Marfan's syndrome and other aortopathies in pregnancy

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Abstract

Aortopathies, or disease affecting the aorta, are associated with a significant mortality risk for the mother and foetus during pregnancy because of an increased rate of aortic dissection. The hereditary aortopathies; Marfan's syndrome, bicuspid aortic valve, Loeys–Dietz syndrome, Ehlers–Danlos (type IV) syndrome, Turner's syndrome and nonsyndromic familial thoracic aortic aneurysm and dissection are all associated with an increased risk of aortic dissection particularly during the third trimester and early postpartum period. Maternal outcome in pregnancy depends on the underlying disorder and the aortic dimensions prior to pregnancy. The foetus has up to 50% chance of inheriting the underlying genetic defect. Vasculitis, particularly Takayasu's arteritis may also be a problem in pregnancy and predispose to aortic dissection. Prepregnancy review, including careful assessment of the aorta and prophylactic aortic surgery for an aortic aneurysm may reduce the risk of aortic dissection in pregnancy for some of the aortopathies but for women with Marfan's syndrome, Loeys–Dietz syndrome and Ehlers–Danlos (vascular type IV) who have had surgery, the risk of death remains high. A subgroup of women with Marfan's syndrome or a bicuspid aortic valve and normal aortic dimensions prepregnancy should do well in a pregnancy. Multidisciplinary pregnancy care with agreement on pregnancy follow-up, delivery and postpartum care with a crisis plan for an aortic dissection can improve pregnancy outcome and ensure prompt management of an aortic dissection should it occur.

Keywords

Cardiovascular, high-risk pregnancy, aorta

Aortopathies in pregnancy

Aortopathies or diseases affecting the aorta have long been recognised as a significant cause of maternal death in pregnancy. In an autopsy series of 580 patients who died from aortic dissections 49 were women under the age of 40 and 24 of these women were pregnant at the time of death.¹ Cardiac disease is now the leading indirect (pre-existing) cause of maternal death in the United Kingdom, Australia and New Zealand.^{2–4} Despite improvements in diagnosis, imaging and surgical management of these women in recent years the mortality rate from aortic dissection in pregnancy and the early postpartum period has remained remarkably stable over the past 15 years in the United Kingdom.² It is hoped that this mortality risk can be reduced by a greater understanding of the aortopathies, screening of at risk families, pre-pregnancy assessment and counselling coupled with close surveillance in pregnancy and awareness of the risk of aortic dissection.

Hypertensive and atherosclerotic disease are the main cause of aortic dissections in the wider population but in the younger age group hereditary aortopathies are the main cause of thoracic aortic dissection. Thoracic aortic disease is usually asymptomatic until the time of dissection. With improved awareness of aortopathies, their mode of inheritance and associated abnormalities we can better identify at risk women. Imaging has improved identification of an abnormal aorta and there have been major advances in surgical management.

Hereditary aortopathies

Marfan's syndrome

Marfan's syndrome is the most commonly described aortopathy occurring in pregnancy. The incidence in the general population is 2–3/10,000. It is an autosomal dominant condition with variable penetrance due to mutations in the FBN1 gene on chromosome 15q21 encoding for fibrillin-1 a glycoprotein found in the microfibrils of the elastic fibres⁵ (Table 1). Over 600 mutations have been described in the FBN1 gene and more recently a second locus for Marfan's syndrome, MFS2 has been described caused by mutations in the transforming growth factor-beta type II receptor (TGFB2). This diversity coupled with approximately 25% of patients having a sporadic mutation causing Marfan's syndrome makes genetic typing of the condition difficult,

although for families with a well-identified genetic abnormality preimplantation genetic diagnosis is available to prevent transferring the condition to the next generation. Diagnosis of the condition remains primarily clinical according to the revised Ghent criteria.^{6,7} Life expectancy is reduced mainly due to aortic dissection but is improving with prophylactic aortic surgery. Aortic dissection can occur in any segment of the aorta but dilatation is usually seen first in the aortic root (sinus of Valsalva) extending to the proximal ascending aorta (Figures 1 and 2). In a study of 113 non-pregnant patients with Marfan's syndrome, aortic dilatation was present in 80% of patients, localised to the sinus of Valsalva in 28% and generalised in 51%. No dissections occurred in an average follow-up time of four years in the group with a normal aortic root measurement on echocardiography.⁸ The risk of aortic dissection is related to the length of ascending aorta involved in an aneurysm, the maximum dimension of the ascending aorta and the presence of a family history of aortic dissection, aortic surgery under 40 years of age or sudden cardiac death.⁸ A complete review of the aorta with magnetic resonance (MR) angiography or computerised tomography (CT) is important though, as dissections can be confined to the descending aorta or aortic arch (Table 2 and Figure 3).

