Presse Med. 2015; 44: 1126–1135

en ligne sur / *on line on*
www.em-consulte.com/revue/lpm
www.sciencedirect.com

Thoracic aortic aneurysms and pregnancy

Capucine Coulon

Available online: 9 October 2015

CHRU de Lille, hôpital Jeanne-de-Flandres, clinique d'obstétrique, 59037 Lille cedex, France

capucine.coulon@chru-lille.fr

Summary

Half of acute aortic dissection in women under the age of 40 occurs during pregnancy or peripartum period. Marfan syndrome is the most common syndromic presentation of ascending aortic aneurysm, but other syndromes such as vascular Ehlers-Danlos syndrome, Loeys-Dietz syndrome and Turner syndrome also have ascending aortic aneurysms and the associated cardiovascular risk of aortic dissection and rupture. Management of aortic root aneurysm has been established in recent recommendations, even if levels of evidence are weak. Pregnancy and postpartum period should be followed very closely and determined to be at high risk. Guidelines suggest that women with aortopathy should be counseled against the risk of pregnancy and about the heritable nature of the disease prior to pregnancy.

Résumé

Anévrysmes de l'aorte thoracique et grossesse

Cinquante pour cent des dissections de l'aorte observées chez la femme de moins de 40 ans surviennent pendant la grossesse ou la période du post-partum. Le syndrome de Marfan constitue la pathologie syndromique la plus souvent responsable d'un anévrysme de l'aorte ascendante, mais d'autres maladies (syndrome d'Ehlers-Danlos vasculaire, syndrome de Loeys-Dietz, syndrome de Turner) peuvent également se compliquer d'un anévrysme de l'aorte thoracique et/ou de dissection ou rupture de l'aorte. La surveillance d'un anévrysme de l'aorte est relativement bien établie selon des recommandations récentes, même si leurs niveaux de preuves sont faibles. La grossesse et le post-partum sont des périodes à haut risque et doivent bénéficier d'une surveillance attentive. Les recommandations suggèrent que les patientes présentant une aortopathie soient informées du caractère à haut risque de la grossesse. La consultation préconceptionnelle doit également insister sur le risque de transmission génétique de la pathologie à leur descendance.

http://dx.doi.org/10.1016/j.lpm.2015.02.024

Methodology

Search of medical and scientific literature through the use of PubMed/Medline. Mesh terms: "pregnancy", "aortic root aneurysm", "thoracic aortic aneurysm", "Marfan syndrome", "Loeys-Ditz syndrome", "vascular Ehlers-Danlos syndrome", "familial TAA", "biscuspid aortic valve".

Introduction

Cardiovascular disease complicates approximately 1–3% of pregnancies and is the second commonest cause of maternal mortality for 10 to 15% [1–3]. Nearly half of maternal deaths secondary to cardiovascular diseases are caused by aortic dissection [4].

Recent recommendations classified risk of heart diseases during pregnancy in 4 stages (World Health Organization modified classification) [5,6].

Aorta aneurysm is a permanent localized dilatation of aorta, having at least a 50% increase of diameter compared with the expected normal diameter of the aorta.

Thoracic aortic root diameter is measured at the sinuses of Valsalva, and has been evaluated with computed tomographic imaging. Normal values are about 35 to 37.2 mm, SD 3.8 for women [7].

Management of aortic root aneurysm has been established in recent recommendations, even if levels of evidence are weak (*table I*). Pregnancy and postpartum period should be followed very closely and determined to be at high risk.

Marfan syndrome is the most common syndromic presentation of ascending aortic aneurysm, but other syndromes such as vascular Ehlers-Danlos syndrome, Loeys-Dietz syndrome and Turner syndrome also have ascending aortic aneurysms and the associated cardiovascular risk of aortic dissection and rupture. Ascending aortic aneurysm can also occur in the absence of associated systemic findings of a connective tissue abnormality in patients with familial aortic aneurysm and dissection or bicuspid aortic valve.

Pregnancy is an important consideration in the management of women with TAA disease. Multidisciplinary team, with obstetrics, cardiovascular surgeon, anaesthesists, and cardiologist should discuss with the woman, about birth control methods and the risk of aortic dissection before conception in women at risk. It is extremely difficult to estimate the individual risk of aortic dissection, and the information is principally extracted from series of women with Marfan syndrome [8].

Table I

Recommendations for the management of aortic disease (ESC guidelines 2011) [6]

Recommendations	Class	Level of evidence
Women with Marfan syndrome or other known aortic disease should be counseled about the risk of aortic dissection during pregnancy and the recurrence risk for the offspring	I	C
Imaging of the entire aorta (CT/MRI) should be performed before pregnancy in patients with Marfan syndrome or other known aortic disease	I	C
Women with Marfan syndrome and an ascending aorta > 45 mm should be treated surgically pre-pregnancy	I	C
In pregnant women with known aortic dilatation, (history of) type B dissection or genetic predisposition for dissection strict blood pressure control is recommended	I	C
Repeated echocardiographic imaging every 4-8 weeks should be performed during pregnancy in patients with ascending aorta dilatation	I	C
In patients with an ascending aorta < 40 mm, vaginal delivery is favoured	I	C
In patients with an ascending aorta > 45 mm, caesarean delivery should be considered	I	C
Women with aortic dilatation or (history of) aortic dissection should deliver in a center where cardiothoracic surgery is available	I	C
Surgical treatment pre-pregnancy should be considered in women with aortic disease associated with a bicuspid aortic valve when the aortic diameter is > 50 mm (or > 27 mm/m^2 body surface area)	IIa	C
Prophylactic surgery should be considered during pregnancy if the aortic diameter is $\geq$ 50 mm and increasing rapidly	IIa	C
In Marfan syndrome, and other patients with an aorta 40–45 mm, vaginal delivery with epidural anaesthesia and expedited second stage should be considered	IIa	C
In Marfan syndrome, and other patients with an aorta 40–45 mm, caesarean section may be considered	IIb	C
Patients with (or history of) type B dissection should be advised against pregnancy	III	C

We are reporting in this review the principal causes of thoracic aortic aneurysm in pregnant women, and their management during pregnancy and postpartum period.

