionated heparin) do not cross the placenta, and are not associated with fetal toxicity. However, the risk of valve thrombosis is higher with heparins than with VKA therapy, despite dose adjustments according to peak anti-Xa levels. The safest anticoagulation strategy for MHV in pregnancy from a maternal standpoint is indisputably VKA throughout pregnancy, with lower rates of maternal mortality and thromboembolic complications compared with LMWH, unfractionated heparin, or with sequential treatment with heparin in the first trimester followed by VKA for the remainder of the pregnancy (Table 2). However, the increased fetal risks associated with VKAs may not be acceptable to some patients despite their well-established superior maternal safety profile, as in this case.

Choosing an anticoagulation strategy and targeted therapeutic range should consider patient-related factors (i.e. mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis of any degree, or left ventricular ejection fraction <35%), valve-related factors, and patient preferences. In addition, adherence to therapy is a significant issue in anticoagulation management for MHV during pregnancy, and barriers to adherence should be identified and addressed before deciding on the specific anticoagulation regimen. Our patient’s history of atrial fibrillation and severely enlarged left atrium, and the mitral valve position of the prosthesis conferred a higher risk of thrombosis, while a recent St-Jude Medical mechanical valve was associated with relatively lower thrombogenicity. By the time she was referred to our centre and provided with counseling about her management options, she was near the end of her first trimester, highlighting the importance of early referral to facilitate patients’ informed choices regarding their care throughout pregnancy. Although LMWH was given early in pregnancy and it was decided to carry on with this treatment modality throughout pregnancy, VKA therapy, including during the first trimester, would have been an appropriate option.

Management of MHV thrombosis in pregnant patients is comparable with non-pregnant patients. As per guidelines published by the European Society of Cardiology (ESC), surgery is the treatment of choice for critically ill patients with an obstructive thrombus, when adequate anticoagulation has failed, or for a large (i.e. > 10 mm) non-obstructive thrombus complicated by embolism. Fibrinolysis should be considered when surgery is unavailable or contraindicated, or for right-sided prostheses. The American Heart Association recommends either slow-infusion low-dose fibrinolytic therapy or emergency surgery depending on multiple factors, including the patient’s surgical risk, clot size, availability of surgical expertise, and the clinical experience with both treatments.

Fibrinolysis may warrant greater consideration in the setting of MHV thrombosis in pregnancy. Notably, the complication rate of fibrinolysis does not seem higher in pregnant than in non-pregnant individuals, and favourable outcomes have been described using fibrinolysis in pregnancy for MHV thrombosis. However, studies with non-pregnant patients have demonstrated that fibrinolysis is associated with a
greater risk of major bleeding, thromboembolism, and valve thrombosis recurrence than surgery. Considering the available evidence and the fact that our patient was critically ill with a very large obstructive mobile thrombus of her mitral valve, multidisciplinary assessment deemed that surgical management was indicated.

Cardiopulmonary bypass is associated with a high risk of neonatal complications, adverse birth outcomes, and a fetal mortality rate of up to 33%. For this reason, emergency caesarean section is recommended prior to cardiac surgery in women who are in their third trimester. We estimated that the benefits of delivering the fetus at 30 weeks of gestation outweighed the maternal obstetrical bleeding risks associated with caesarean section while on therapeutic anticoagulation, as well as the fetal risks of attempting to maintain the pregnancy while on cardiopulmonary bypass.

The decision to replace her mechanical valve with a bioprosthetic one appeared to be the safer option considering her post-operative bleeding complications, which necessitated that she only receives prophylactic LMWH for nearly 2 weeks following her surgery. Moreover, a bioprosthetic valve was justified by the possibility of a future percutaneous intervention rather than redo surgery, with valve-in-valve interventions using percutaneous devices. It should be noted however that bioprosthetic mitral valves still incur a non-negligible risk of thromboembolism (i.e. 2.4% per patient-year), with the highest risk period being the first 90–180 days following surgery.

It was imperative that a multidisciplinary approach be used in this case. A meeting with medical and surgical specialties involved with her care allowed each team member to participate in the decision-making process, to clarify the plan and each other’s roles at every stage, and to ensure adequate backup and resources. For example, the ECMO, vascular neurology, and neuro-interventional radiology teams, as well as the blood bank in case of massive obstetrical haemorrhage were all made aware of the case and the possible need to involve them further on an emergent basis throughout the course of the day (Table 1). Of note, pre-emptive ECMO cannulation as a standby modality has been described previously for pregnant patients undergoing high-risk surgery but is currently limited to case reports. We advise that ECMO cannulation be considered as a potentially life-saving proactive measure during the perioperative planning of similar cases.

We have presented the clinical course and management of a patient with a MHV thrombosis, outlining the rationale for the decisions that were made in her care. A multidisciplinary approach in a specialized centre with a cardio-obstetrics programme helped to maximize the chances of a successful outcome. We highlight the importance of referring patients with MHV to centres that can offer the resources and expertise to counsel and monitor these patients, as well as manage potential complications. The referral should occur when the patient is contemplating pregnancy or on an urgent basis if the pregnancy is unplanned. Moreover, considering a lifetime perspective when planning for valve replacement surgery, referral for pre-emptive pre-conception evaluation may help with informed decision-making regarding valve replacement options. In addition to diligent anticoagulant therapy monitoring and dose titration, frequent echocardiographic surveillance of the valves should be performed during pregnancy, as MHV are prone to thrombus formation, despite uninterrupted therapeutic anticoagulation. Future research comparing the safety and effectiveness of cardiac surgery vs. fibrinolysis in pregnant patients with MHV thrombosis is warranted, as well as the development of anticoagulation strategies with better safety profiles for both the mother and fetus. Moreover, the optimal strategy for peripartum anticoagulation of women with MHV, including bridging strategies close to delivery, needs to be clarified. Importantly, we advocate for the creation of ‘Cardio-Obstetrics Valve Teams’ to provide close collaborative care to this complex, and high-risk patient group.

Lead author biography

Jennifer Wright, MD PhD, graduated from McGill’s General Internal Medicine residency programme in June 2022. She is pursuing a Masters of Health Professions Education at the University of Ottawa and clinical fellowship training in Perioperative Medicine at McMaster University.

Supplementary material

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

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