Whilst there are a number of case reports of aortic dissection occurring in pregnancy or the early postpartum period in women with Marfan's syndrome, researchers have identified a relatively low risk group of women who have tolerated pregnancy well, with a low risk of adverse cardiac events.^{5,8,15} These women had an aortic root diameter of <40 mm. With an aortic diameter of 40–45 mm additional risk factors such as increasing aortic diameter in pregnancy, a family history of aortic dissection, aortic surgery under 40 years of age or sudden cardiac death identify a high risk subgroup. Pregnancies are not recommended with an aortic root measurement >45 mm.^{5,10} Immer and

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Table 1. Genetic syndromes predisposing to thoracic aortic aneurysm and dissection.

	Genetic mutations	Associated features
Marfan's syndrome	FBN1 (fibrillin-1) TGFB2	Cardiovascular – mitral valve prolapse Skeletal – pectus excavatum, arachnodactyly, kyphoscoliosis, joint laxity Ocular – ectopia lentis Dural ectasia
Ehlers–Danlos type IV	COL3A1 (type III collagen defect)	Easy bruising, thin skin Uterine, GI, arterial rupture
Loeys–Dietz syndrome	TGFB1 TGFB2	Arterial tortuosity and aneurysms Hypertelorism Bifid uvula or cleft palate
FTAAD	TGFB2 MYH11 ACTA2	Nil
Bicuspid aortic valve		Coarctation of the aorta Ascending aortic aneurysm
Turner syndrome	45X	Ovarian failure Bicuspid aortic valve (10 – 25%) Coarctation of the aorta (8 – 10%)

FBN1 encodes fibrillin-1; TGFB2: transforming growth factor-beta type receptor; FTAAD: nonsyndromic familial thoracic aortic aneurysms and dissection.

Figure 1. Transthoracic echocardiogram showing a Type A aortic dissection (a, b) and aortic regurgitation (c).

colleagues¹⁴ also assessed the risk for Type B dissection (21%) in women with aortopathies in pregnancy. There were no predictive clinical features in these women.

Prophylactic aortic surgery is recommended pre-pregnancy for women with an ascending aorta ≥ 45 mm. During pregnancy, aortic surgery is recommended for progressive dilatation of the ascending aorta, ascending aortic (Type A) dissection and for Type B dissections where there are problems of malperfusion or aortic rupture.^{5,10} Some women are first diagnosed with an ascending aortic aneurysm during pregnancy. There is no consensus for these women as to whether prophylactic surgery should be offered in pregnancy and if so at what aortic dimension. Prophylactic surgery is recommended to be performed, where possible, during the second trimester of pregnancy to minimise foetal risk. When the foetus is viable, delivery by caesarean section immediately prior to aortic surgery is recommended.^{5,10}

Bicuspid aortic valve

Bicuspid aortic valves are found in 1–2% of the population. The abnormality is associated with dilatation of the ascending aorta due to abnormal blood flow in the ascending aorta and degenerative histopathological changes including cystic medial necrosis, changes in smooth muscle orientation and elastic fibre fragmentation.¹⁶ Aortic dissections are confined to the ascending aorta.⁵ There is an association with coarctation of the aorta.

There is a significant familial predisposition with variable involvement of the aortic valve and ascending aorta.¹⁷ Aortic root dilatation with a trileaflet valve was seen in 32% of first degree relatives with a bicuspid aortic valve.¹⁸ The genetic abnormality has not yet been identified. Consideration should therefore be given to performing a screening echocardiogram pre-pregnancy in women who have a first degree relative with a bicuspid aortic valve or aortopathy.

Figure 2. Magnetic resonance image showing dilated aortic root (a) and dural ectasia (b) in a patient with Marfan syndrome.

Table 2. Aortic dissection classification systems.

Stanford	De Bakey (origin of intimal tear)	
A (involves ascending aorta)	I	Ascending aorta extending to arch or descending aorta
A	II	Ascending aorta only
B (arch or descending aorta)	IIIa	Descending thoracic aorta
B	IIIb	Extending below the diaphragm

In the series of aortic dissections in pregnancy by Immer et al.¹⁴ 10% had a bicuspid aortic valve. These dissections tended to occur in younger patients, earlier in pregnancy (average 26.8 weeks gestation), with a poor foetal outcome compared to aortic dissections in women with Marfan’s syndrome. The European Society of Cardiology recommends pre-pregnancy surgery when the aortic root is >50 mm.¹⁰ Bicuspid aortic valve repair for aortic regurgitation has excellent long-term results in specialised centres and should be considered where possible pre-pregnancy with aortic aneurysm repair as necessary.⁵