Cardiovascular diseases

Marfan syndrome

Marfan syndrome is due to mutations in the *FBN1* gene and leads to manifestations including skeletal and connective tissues features (such as tall stature, kyphoscoliosis, elongated fingers and toes, pectus deformities, hypererlaxity, dural ectasia), ocular pathology (high myopia, ectopia lentis, lens dislocation), and cardiovascular disease (aortic root aneurysm, aortic dissection, primarily mitral valve prolapse and regurgitation) which criteria for his diagnosis have been revised recently (Ghent nosology), [9,10] to facilitate accurate of diagnosis of this genetic aneurysm syndrome and to improve patient management and counseling. Most patients with Marfan syndrome present a dilatation of the aortic root/ascending aorta or type A dissection. This is very important to relate this measurement to normal values based on age and body surface area [11]. After diagnosis, follow-up imaging studies are recommended at 6 months and then annually if stability is documented [12].

In Marfan syndrome, we consider that thoracic aortic aneurysm exists when aortic diameter is larger than 40 mm, measured on the Valsalva sinuses.

Vascular Ehlers-Danlos syndrome

Vascular Ehlers-Danlos syndrome is a rare genetic disease transmitted as an autosomal dominant trait. This is characterised by a deficiency of synthesis, secretion and structure of procollagen type III affecting the entire arterial tree, together with the skin and the intestine. The disease results from heterozygous mutations in the *COL3A1* gene, causing structural defect in the pro1 (III) chain of collagen type III. It is distinguished from other forms of Elhers-Danlos syndrome by its unstable acrogeric morphotype and by vascular, gastrointestinal and obstetrical complications. Clinically, it is characterised by four major and nine minor diagnostic criteria [13]. The combination of two major diagnostic criteria has a high specificity, but further biochemical testing and mutational analysis of *COL3A1* gene is recommended to formally confirm the diagnosis, which provides diagnosis certainty but has a sensitivity of only 61% [14].

Turner syndrome

Turner syndrome is also associated with aortic disease. The prevalence of cardiovascular abnormalities is about 25–50% in Turner syndrome. The risk of an aortic dissection is probably higher in women with additional risk factors such as bicuspid aortic valve or coarctation of the aorta, and/or hypertension. Those with aortic dilatation are at highest risk of dissection, but dissection may also occur in the absence of any dilatation. Thoracic aortic diameters must be evaluated in relation to body surface area as these patients often have short stature. An aortic index > 27 mm/m^2 is associated with a high risk of dissection, and prophylactic surgery should be considered. Aortic dissection during pregnancy is associated with maternal mortality of 2% [15–17].

In Turner syndrome, aorta is considered dilated with a majored risk of dissection when her diameter is larger than 35 mm, or larger than 27 mm/m^2 in small maternal height.

Loeys-Dietz syndrome

Loeys-Dietz syndrome is a recently described autosomal dominant aortic aneurysm syndrome with involvement of many other systems [18,19]. It is due to mutations in transforming growth factor beta receptor type I or II (*TGFBR1* and *TGFBR2*) genes [20] and has a characteristic triad of craniofacial features (craniosynostosis, bifid uvula or cleft palate, hypertelorism), aortic root and branch vessel aneurysm and dissection, and arterial tortuosity of the head and neck vessels but can occur in other vessels [19]. The vascular disease in these patients is particularly aggressive with a strong predisposition for aneurysms and dissections throughout the arterial tree (mean age of death of 26 years) [20] and a high incidence of pregnancy-related complications [19]. Most patients have aortic root aneurysms (98%) that lead to aortic dissection. Repair is recommended for smaller diameters of aorta because of many reports of aortic dissection occurring when the aortic diameter was less than 50 mm [19]. Major complications are described during pregnancy or postpartum period [19].

Bicuspid aortic valve

The partial or complete fusion of aortic valve commissures (bicuspid aortic valve) represents the most common form of congenital heart disease and affects approximately 1% of the population. It may be familial in approximately 9% of cases. A subset of individuals and families with BAV disease has associated ascending aortic aneurysm [21]. Abnormal elastic properties, similar to the findings in patients with Marfan syndrome, have been described [22–25], but it has not been confirmed by prospective studies.

Bicuspid aortic valve is known to coexist with other congenital vascular defects; the most common of which is coarctation of the aorta. Of patients with coarctation, approximately 25 to 50% have bicuspid aortic valve [26]. Approximately 50% of the patients with a bicuspid aortic valve and aortic stenosis have dilatation of the ascending aorta [27]. Dilatation is often maximal in the distal part of the ascending aorta, which cannot be adequately visualized echocardiographically, MRI or CT should be performed pre-pregnancy.

Dissection does occur, although less frequently than in Marfan patients [28].

Aortic root dilatation has been documented in childhood, suggesting that this process begins early in life [29–31].

Guidelines suggest that women with bicuspid aortic valve and significant aortopathy (aortic root dilatation > 45 mm) should be counseled against the risk of pregnancy, and surgery should be considered in patients with aortic root > 50 mm [6].

Familial thoracic aortic aneurysm

Familial thoracic aortic aneurysm has been used to designate a heritable predisposition for ascending aortic aneurysm and dissection in the absence of systemic features of a connective tissue disorder. They are affected of ACTA2 gene mutations in 14% of individuals with familial TAA disease and are associated with cerebral aneurysms, premature coronary and cerebrovascular disease, livedo reticularis and iris flocculi [12]. Up to 20% of patients with TAA will have another first-degree relative with thoracic aortic disease [12]. Regalado et al. [32] described 53 women with ACTA2 mutations, who had a total of 137 pregnancies. Eight of them had an acute aortic dissection in the third trimester or the postpartum period (6% of pregnancies). The majority of the aortic dissections were type A, half of which were fatal. The rate of aortic dissection in the peripartum in women with ACTA2 mutation was much higher, compared to the population-based frequency of peripartum dissection of 0.6% [33]. These findings indicate that pregnancy in women with ACTA2 mutations is associated with an increased risk for ascending and descending thoracic aortic dissections with minimal aortic dilatation. Women with ACTA2 mutations who are planning to get pregnant should be counseled about the risk of aortic dissection and aortic root diameter follow-up should be controlled during pregnancy.