Loeys–Dietz syndrome

Loeys–Dietz syndrome has recently been identified as an autosomal dominant condition due to mutations in the genes encoding for transforming growth factor beta receptor 1 or 2 (TGFBRI or 2).¹⁹ In addition to arterial and aortic aneurysms and tortuosity, hypertelorism and a cleft palate or bifid uvula is seen. Aortic dissection and rupture is usually seen in the proximal ascending aorta with tortuosity of the head and neck vessels. Expansion of the aorta is described throughout its length. Only 25% have an affected parent with 75% having *de novo* mutations. Bicuspid aortic valve, patent ductus arteriosus, ventricular and atrial septal defects are also seen in some affected patients. Prophylactic surgery of the ascending aorta is recommended when the aortic root is >40 mm or expands by >5 mm over 1 year.

Successful pregnancies have been described in women with Loeys–Dietz syndrome but complication rates are high (6 events in 12 women

who had 21 pregnancies).²⁰ Complications included aortic dissection and uterine rupture occurring during pregnancy or the early postpartum period. Early delivery by caesarean section has been recommended.^{19,21}

Ehlers–Danlos syndrome (type IV, vascular form)

Ehlers–Danlos syndrome, type IV, due to mutations in the gene for type III procollagen (COL3A1), is an autosomal dominant condition characterised by easy bruising, thin skin with visible veins, characteristic facial features and rupture of arteries, uterus or intestine. Diagnosis is usually made in the 20s and life expectancy is reduced.²²

In a review of 81 women who had 183 pregnancies, 12 women died peripartum or in the first two weeks after delivery: five from uterine rupture in labour and seven from vessel rupture (five at delivery and five postpartum).²² Successful pregnancies have occurred with vascular Ehlers–Danlos syndrome²³ but the condition remains very high risk for the mother and is considered a contraindication for pregnancy.¹⁰ There is no evidence that prophylactic aortic surgery reduces the risk of aortic dissection.⁵

Nonsyndromic Familial Thoracic Aneurysm and Dissection

A strong familial risk for thoracic aortic dissection has been recognised in the absence of features of other syndromes such as Marfan’s syndrome probably accounting for at least 20% of thoracic aortic aneurysms in young people.²⁴ Several genetic defects have now been described to explain this autosomal dominant condition with variable penetrance leading to cystic medial degeneration of the ascending aorta⁵ (Table 1). As there are no classical phenotypic abnormalities it is important that first degree relatives of a patient with an aortic dissection are screened, preferably pre-pregnancy. With some of the genetic abnormalities dissections have occurred in patients with aortic diameters <50 mm. Prophylactic aortic surgery is recommended at 42 mm in pre-pregnant women.⁵ Familial thoracic aneurysm and dissection (FTAAD) has been described as the cause of aortic dissection in postpartum women but there are no significant case series published on pregnant women with this syndrome. Women who have had valve sparing aortic root replacement surgery for a thoracic aneurysm

Figure 3. Magnetic resonance image of the thoracic (a) and abdominal (b) aorta in a woman who presented with an aortic arch dissection (red arrows) at 23 weeks in her first pregnancy that required urgent repair. At 32 weeks a further dissection occurred complicated by left renal and splenic infarction (b) with collateral formation (yellow arrow). A Bentall's procedure was performed at a later date for ascending aortic aneurysm.

or dissection would be expected to do well in pregnancy as the remainder of the aorta should not be at risk.

Turner's syndrome

Turner's syndrome occurs in phenotypic women with a complete or partial absence of one X chromosome (45X). Infertility is common in women with Turner's syndrome due to premature ovarian failure resulting in spontaneous pregnancies in only 2–5%. Increasing numbers of women are having successful pregnancies with oocyte donors.²⁵ Women with Turner's syndrome have an increased risk of a bicuspid aortic valve (10–25%), coarctation of the aorta (8–10%) and hypertension.^{5,24} All these predispose to the development of ascending aortic aneurysms and dissection. Women with Turner's syndrome are short in stature so measurement of the aorta should be indexed for body surface area. Surgery is recommended if the aorta measures more than 25 mm/m². There are no comprehensive reviews of the risk of pregnancy in women with Turner's syndrome and aortopathies but the Collège National des Gynécologues et Obstétriciens Français has produced excellent clinical practice recommendations for Turner's syndrome and pregnancy.²⁶ They list as contraindications to pregnancy; a history of aortic surgery or aortic dissection, a dilated aorta with the largest aortic diameter greater than 25 mm/m² or 35 mm, coarctation of the aorta or uncontrolled hypertension. Portal hypertension with oesophageal varices is a noncardiac contraindication. Monitoring throughout the pregnancy with echocardiography performed at the end of the first and second trimesters then monthly until delivery is recommended with delivery if the aortic dimension increases by 10% or is greater than 25 mm/m² on confirmatory MR scanning. Routine beta-blockade should be considered during pregnancy with additional anti-hypertensive treatment as needed. Anaesthetic review predelivery is important because of the increased rate of problems with both intubation and insertion of spinal or epidural anaesthesia. About 85% of

deliveries in stable women are by caesarean section because of narrow pelvic outlets and assisted delivery is recommended for women undergoing vaginal delivery. Follow-up echocardiography to record aortic dimensions is recommended between days 5 and 8 postpartum. The French website also has excellent material for patient education.

Coarctation of the aorta

Coarctation of the aorta is a congenital aortic abnormality characterised by a discrete narrowing of the aorta distal to the left subclavian artery. Seventy-five per cent will have a bicuspid aortic valve. Coarctation is also described occurring with a patent ductus arteriosus, Turner's and Noonan's syndromes. Most aortic coarctations are diagnosed in infancy and repaired surgically with an end-to-end anastomosis, Dacron graft, subclavian artery patch or bypass of the coarctation. Balloon aortoplasty or stenting is also performed on both native aortic vessels and restenosed aortas. Residual gradients within the aorta will predispose to hypertension. Aneurysms may occur at the anastomotic sites and some Dacron grafts have been associated with an increased risk of aortic rupture. Ten per cent of adult patients with coarctation in a Mayo Clinic series were found to have intracranial aneurysms on routine review compared to 2% in the general population.²⁷

There are two comprehensive reviews of pregnancies in women with coarctation of the aorta.^{28,29} In the Mayo Clinic series, 50 women, of whom 34 had a repair of their coarctation pre-pregnancy, had 118 pregnancies. All aortic repairs were surgical. Persistent hypertension following aortic repair occurred in 59% of the women and was more common if the initial surgery was at an older age. Two women developed pre-eclampsia and 15, hypertension during the pregnancy. The hypertensive women were more likely to have a residual coarctation. One woman, who had Turner's syndrome, died of an aortic dissection at 36 weeks' gestation. Thirty-six per cent of deliveries were by

caesarean section, predominantly for perceived maternal cardiovascular risk. No cerebral bleeds were recorded.

Vriend et al.²⁹ report the pregnancy results in women with coarctation of the aorta entered on The Netherlands, CONCOR national registry. Fifty-four of the 100 women over 18 years of age had 126 pregnancies resulting in 98 successful pregnancies, 22 miscarriages and six terminations of pregnancy. Women with Turner's syndrome were excluded. All the women had prior surgical repair of their coarctation, 89% with resection and end-to-end anastomosis. Thirty had residual hypertension. Fourteen women with 26 pregnancies had pregnancies complicated by hypertension and four women with five pregnancies developed pre-eclampsia. In contrast to the Mayo Clinic series, 85 of the deliveries were vaginal. There were no aortic dissections.

Management of hypertension is critical in these pregnancies with recent imaging of the aorta by magnetic resonance imaging (MRI) to exclude residual coarctation or aneurysm formation. The choice of method for delivery will depend on the surgical result from the coarctation and the presence of significant co-morbidities such as Turner's syndrome or aortic stenosis.

Vasculitis

Limited data are available on the risk to the aorta of pregnancy in women with pre-existing vasculitides. Behçet's syndrome and giant cell arteritis have not been described causing problems in pregnancy.

Takayasu's arteritis

Takayasu's arteritis is an idiopathic vasculitis involving the aorta and its branches causing aneurysm formation and stenosis.⁵ Pregnancy outcome is strongly correlated with abdominal aortic and renal involvement with increased risk of pre-eclampsia (60%), congestive cardiac failure (5%), cerebral haemorrhage (5%), progressive renal impairment and intrauterine death.³⁰ Cytotoxic agents should be stopped where possible pre-pregnancy although azathioprine has been used successfully in pregnancy for transplant recipients. Steroid therapy can be safely continued. Thromboprophylaxis is recommended due to an increased risk of thromboembolic complications. Pregnancy has not been shown to adversely affect the disease process.³¹ A full assessment of the woman including an MR scan of the aorta is recommended pre-pregnancy. Pregnancy is safest during a period of remission. Patients with Takayasu's disease and prior aortic grafts have a higher risk of graft failure with a report documenting a 12% incidence of anastomotic aneurysms over 20 years following surgery.⁵

Management of pregnancy with aortopathies

Prepregnancy assessment

Prepregnancy assessment is done based on the following history:

- personal history of aortic dissection or surgery;
- family history of aortic dissection, surgery or sudden cardiac death;
- genetic abnormality if known;
- concomitant cardiac problems – bicuspid aortic valve, coarctation of the aorta, aortic regurgitation, mitral valve prolapse, left ventricular impairment, arrhythmias, prosthetic valve and
- current dimensions of the aorta and serial data if known.