Effects of pregnancy on the aorta

The period of pregnancy is characterized by increases in maternal blood volume, heart rate, blood pressure, stroke volume, and cardiac output [34]. Pregnancy-induced alterations in plasma estrogen and progesterone concentrations produce changes in vascular structure that render the aortic media more susceptible to injury imposed by hemodynamic forces [35]. These different effects lead to greater arterial wall tension as well as intimal shear forces. These changes begin in the first and second trimester but are maximal in the third trimester, during labor and in the postpartum period. Arterial wall fragility during pregnancy remains controversial, even if 50% of aortic dissections occur during pregnancy in women under age of 40 [36]. The highest incidence period for arterial dissection and/or rupture during pregnancy is the third trimester (50%) and peripartum period (33%).

Most dissections occur in the ascending aorta, although dissection or rupture of any artery in the body has been described. Recommendations about counseling and management of chronic aortic diseases in pregnancy have been established in 2010, even if levels of evidence are weak [12].

Medical management and follow-up

Patients with aortic pathology should be monitored by echocardiography at 4–12 week intervals throughout the pregnancy and the 6 months postpartum period.

Pharmacologic therapy includes treatment of hypertension, optimal lipid control and smoking cessation [12].

For pregnant women with known thoracic aortic dilatation or a familial or genetic predisposition for aortic dissection, strict blood pressure control, specifically to prevent stage II hypertension, is recommended [12].

Basic treatment involves medications to lessen blood pressure and reduce aortic wall stress and guidelines to modify lifestyle (physical activity, weight-lifting restrictions) and pregnancy recommendations [12]. Angiotensin receptor blocker and angiotensin-converting enzyme inhibitors are contraindicated during pregnancy, because of their risk of teratogenic effects.

Beta-blockers, which decrease the impact force of ejected blood on the aorta, and lower heart rate and blood pressure, are important in the treatment of TAA [12]. It has been suspected for a long time that beta-blockers may reduce the risk of aortic dissection in patients with Marfan syndrome [37]. Indeed, in a 10-year study of beta-blockers in Marfan syndrome, the patients treated with propranolol had a lower rate of aortic root dilatation, and fewer cardiovascular endpoints (defined as aortic regurgitation, dissection, surgery, heart failure or deaths), and improved survival than untreated patients [37].

The recently thoracic aortic disease guidelines have recommended the utility of beta-blockers in patients with Marfan syndrome and aortic aneurysm to reduce the risk of aortic dissection [12], even if a meta-analysis including mostly studies with non-pregnant patients, a beneficial effect was not confirmed [38].

In patients with vascular Ehlers-Danlos syndrome, celiprolol is recommended because of the very high risk of dissections, and the benefit demonstrated in non-pregnant patients [39]. Ong et al. published the results of the Beta-Blockers in the Ehlers-Danlos Syndrome Treatment (BBEST) study, which is a prospective randomised, open, blinded-endpoints trial on the effects of celiprolol (β1-adrenoceptor antagonist with a β2-adrenoceptor agonist action) on primary prevention of cardiovascular events in vascular Ehlers-Danlos syndrome. They randomised 53 patients, assigned to celiprolol (n = 25) or control group (n = 28), to 5 years of treatment.

Treatment of patients with celiprolol compared with no treatment reduces arterial events, such as rupture or dissection, by three times, but this trial did not include pregnant women [39]. Monitoring of fetal growth should be proposed when the mother is taking beta-blockers (risk of fetal growth restriction).

Follow-up of pregnant women with genetic syndromes associated with TAA and dissection

Marfan syndrome

Pregnant women with Marfan syndrome are at increased risk of aortic dissection if the aortic diameter is greater than 40 mm. Women with Marfan syndrome require frequent cardiovascular

monitoring throughout pregnancy and into the postpartum period. We suggest that measurements of aortic root should be practiced once a trimester during first and second trimester and once a month during the third trimester. Evaluation of the aortic diameter during the early postpartum period (first week) is also necessary. Indeed, a few cases of aortic dissections in the postpartum period are described [28,40].

An echocardiogram is recommended at the time of the diagnosis of Marfan syndrome to determine the aortic root and ascending aortic diameter and 6 months thereafter to determine the rate of enlargement of the aorta [12].

For all pregnant women with known aortic root or ascending aortic dilatation, monthly or bimonthly echocardiographic measurements of the ascending aortic dimensions are recommended to detect aortic expansion until birth [12].

For imaging of pregnant women with aortic arch, descending, or abdominal aortic dilatation, magnetic resonance imaging (without gadolinium) is recommended over computed tomographic imaging to avoid exposing both mother and fœtus to ionizing radiation. Transesophageal echocardiogram is an option for imaging of the thoracic aorta [12].

Women with Marfan syndrome and aortic dilatation, as well as patients without Marfan syndrome, who have known aortic disease, should be counselled about the risk of aortic dissection as well as the heritable nature of the disease prior to pregnancy [12,21,41].

If progressive aortic dilatation and/or advancing aortic valve regurgitation are documented, prophylactic surgery may be considered [12,28].

The risk of major aortic complication during pregnancy seems to be low when aortic diameter is less than 40 mm. For patients with an aortic diameter larger than 40 mm and Marfan syndrome, half of them will have come to prophylactic surgery during pregnancy, will have a rupture, or will have life-threatening growth. Use of beta-blockers for women with aortic dilatation to control heart rate and reduce shear forces, particularly in the third trimester and postpartum period is recommended. Other cardiotropics medications such as angiotensin-converting enzyme inhibitors and angiotensine receptor blockers are contraindicated during pregnancy.

Pyeritz [42] using phone interview did not report aortic complications during 105 pregnancies in 26 women with Marfan syndrome, but one death due to mitral endocarditis at the end of pregnancy.

Rossiter et al. [43] reported follow-up and outcomes of 45 prospectively observed pregnancies in 21 patients with Marfan syndrome. No adverse outcomes and no dissections occurred when aortic diameter was lower than 40 mm.