A prepregnancy review involves a current assessment of the mother's history including any previous history of aortic dissection or cardiovascular surgery. In conditions where the aortic pathology is confined to the ascending aorta (bicuspid aortic valve, FTAAD) and a good repair has been achieved sparing the aortic valve,

pregnancy should be relatively low risk. In contrast, women with a previous dissection and Marfan's, Turner's, Loeys-Dietz and Ehlers-Danlos type IV syndromes are at high risk of having a further aortic dissection particularly in late pregnancy or the early postpartum period. The risk for a woman with vasculitis depends on the activity of the disease at the time of pregnancy.

Prosthetic valves have specific issues associated with anticoagulation and the choice of low molecular weight heparin or warfarin.^{10,32}

A family history of aortic dissection in a first degree relative in the absence of a known syndrome may be due to FTAAD or bicuspid aortic valve. A baseline echocardiogram is recommended.

Counselling should include the risk of foetal inheritance and where there is an identified genetic mutation in a parent, there is the possibility of preimplantation genetic screening.

A comprehensive assessment should be made of the aorta. Echocardiography remains the main imaging tool to screen the ascending aorta and to assess any valvular or concomitant structural cardiac lesions. The distal ascending aorta and aortic arch are not well visualised by transthoracic echocardiography and MR scanning provides complimentary information on the remainder of the aorta. (Figures 2 and 3) Although CT scanning will provide good views of the aorta MR scanning is preferred in this age group to avoid unnecessary radiation exposure. Gadolinium should be avoided in pregnancy.

In women with FTAAD or Loeys-Dietz syndrome prophylactic surgery is recommended at an aortic dimension of 42mm, in Marfan's syndrome at 45mm, with a bicuspid aortic valve at 50mm and in Turner's syndrome at >25mm/m² or earlier if there is a rapid increase in aortic dimensions.

When the assessment is complete a full discussion with the woman, her partner, cardiologist, obstetrician and obstetric physician is important to outline the likely risks of pregnancy to the mother, the inheritance risk for the foetus (including preimplantation genetic screening if available), the likely course of the pregnancy, including risk of maternal death and major morbidity and regularity of cardiac and obstetric follow-up, symptoms of aortic dissection to be aware of and report immediately, and likely delivery plans. Where appropriate, alternatives to a pregnancy either by adoption or surrogacy may also be discussed.

Aortic surgery

When technically possible a prophylactic aortic root replacement with resuspension and repair of the aortic valve (David procedure) is preferred to Bentall's procedure where the aortic valve is replaced, to remove the risk of prosthetic valves and anticoagulation in pregnancy.³² Homograft (cadaveric aortic root) or bioprosthetic grafts can be used to avoid the need for anticoagulation but have a limited life expectancy before needing replacement.^{5,32} Aortic stents are increasingly being used to treat residual aortic coarctation or aneurysms of the descending thoracic aorta greater than 55mm in diameter but are not recommended for treating ascending aortic or arch aneurysms.⁵

Medical therapy

Medical therapy is aimed firstly at carefully controlling blood pressure. Tight control of blood pressure is important throughout pregnancy and the postpartum period. The early detection and management of gestational hypertension and pre-eclampsia is also important.

Beta-blockade has been shown in one randomised study³³ and a number of observational studies to slow the progression of aortic dilatation in Marfan's syndrome. Beta-blockers are well tolerated in pregnancy and are recommended for all women with aortopathies throughout pregnancy despite the small risk of intrauterine growth restriction.

Angiotensin II blockers have also been shown to reduce the rate of aortic dilatation in animal studies and a preliminary study in children with Marfan's syndrome.³⁴ This class of drugs is contraindicated in pregnancy and with breast feeding.

Pregnancy review

Regular cardiac and obstetric review, including echocardiography to assess the ascending aorta, is recommended throughout the pregnancy. Imaging of the aorta is recommended at 4 to 8 week intervals¹⁰ although serial echocardiographic studies may not predict an aortic dissection particularly of the descending aorta or aortic arch.³⁵ In women with Marfan's syndrome and a baseline aortic root measurement of <40 mm, imaging does not need to be so intensive but is still recommended at the time of peak increase in cardiac output at 20 to 28 weeks and at 34 weeks or later if the blood pressure were to rise suddenly.

Delivery

Forming delivery plans, in discussion with the mother, is important to minimise complications at this important time. A multidisciplinary approach involving the Obstetrician, Obstetric Physician, Obstetric and Cardiac Anaesthetists, Cardiologist and if necessary the Cardiac Surgeons will minimise risk. Plans need to include the timing and location of delivery, elective or spontaneous labour and mode of delivery. More detailed recommendations according to aortic dimensions and the underlying pathology are available in Table 3. Where there has been an increase in aortic diameter during pregnancy or there is a family history of aortic dissection, aortic surgery under the age of 40

or sudden cardiac death, delivery by caesarean section is recommended. It is recommended that women with aortopathies deliver in a hospital with cardiac surgical facilities.