One dissection on the descending aorta and one extension of a pre-existing aortic dissection were reported. He found a similar risk for aortic complication and dilatation in a group of non-pregnant women with Marfan syndrome, matched for age during follow-up of 6 years [43]. Most patients had little to no demonstrable change in aortic root diameter during the course of pregnancy and postpartum period. Follow-up of these patients showed no worsening in long-term cardiovascular prognosis or accelerated dilatation of the aortic root when compared with women with Marfan syndrome who have never been pregnant.

Lipscomb reported 6 aortic complications (including 4 aortic dissections) in 91 pregnancies of 36 women with Marfan syndrome [44].

Lind reported 117 pregnancies complicated by 5 aortic dissections [45].

Meijboom et al. [46] prospectively studied aortic diameter in 127 women with Marfan syndrome, (33 pregnancies in 23 women) using serial echocardiographic examinations. They showed that aortic root enlargement was minimal during pregnancy when the aortic root diameter was less than 45 mm before conception, but diagnosis of Marfan syndrome was known for each woman prior to pregnancy. The authors concluded that pregnancy in women with Marfan syndrome seems to be safe up to an aortic root diameter of 45 mm.

Immer et al. [28] identified in a retrospective review of reports, only 5 of 45 (8.9%) total cases of pregnancy-related aortic dissection occurring after delivery.

Pacini et al. [47] studied the occurrence of aortic complications in their population of Marfan syndrome in 160 pregnancies (n = 85 women) and compared this with the aortic complication rate occurring in women with Marfan syndrome, who had never been pregnant (n = 68). They observed 7 aortic complications during or immediately after pregnancy, with a risk of aortic complication of 4.4% per pregnancy, mainly in the third trimester of pregnancy or after delivery, carefully monitored, in a prospective study [47]. The incidence of aortic complication during a pregnancy was not related to the number of prior pregnancies. They observed 14 aortic complications occurring in women with Marfan syndrome when they had never been pregnant (risk for aortic complication was 1.5% per year of follow-up). Marfan syndrome diagnosis was made later in women when they had never been pregnant (33 $\pm$ 15 vs 22 $\pm$ 14 years old, $P < 0.05$). During pregnancy, the relative risk of aortic complication was 5.5 (95% CI 2.0–15.5, $P = 0.001$).

Donnelly et al. [48] prospectively studied 98 women with Marfan syndrome, and tried to assess the impact of pregnancy on the rate of aortic growth as well as on short or long term clinical outcomes. Of these 98 women, 69 had 199 pregnancies, and 35 women with 55 pregnancies could be followed prospectively during their pregnancy with multiple cardiac ultrasonographies, of which 14 entered pregnancy with an aortic root diameter more than 40 mm. No acute dissections were observed during all pregnancies. Two women developed symptomatic carotid artery dissections and 1 patient showed worsening of aortic regurgitation from mild to severe at 38 weeks

with a 49 mm aortic root, necessitating aortic root replacement 6 months after delivery. They described a significantly higher rate of aortic growth during pregnancy compared to the prior baseline aortic growth for each woman [48].

Patients with Marfan syndrome and dilatation of the aorta more than 45 mm are classified in WHO IV, with an extremely high risk of mortality or severe morbidity and the pregnancy is indeed contraindicated [5,6]. In this situation, termination of the pregnancy should be discussed with the woman if pregnancy occurs. If pregnancy continues, specific care throughout the antenatal and peripartum period should be performed.

Pregnancy should be discouraged in women with previous aortic dissection because of the high risk for aortic complications.

Some cases of women with aortic root aneurysm with repair in the end of the first trimester of pregnancy are described, with positive outcome for both mother and child [49].

Vascular Ehlers-Danlos syndrome

During pregnancy, women may show increased bruising, hernias, and varicosities, and suffer rupture of large vessels or rupture of the uterus. Because of the risk of uterine rupture, vascular Ehlers-Danlos syndrome is a contraindication for pregnancy. Aortic dissection may occur without dilatation.

Twenty-five percent of the patients had a first complication by the age of 20 years, and more of 80 percent had had at least one complication by the age of 40 years. The mortality reported for each complication is about 12%.

The first complication of the disease is an arterial complication in 46% of cases, an intestinal perforation in 19% of cases and an organic rupture (kidney, spleen or liver) in 5% of cases [14].

Arterial lesions suggestive of the disease include dissecting aneurysms of the internal carotid and iliac arteries and of the anterior visceral branches of the abdominal aorta, fusiform aneurysms of the splenic artery and early onset non-traumatic direct carotid-cavernous fistulae.

No treatment has been proven to prevent acute arterial events for patients with Ehlers-Danlos syndrome.

Women with Ehlers-Danlos syndrome type IV have an increased risk of complications of pregnancy as well as 50 percent risk of having an affected child.

Death was most common following organ rupture (45%) and less common after bowel rupture (2%).

Pepin et al. [14] described 81 women with Ehlers-Danlos syndrome type IV, which had had a total of 183 pregnancies. Twelve women died during the peripartum period or within two weeks after delivery (5 of rupture uterine during labor, 2 of vessel rupture at delivery, and 5 in the postpartum period after vessel rupture). Although several pregnant women died of uterine rupture at term, we do not know whether the use of elective caesarean section would decrease mortality.

Lurie et al. [50] reviewed the cases of 26 previously documented pregnant women with Ehlers-Danlos syndrome type IV who had 50 pregnancies and found 20% mortality per pregnancy and 38.5% mortality for each patient. The majority of the deaths occurred in the peripartum period and were due to uterine rupture in two cases and vascular rupture in the other cases.

Turner syndrome

Patients with Turner syndrome should undergo imaging of the heart and aorta for evidence of bicuspid aortic valve, coarctation of the aorta, or dilatation of the ascending thoracic aorta. If initial imaging is normal and there are no risk factors for aortic dissection, repeat imaging should be performed every 5 to 10 years or if otherwise clinically indicated. If abnormalities exist, annual imaging or follow-up imaging should be done [12].

Turner syndrome is associated with risk of aortic root dilatation or aortic dissection. Turner syndrome is characterized by an ovarian failure, which leads to infertility. Less than 10% of women with Turner syndrome may have a spontaneous pregnancy, and most of them required in vitro fertilization to become pregnant. Deaths and severe morbidity during pregnancy and peripartum period are described in women with Turner syndrome, due to acute aortic dissection; this risk of aortic dissection is evaluated to 2%, with an increased risk of maternal death as much as 100-fold during pregnancy [15]. Aortic dissection may occur even there is no dilatation of the aorta [16,51–54]. The severity of morbidity depends on the karyotype, the monosomy 45, X karyotype representing the most affected women and the low-grade mosaic women representing more healthy women [55].