Regional anaesthesia has been used successfully for labour and caesarian section for women with Marfan's syndrome but dural ectasia in two women with Marfan's syndrome was associated with inadequate spinal anaesthesia probably through erratic spread of the anaesthetic agent.³⁶

The cardiovascular stress of labour can be reduced with early continuous epidural infusion and assisted delivery with forceps or vacuum extraction to avoid maternal pushing and hypertension in active labour.

Additional planning is required for women with prosthetic valves on anticoagulants. Most will therefore be delivered electively either by induction of labour or caesarean section.

Syntocinon can be safely administered as a uterotonic to reduce the risk of postpartum haemorrhage but ergotamine preparations should be avoided because of vasoconstriction leading to hypertension.

Postpartum care is critical as many aortic dissections occur during this time. Close monitoring with meticulous control of maternal blood pressure can reduce the risk of dissection. There is no consensus on the optimal duration of hospitalisation postpartum but women should be advised to remain in hospital for a minimum of 72 h postpartum and until their blood pressure is stable. Postpartum echocardiography is also useful to assess any change in aortic dimensions. Suitable contraception should be considered before discharge from hospital.

Acute aortic dissection

Aortic dissection (Figures 2 and 3) can occur at any gestation but most commonly occurs during the third trimester or in the first few weeks

Table 3. Delivery recommendations according to type and severity of aortopathy.

	Aortic dimensions	Recommended mode of delivery	Associated concerns	Anaesthetic concerns
Marfan's syndrome	<40 mm	Vaginal	FHx – Aortic dissection – Sudden cardiac death (consider caesarean)	Dural ectasia may preclude spinal ³⁶ (fig 2)
	>45 mm or Increasing in pregnancy	Caesarean		
Bicuspid AV	<50 mm Aortic graft	Vaginal	Aortic stenosis Coarctation of the aorta	Epidural contraindicated with severe AS
	>50 mm	Caesarean		
Loeys–Dietz		Caesarean	Uterine rupture Bicuspid AV, VSD, ASD	
Ehlers–Danlos		Caesarean	Uterine rupture	
Turner's syndrome	<25 mm/m ²		Pelvic obstruction Coarctation aorta Bicuspid aortic valve	Difficult intubation Difficult insertion of spinal/epidural
	>25 mm/m ² >10%↑aorta	Caesarean		
FTAAD	Aortic graft	Vaginal		
	>42 mm	Caesarean	No published series on outcomes in pregnancy	
Coarctation of the aorta		Uncertain	Hypertension 10% intracranial aneurysm	

FHx: family history, AS: aortic stenosis, AV: aortic valve, VSD: ventricular septal defect, ASD: atrial septal defect, FTAAD: familial thoracic aneurysm and dissection.

Mode of delivery: where vaginal delivery is recommended a caesarean section should be performed if there are obstetric indications. Recommendations may change with prosthetic valves and anticoagulation.

postpartum. In the most extensive review of aortic dissection in pregnancy, 47 women had aortic dissections antepartum and 10 postpartum.¹⁴ The presentation is classically with severe chest pain radiating to the back or haemodynamic compromise but in a single centre series from Melbourne, Australia only one woman presented with typical pain, one with a persistent cough and shortness of breath, one with epigastric pain, another with pleuritic pain and the fifth with features of a stroke in the middle cerebral artery territory.³⁷ We have also seen a patient present with an ischaemic limb. Only one of the five women in the Melbourne series was known to have an underlying condition (Turner's syndrome) predisposing to aortic dissection at the time of presentation although two were later diagnosed with Marfan's syndrome, one with a bicuspid aortic valve and the fourth died before a diagnosis was made. This highlights the significant incidence of women with undiagnosed aortopathies in pregnancy. The woman with Turner's syndrome had not had an echocardiogram performed before or during her donor egg pregnancy.

Early pain relief and management of hypertension are essential while initiating investigations. Rapid diagnosis of an aortic dissection is important as the mortality increases by 1–2% per hour during the first 48 h. The differential diagnosis includes acute myocardial infarction (ECG changes may be present due to coronary artery involvement), pulmonary embolism, pre-eclampsia and pancreatitis. A transthoracic echocardiogram is the first line investigation but a negative scan does not rule out an aortic dissection. Transoesophageal echocardiography, if there is a high index of suspicion or CT angiography with lead shielding of the foetus will help rule out a pulmonary embolus or aortic dissection. MRI can provide excellent images without radiation exposure but is time consuming and the patient is lying supine isolated in the imaging room where an acute deterioration in her status may go undetected.