It is therefore absolutely necessary for all women with Turner syndrome to undergo a full cardiological assessment before seeking to become pregnant including echocardiography, thoracic magnetic resonance imaging to verify aortic root, cardiac valves and left ventricular function, hypertension monitoring and treatment. Pregnancy should be contraindicated if exists a history of aortic repair, a history of aortic dissection, an aortic dilatation > 25 mm/m^2 or > 35 mm, an aortic coarctation or a treated uncontrolled hypertension. Recommendations have been edited by the French National Authority of Health (HAS). Aortic root diameter should be carefully monitored during pregnancy and postpartum period, with an echocardiography in the first and second trimester, a monthly echocardiography during the third trimester, repeated between the fifth or eighth postpartum day. Increase of diameter > 10% should be confirmed with a magnetic resonance imaging. If diameter is > 25 mm/m^2 or > 35 mm, or increase of the diameter > 10%, intensive monitoring close to a cardiovascular team should be proposed, caesarean delivery should be considered. If aortic root diameter is < 25 mm/m^2 or < 35 mm, vaginal delivery with expedited second stage and instrumental delivery, and with epidural anaesthesia may be considered, but 85% of women with Turner

syndrome will finally deliver by caesarean due to cephalopelvic disproportion.

Loeys-Dietz syndrome

Patients with Loeys-Ditz syndrome or a confirmed genetic mutation known to predispose to aortic aneurysm and aortic dissections (*TGFBR1, TGFBR2, FBN1, ACTA2, or MYH11*) should undergo complete aortic imaging at initial diagnosis and 6 months thereafter to establish if enlargement is occurring.

Patients with Loeys-Ditz syndrome should have yearly magnetic resonance imaging from the cerebrovascular circulation to the pelvis [12].

Loeys described 21 pregnancies among 12 women with Loeys-Dietz syndrome, 6 of them had a major complication during pregnancy or immediate postpartum period (aortic dissection in four and uterine rupture in two) [19].

We did not find any recommendations about the follow-up during pregnancy and mode of delivery, but we consider that Loeys-Dietz syndrome is at high risk of maternal complications during pregnancy (aortic dissection as well as uterine rupture), a closely follow-up of aortic root diameter should be proposed (every month) and a prophylactic premature caesarean after fetal lung maturation should be considered.

Bicuspid aortic valve

Siu and Silversides [56] studied prospectively a group of patients affected by bicuspid aortic valve and they showed that 28% of them had an aortic root dilatation and after 9 years of follow-up, the prevalence had increased to 45% with a median increase in the aortic sinus dimension of 0.2 mm/year.

Even though the group of pregnant women which continues to represent a high-risk for maternal and fetal morbidity, their overall mortality risk is < 1% based on recent studies [57–59].

Mode of delivery

During active labor, further hemodynamic changes occur. A 30–50% increase in cardiac output occurs in normal pregnancy. During labor and postpartum period, uterine contractions, pain, positioning, anxiety, bleeding, and uterine involution cause significant hemodynamic changes. Each uterine contraction forces an additional 300 to 500 mL of venous blood back into the central venous system. During the second stage of labor, blood pressure and heart rate can increases markedly with pain while Valsalva manoeuvres during pushing efforts can result in large fluctuations in central venous system. Immediately after delivery of the placenta, 500 mL of blood is diverted from the uteroplacental bed back into the maternal circulation like an "auto-transfusion", increasing central venous pressures, ventricular preload and cardiac output.

The following of these high-risk pregnancies should be proposed in a specialized center and the choice and management of the delivery discussed in multidisciplinary team.

The principal aim of peripartum management of women with aortic root aneurysm is to limit and reduce the cardiovascular stress of labor and delivery. Beta-blockers should be continued during peripertum period if the women are treated during pregnancy.

Locoregional anaesthesia techniques can be difficult in Marfan women, if they particularly have severe scoliosis or dural ectasia, and locoregional anaesthesia is advised to prevent blood pressure peaks (medical indication).

If the aortic root diameter is 40–45 mm, vaginal delivery with expedited second stage (instrumental delivery) may be considered, as well as caesarean delivery, based on each individual situation.

For patients with Marfan syndrome, if the aortic root diameter exceeds 45 mm, caesarean delivery is advised. If the aortic diameter is lesser than 40 mm, vaginal route with maternal efforts can be allowed. If this diameter is greater than 45 mm, caesarean section before labor should be considered, according to the risk of aortic dissection during labor or postpartum period, but data are limited. If dissection occurs during pregnancy, better outcome is obtained when surgical repair of the aorta is concomitant to caesarean section [60]. If gestational age is very pre-term, repair of the aorta is realized during the pregnancy.

Pregnant women with aortic aneurysms should be delivered where cardiothoracic surgery is available, with inborn in the treating center [12]. Delivery by caesarean section is reasonable for patients with significant aortic enlargement, dissection, or severe aortic valve regurgitation [12,41].

Caesarean section before labor allows limitation of blood pressure and cardiac output variations, which increase arterial rupture's risk. This mode of delivery also limits risk of uterine and perineal complications. If the vaginal route is preferred, use of forceps should be very careful with the risk of perineal lesions, but forceps delivery leads to shorten the second stage of labor to reduce cardiovascular stress. Arterial micro-dissections constitution during the labor could explain the dramatically late postpartum vascular complications.

For women with vascular Ehlers-Danlos syndrome and Loeys-Dietz, early caesarean delivery after fetal lung maturation must be considered.

Acute aortic syndrome during pregnancy

Half of acute aortic dissection in women under the age of 40 occurs during pregnancy or peripartum period.

Acute aortic dissection is a life-threatening medical emergency associated, even in-hospital arisen, with high rates of mortality and morbidity. Sudden onset of severe sharp pain is the single most common presenting complaint, but clinical presentation can be very diverse. Any pregnant women with aortic disease may present, during pregnancy, an acute aortic syndrome. The third trimester, the delivery and the early postpartum period

are the most risked periods for these complications. Unfortunately, these complications are often inaugural in the discovery of the aortic disease. Acute aortic dissection occurring during pregnancy is a surgical emergency; this could be dramatic for both the mother and the unborn child. Optimal care includes involvement with a high-risk maternal-fetal team along with a cardiovascular surgery team, aortic speciality team and anaesthesiologist team.

The commonly used Stanford classification divides aortic dissections into 2 groups. Stanford type A dissection involves ascending aorta, whereas Stanford type B dissection primarily involves descending aorta. In rare cases, type B dissection may show a retrograde propagation and involve the aortic arch and ascending aorta.

For type A aortic dissection occurring during the first or second trimester, urgent surgical repair is preferred. The fetus will be particularly monitored. Unfortunately, fetal death during cardiopulmonary bypass and hypothermia is common. The overall maternal mortality rate is high (5%) and the fetal and neonatal mortality also (about 15 to 30%) [61,62].

Ch'ng et al. [63] reported their experience of aortic dissections, this is the largest study (n = 233 patients). Of the dissections occurring in women (n = 73), five occurred in pregnant women. Four women were at gestational age more than 32 weeks and aortic surgery followed the caesarean section. One patient died from multi-organ failure *malgré la chirurgie* and returned to theatre for bleeding prolonged intensive care unit stay and fetal death at 21 weeks of gestational age was diagnosed.

When aortic dissection occurs during the third trimester, the foetus is viable and urgent caesarean section is performed in cardiac theatres, followed by surgical aortic repair, this management offers the best survival chance for the unborn child and the mother [64].

For acute arch or type B aortic dissection, medical treatment is preferred, unless percutaneous stent grafting or open surgery is performed in case of aortic rupture, or subacute aortic leaking. Many cases of acute aortic dissection occurring during pregnancy are described.

When progressive dilatation occurs during pregnancy, before the fetus is viable, aortic repair with fetus in utero should be considered. When the fetus is viable, caesarean delivery followed directly by aortic surgery is recommended.

Pre-pregnancy counseling

Guidelines have been established by European Society of Cardiology in 2011 for management of patients with cardiovascular diseases during pregnancy [6]. Preconceptional counseling for women with Marfan syndrome, Loeys-Dietz syndrome or vascular Ehlers-Danlos syndrome should discourage from becoming pregnant if their aortic root exceeds 45 mm, or undergo surgery before pregnancy.

In other patients with dilatation of the aorta, pre-pregnancy surgery should be considered when the ascending aorta is more than 50 mm. Body surface area should probably be taken into account in small women (aortic diameter index > 27 mm/m^2 is associated with a high risk of dissection, and prophylactic surgery should be considered).

Patients with a known bicuspid aortic valve and enlarged aortic root should to be counseled like Marfan syndrome. Normal size patients with an aortic root size more than 40 mm or an increase of aortic root size during pregnancy are at high risk of aortic dissection, mainly in the third trimester. If possible, surgical repair of the enlarged aortic root should be done prepartum. If the diagnosis of enlarged aortic root is done during pregnancy, a close echocardiography follow-up is recommended (4 to 6 weeks). In aortic root larger than 40 mm or increasing in size during pregnancy, beta-blockers medication should be proposed. During pregnancy and delivery, hypertension blood pressure should be avoided.

Patients with Marfan syndrome with an aortic root diameter more than 40 mm should undergo preconceptional counseling for surgical aortic repair before pregnancy.

Patients with Marfan syndrome with an aortic aneurysm should be evaluated closely and continuously during pregnancy by multidisciplinary specialists to prevent aortic dissection that could be fatal for both mother and child.

Women with Turner syndrome should be contraindicated for pregnancy if exists a history of aortic repair, a history of aortic dissection, an aortic dilatation > 25 mm/m^2 or > 35 mm, an aortic coarctation or a treated uncontrolled hypertension.

In patients with Turner syndrome with additional risk factors, including bicuspid aortic valve, coarctation of the aorta and/or hypertension, and in patients who attempt to become pregnant or who become pregnant, it may be reasonable to perform imaging of the heart and aorta to help determine the risk of aortic dissection.

Women should be also counseled about the heritable nature of the disease prior to pregnancy.

Conclusion

Several genetic disorders involving aorta have been reported to result in a risk of aortic dissection or rupture during pregnancy. Following and management of the pregnancy and peripartum period should be proposed in a center, where cardiovascular surgery is available.

Beta-blockers are commonly used in case of aortopathy.

Mode of deliver should be discussed in a multidisciplinary team, involving obstetrics, anaesthesia and cardiovascular surgeon.

Disclosure of interest: the author declares that she has no conflicts of interest concerning this article.

References

[1] Chang J, Elam-Evans LD, Berg CJ, Herndon J, Flowers L, Seed KA, et al. Pregnancy-related mortality surveillance – United States, 1991–1999. Morb Mortal Wkly Rep 2003;52(2):1–8.

[2] Arafeh JMR, Baird SM. Cardiac disease in pregnancy. Crit Care Nurs Q 2006;29(1):32–52.

[3] Weindling AM. The confidential enquiry into maternal and child health (CEMACH). Arch Dis Child 2014 [cité 11 mai 2014. Disponible sur Internet: http://adc.bmj.com.].

[4] Huisman CM, Zwart JJ, Roos-Hesselink JW, Duvekot JJ, van Roosmalen J. Incidence and predictors of maternal cardiovascular mortality and severe morbidity in the Netherlands: a prospective cohort study. PLoS one 2013;8(2): e56494 [Frasch MG, éditeur].

[5] Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart Br Card Soc 2006;92(10):1520–5.

[6] Regitz-Zagrosek V, Lundqvist CB, Borghi C, Cifkova R, Ferreira R, Foidart J-M, 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 (ESC). Eur Heart J 2011;32(24):3147–97.

[7] Johnston KW, Rutherford RB, Tilson MD, Shah DM, Hollier L, Stanley JC. Suggested standards for reporting on arterial aneurysms. Subcommittee on reporting standards for arterial aneurysms, ad hoc committee on reporting standards, society for vascular surgery and north American chapter, international society for cardiovascular surgery. J Vasc Surg 1991;13(3):452–8.