Aortic dissections are classified by either the Stanford criteria (Table 2) defined by whether the dissection flap is in the ascending aorta (Type A) or aortic arch or descending aorta (Type B) or the De Baake classification that describes the location of the dissection (Table 2).

Ascending aortic aneurysms have a high mortality and require urgent surgery. For women in the first and second trimester immediate surgical repair is recommended but for women with a viable foetus caesarean section followed by immediate repair of the dissection gives the best result for mother and baby.¹⁰ A team approach to the surgery is important with Obstetrician, Cardiac Surgeon, Obstetric and Cardiothoracic Anaesthetists and Neonatologist present in theatre. Ch'ng et al.³⁷ recommended sternotomy prior to caesarean section to enable rapid cardiopulmonary bypass if the mother deteriorates. Uterine bleeding can be a major problem with coronary bypass.⁵ Syntocinon may be given but vasopressors such as ergotamine should be avoided.

Type B aortic dissections are usually managed medically unless there is a problem with malperfusion or aortic rupture. Aortic stenting has been used for Type B dissections but there are no published reports of this in pregnancy and there would be significant radiation exposure for the foetus.

Where a pregnancy is not yet viable foetal outcome can be improved by; normothermic cardiopulmonary bypass, avoiding vasoconstrictors to maximise placental blood flow, maintaining a high maternal haematocrit and high bypass flow rates. Sustained uterine contractions increase the rate of foetal death but there is no benefit seen from β -agonist tocolytics and they should be avoided.³⁸

Further pregnancies are contraindicated in women with an aortic dissection due to the high risk of further aortic dissections.

Conclusion

Aortic dissection is a life-threatening event for the mother and foetus. A better understanding of the underlying aortopathy and careful pre-pregnancy assessment may help differentiate between high and lower

risk women and help reduce but not eliminate the associated maternal mortality. Women should be advised of the risk of aortic dissection, of the symptoms to be alert to and to which cardiac surgical hospital they should present if symptomatic. Meticulous planning of delivery and the postpartum period will also reduce maternal risk.

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References

1. Schnitker MA and Bayer CA. Dissecting aneurysms of the aorta in young individuals, particularly in association with pregnancy. *Ann Intern Med* 1944; 20: 486.
2. CEMACH. *CEMACH saving mothers' lives: reviewing maternal deaths to make motherhood safer-2003-2005: The Seventh Report on Confidential Enquiries into Maternal Deaths in the United Kingdom*. London: Centre for Maternal and Child Enquiries, 2008.
3. Sullivan EH, Hall B and King JF. *Maternal deaths in Australia 2003-2005*. Maternal deaths series no. 3. Cat. no. PER 42. Sydney: AIHW National Perinatal Statistics Unit, 2007.
4. PMMRC. *Sixth Annual Report of the Perinatal and Maternal Mortality Review Committee. Reporting mortality 2010*. Wellington: Health Quality and Safety Commission, 2012.
5. Hiratzka LF, Bakris GL, Beckman JA, et al. ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation* 2010; 121: e266–e369.
6. De Paepe A, Devereux RB, Dietz HC, et al. Revised diagnostic criteria for the Marfan syndrome. *Am J Med Genet* 1996; 62: 417–426.
7. Judge DP and Dietz HC. Marfan's syndrome. *Lancet* 2005; 366: 1965–1976.
8. Roman MJ, Rosen SE, Kramer-Fox R, et al. Prognostic significance of the pattern of aortic root dilation in the Marfan syndrome. *J Am Coll Cardiol* 1993; 22: 1470–1476.
9. Pyeritz. Maternal and fetal complications of pregnancy in the Marfan syndrome. *Am J Med* 1981; 71: 784–790.
10. Regitz-Zagrosek V, Lundqvist C, Borghi C, et al. ESC Guidelines on the Management of Cardiovascular Diseases During Pregnancy. The Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology. *Eur Ht J* 2011; 32: 3147–3197.