[8] Goland S, Elkayam U. Cardiovascular problems in pregnant women with marfan syndrome. Circulation 2009;119(4):619–23.

[9] Loeys BL, Dietz HC, Braverman AC, Callewaert BL, Backer JD, Devereux RB, et al. The revised Ghent nosology for the Marfan syndrome. J Med Genet 2010;47(7):476–85.

[10] Levenson D. New guidelines for diagnosis of Marfan and Loey-Dietz syndromes. Am J Med Genet A 2010;152A(11):fm vii–i.

[11] Roman MJ, Devereux RB, Kramer-Fox R, O'Loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. Am J Cardiol 1989;64(8):507–12.

[12] Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey Jr DE, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. J Am Coll Cardiol 2010;55(14):e27–129.

[13] Beighton P, Paepe AD, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: revised nosology, Villefranche, 1997. Am J Med Genet 1998;77(1):31–7.

[14] Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers–Danlos syndrome type IV, the vascular type. N Engl J Med 2000;342(10):673–80.

[15] Karnis MF, Zimon AE, Lalwani SI, Timmreck LS, Klipstein S, Reindollar RH. Risk of death in pregnancy achieved through oocyte donation in patients with Turner syndrome: a national survey. Fertil Steril 2003;80(3):498–501.

[16] Karnis MF. Catastrophic consequences of assisted reproduction: the case of Turner syndrome. Semin Reprod Med 2012;30(2):116–22.

[17] Chevalier N, Letur H, Lelannou D, Ohl J, Cornet D, Chalas-Boissonnas C, et al. Materno-fetal cardiovascular complications in Turner syndrome after oocyte donation: insufficient prepregnancy screening and pregnancy follow-up are associated with poor outcome. J Clin Endocrinol Metab 2011;96(2): E260–7.

[18] Singh KK, Rommel K, Mishra A, Karck M, Haverich A, Schmidtke J, et al. TGFBR1 and TGFBR2 mutations in patients with features of Marfan syndrome and Loeys-Dietz syndrome. Hum Mutat 2006;27(8):770–7.

[19] Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, et al. Aneurysm syndromes caused by mutations in the TGF-β receptor. N Engl J Med 2006;355(8):788–98.

[20] Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet 2005;37(3):275–81.

[21] Pearson GD, Devereux R, Loeys B, Maslen C, Milewicz D, Pyeritz R, et al. Report of the National Heart, Lung, and Blood Institute and National Marfan Foundation working group on research in Marfan syndrome and related disorders. Circulation 2008;118(7):785–91.

[22] Niwa K, Siu SC, Webb GD, Gatzoulis MA. Progressive aortic root dilatation in adults late after repair of tetralogy of Fallot. Circulation 2002;106(11):1374–8.

[23] Nistri S, Sorbo MD, Basso C, Thiene G. Bicuspid aortic valve: abnormal aortic elastic properties. J Heart Valve Dis 2002;11(3):369–73 [discussion 373–374].

[24] Bauer M, Pasic M, Meyer R, Goetze N, Bauer U, Siniawski H, et al. Morphometric analysis of aortic media in patients with bicuspid and tricuspid aortic valve. Ann Thorac Surg 2002;74(1):58–62.

[25] Nataatmadja M, West M, West J, Summers K, Walker P, Nagata M, et al. Abnormal extracellular matrix protein transport associated with increased apoptosis of vascular smooth muscle cells in marfan syndrome and bicuspid aortic valve thoracic aortic aneurysm. Circulation 2003;108(10 suppl. 1):II-329–334.

[26] Roos-Hesselink JW, Schölzel BE, Heijdra RJ, Spitaels SEC, Meijboom FJ, Boersma E, et al. Aortic valve and aortic arch pathology after coarctation repair. Heart 2003;89(9):1074–7.

[27] Fedak PWM, de Sa MPL, Verma S, Nili N, Kazemian P, Butany J, et al. Vascular matrix remodeling in patients with bicuspid aortic valve malformations: implications for aortic dilatation. J Thorac Cardiovasc Surg 2003;126 (3):797–806.

[28] Immer FF, Bansi AG, Immer-Bansi AS, McDougall J, Zehr KJ, Schaff HV, et al. Aortic dissection in pregnancy: analysis of risk factors and outcome. Ann Thorac Surg 2003;76 (1):309–14.

[29] Ciotti GR, Vlahos AP, Silverman NH. Morphology and function of the bicuspid aortic valve with and without coarctation of the aorta in the young. Am J Cardiol 2006;98 (8):1096–102.

[30] Beroukhim RS, Kruzick TL, Taylor AL, Gao D, Yetman AT. Progression of aortic dilation in children with a functionally normal bicuspid aortic valve. Am J Cardiol 2006;98(6):828–30.

[31] Gurvitz M, Chang R-K, Drant S, Allada V. Frequency of aortic root dilation in children with a bicuspid aortic valve. Am J Cardiol 2004;94(10):1337–40.

[32] Regalado ES, Guo D, Estrera AL, Buja LM, Milewicz DM. Acute aortic dissections with pregnancy in women with ACTA2 mutations. Am J Med Genet A 2014;164(1):106–12.

[33] Nienaber CA, Fattori R, Mehta RH, Richartz BM, Evangelista A, Petzsch M, et al. Gender-related differences in acute aortic dissection. Circulation 2004;109(24):3014–21.

[34] Chung E, Leinwand LA. Pregnancy as a cardiac stress model. Cardiovasc Res 2014;101(4):561–70.

[35] Manalo-Estrella P, Barker AE. Histopathologic findings in human aortic media associated with pregnancy. Arch Pathol 1967;83(4): 336–41.

[36] Williams GM, Gott VL, Brawley RK, Schauble JF, Labs JD. Aortic disease associated with pregnancy. J Vasc Surg 1988;8(4):470–5.

[37] Shores J, Berger KR, Murphy EA, Pyeritz RE. Progression of aortic dilatation and the benefit of long-term β-adrenergic blockade in Marfan's syndrome. N Engl J Med 1994;330 (19):1335–41.

[38] Gersony DR, McClaughlin MA, Jin Z, Gersony WM. The effect of beta-blocker therapy on clinical outcome in patients with Marfan's syndrome: a meta-analysis. Int J Cardiol 2007;114(3):303–8.

[39] Ong K-T, Perdu J, De Backer J, Bozec E, Collignon P, Emmerich J, et al. Effect of celiprolol on prevention of cardiovascular events in vascular Ehlers-Danlos syndrome: a prospective randomised, open, blinded-endpoints trial. Lancet 2010;376(9751):1476–84.

[40] Gandhi SD, Iqbal Z, Markan S, Almassi GH, Pagel PS. Massive retrograde acute type B aortic dissection in a postpartum woman with a family history of Marfan syndrome. J Clin Anesth 2008;20(1):50–3.
[41] Milewicz DM, Dietz HC, Miller DC. Treatment of aortic disease in patients with Marfan syndrome. Circulation 2005;111(11):e150–7.
[42] Pyeritz RE. Maternal and fetal complications of pregnancy in the Marfan syndrome. Am J Med 1981;71(5):784–90.
[43] Rossiter JP, Repke JT, Morales AJ, Murphy EA, Pyeritz RE. A prospective longitudinal evaluation of pregnancy in the Marfan syndrome. Am J Obstet Gynecol 1995;173(5):1599–606.
[44] Lipscomb KJ, Smith JC, Clarke B, Donnai P, Harris R. Outcome of pregnancy in women with Marfan's syndrome. Br J Obstet Gynaecol 1997;104(2):201–6.
[45] Lind J, Wallenburg HCS. The Marfan syndrome and pregnancy: a retrospective study in a Dutch population. Eur J Obstet Gynecol Reprod Biol 2001;98(1):28–35.
[46] Meijboom LJ, Vos FE, Timmermans J, Boers GH, Zwinderman AH, Mulder BJM. Pregnancy and aortic root growth in the Marfan syndrome: a prospective study. Eur Heart J 2005;26(9):914–20.
[47] Pacini L, Digne F, Boumendil A, Muti C, Detaint D, Boileau C, et al. Maternal complication of pregnancy in Marfan syndrome. Int J Cardiol 2009;136(2):156–61.
[48] Donnelly RT, Pinto NM, Kocolas I, Yetman AT. The immediate and long-term impact of pregnancy on aortic growth rate and mortality in women with Marfan syndrome. J Am Coll Cardiol 2012;60(3):224–9.
[49] Tang GHL, Malekan R, Lansman SL, Spielvogel D. Aortic valve-sparing reimplantation and mitral repair in a pregnant. Second trimester marfan patient: surgical decision. Ann Thorac Surg 2013;95(2):701–3.
[50] Lurie S, Manor M, Hagay ZJ. The threat of type IV Ehlers-Danlos syndrome on maternal well-being during pregnancy: early delivery may make the difference. J Obstet Gynaecol J Inst Obstet Gynaecol 1998;18(3):245–8.
[51] Chevalier N, Bständig B, Galand-Portier M-B, Isnard V, Bongain A, Fénichel P. [Oocyte donation in patients with Turner syndrome: a high-risk pregnancy]. Ann Endocrinol 2009;70(4):246–51.
[52] Hagman A, Källén K, Bryman I, Landin-Wilhelmsen K, Barrenäs M-L, Wennerholm U-B. Morbidity and mortality after childbirth in women with Turner karyotype. Hum Reprod Oxf Engl 2013;28(7):1961–73.
[53] Hagman A, Loft A, Wennerholm U-B, Pinborg A, Bergh C, Aittomäki K, et al. Obstetric and neonatal outcome after oocyte donation in 106 women with Turner syndrome: a Nordic cohort study. Hum Reprod Oxf Engl 2013;28(6):1598–609.
[54] Practice committee of American society for reproductive medicine increased maternal cardiovascular mortality associated with pregnancy in women with Turner syndrome. Fertil Steril 2012;97(2):282–4.
[55] El-Mansoury M, Barrenäs M-L, Bryman I, Hanson C, Larsson C, Wilhelmsen L, et al. Chromosomal mosaicism mitigates stigmata and cardiovascular risk factors in Turner syndrome. Clin Endocrinol (Oxf) 2007;66(5):744–51.
[56] Siu SC, Silversides CK. Bicuspid aortic valve disease. J Am Coll Cardiol 2010;55(25):2789–800.
[57] Yap S-C, Drenthen W, Pieper PG, Moons P, Mulder BJM, Mostert B, et al. Risk of complications during pregnancy in women with congenital aortic stenosis. Int J Cardiol 2008;126(2):240–6.
[58] Hameed A, Karaalp IS, Tummala PP, Wani OR, Canetti M, Akhter MW, et al. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. J Am Coll Cardiol 2001;37(3):893–9.
[59] Silversides CK, Colman JM, Sermer M, Farine D, Siu SC. Early and intermediate-term outcomes of pregnancy with congenital aortic stenosis. Am J Cardiol 2003;91(11):1386–9.
[60] Sakaguchi M, Kitahara H, Seto T, Furusawa T, Fukui D, Yanagiya N, et al. Surgery for acute type A aortic dissection in pregnant patients with Marfan syndrome. Eur J Cardio-Thorac Surg 2005;28(2):280–3. discussion 283-285.
[61] John AS, Gurley F, Schaff HV, Warnes CA, Phillips SD, Arendt KW, et al. Cardiopulmonary bypass during pregnancy. Ann Thorac Surg 2011;91(4):1191–6.
[62] Weiss BM, von Segesser LK, Alon E, Seifert B, Turina MI. Outcome of cardiovascular surgery and pregnancy: a systematic review of the period 1984–1996. Am J Obstet Gynecol 1998;179(6 Pt 1):1643–53.
[63] Ch'ng SL, Cochrane AD, Goldstein J, Smith JA. Stanford type A aortic dissection in pregnancy: a diagnostic and management challenge. Heart Lung Circ 2013;22(1):12–8.
[64] Chang C-Y, Yang J-M, Lam C-W, Chen P-H. Successful management of aortic dissection in a patient with Marfan syndrome during pregnancy. Am J Obstet Gynecol 2013;208(2):e3–6.