11. Elkayam U, Ostrzega E, Shotan A, et al. Cardiovascular problems in pregnant women with the Marfan syndrome. *Ann Intern Med* 1995; 123: 117–122.
12. Rossiter JP, Repke JT, Morales AJ, et al. A prospective longitudinal evaluation of pregnancy in the Marfan syndrome. *Am J Obstet Gynecol* 1995; 173: 1599–1606.
13. Lipscomb KJ, Clayton Smith J, Clarke B, et al. Outcome of pregnancy in women with Marfan's syndrome. *Br J Obstet Gynaecol* 1997; 104: 201–206.
14. Immer FZ, Bansi AG, Immer-Bansi AS, et al. Aortic dissection in pregnancy: analysis of risk factors and outcome. *Ann Thorac Surg* 2003; 76: 309–314.
15. Meijboom LJ, Vos FE, Timmermans J, et al. Pregnancy and aortic root growth in the Marfan syndrome: a prospective study. *Eur Heart J* 2005; 26: 914–920.
16. Sorrell VL, Panczyk E and Alpert JS. A new disease: bicuspid aortic valve aortopathy syndrome. *Am J Med* 2012; 125: 322–323.
17. Plaisance BR, Winkler MA, Attili AK, et al. Congenital bicuspid aortic valve first presenting as an aortic aneurysm. *Am J Med* 2012; 125: e5–e7.
18. Biner S, Rafique AM, Ray I, et al. Aortopathy is prevalent in relatives of bicuspid aortic valve patients. *J Am Coll Cardiol* 2009; 53: 2288–2295.
19. Van Hemelrijk C, Renard M and Loeys B. The Loeys-Dietz syndrome: an update for the clinician. *Curr Opin Cardiol* 2010; 25: 546–551.
20. Loeys BL, Schwarze U, Holm T, et al. Aneurysm syndromes caused by mutations in the TGF- β receptor. *N Eng J Med* 2006; 355: 788–798.
21. Gutman G, Baris HN, Hirsch R, et al. Loeys-Dietz syndrome in pregnancy: a case description and report of a novel mutation. *Fetal Diagn Ther* 2009; 26: 35–37.
22. Pepin M, Schwarze U, Superti-Furga A, et al. Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. *N Eng J Med* 2000; 342: 673–680.
23. Palmquist M, Pappas JG, Petrikovsky B, et al. Successful pregnancy outcome in Ehlers-Danlos syndrome, vascular type. *J Matern Fetal Neonatal Med* 2009; 22: 924–927.
24. Hovatta O. Pregnancies in women with Turner's syndrome. *Ann Med* 199; 31: 106–110.
25. Isselbacher EM. Thoracic and abdominal aortic aneurysms. *Circulation* 2005; 111: 816–828.
26. Collège National des Gynécologues et Obstétriciens Français. Turner syndrome and pregnancy. Clinical practice recommendations. April 2009. (http://www.cngof.asso.fr/D_TELE/RPC_Turner_et_gro_090723_en.pdf).
27. Connolly HM, Huston J, Brown RD, et al. Intracranial aneurysms in patients with coarctation of the aorta: a prospective magnetic resonance angiographic study of 100 patients. *Mayo Clin Proc* 2003; 78: 1491–1499.
28. Beauchesne LM, Connolly HM, Ammass NM, et al. Coarctation of the aorta: outcome of pregnancy. *J Am Coll Cardiol* 2001; 38: 1728–1733.
29. Vriend JWJ, Drenthen W, Pieper PG, et al. Outcome of pregnancy in patients after repair of aortic coarctation. *Eur Ht J* 2005; 26: 2173–2178.
30. Vitthala S and Misra PK. Takayasu's arteritis and pregnancy: A review. *Internet J Gynecol Obstet* 2008; 9(2): DOI: 10.5580/963.
31. Hauenstein E, Frank H, Bauer JS, et al. Takayasu's arteritis in pregnancy: review of literature and discussion. *J Perinat Med* 2010; 38: 55–62.
32. Sadler L, McCowan L, White H, et al. Pregnancy outcomes and cardiac complications in women with mechanical bioprosthetic and homograft valves. *BJOG* 2000; 107: 245–253.
33. Shores J, Berger KR, Murphy EA, et al. Progression of aortic dilatation and the benefit of long-term β -adrenergic blockade in Marfan's syndrome. *N Engl J Med* 1994; 330: 1335–1341.
34. Brooke BS, Habashi JP, Judge DP, et al. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. *N Eng J Med* 2008; 358: 2787–2795.
35. Rosenblum NG, Grossman AR, Gabbe SG, et al. Failure of serial echocardiographic studies to predict aortic dissection in a pregnant patient with Marfan's syndrome. *Am J Obstet Gynecol* 1985; 146: 470–471.
36. Lacassie HJ, Millar S, Leithe LG, et al. Dural ectasia: a likely cause of inadequate spinal anaesthesia in two parturients with Marfan's syndrome. *Br J Anaesth* 2005; 94: 500–504.
37. Ch'ng SL, Cochrane AD, Goldstein J, et al. Stanford Type A aortic dissection in pregnancy: a diagnostic and management challenge. *Ht Lung Circ* 2013; 22: 12–18.
38. Patel A, Asopa S, Tang ATM, et al. Cardiac surgery during pregnancy. *Tex Heart Inst J* 2008; 35: 307–312.