



MARFAN SYNDROME

Background

Marfan syndrome is an autosomal dominant connective disease which primarily involves the cardiovascular, musculoskeletal and ocular systems. Diagnosis is based on Ghent criteria including; a detailed history, physical examination, imaging (primarily heart and spine), and/or molecular genetic testing.

Aortic dilation and dissection are the major causes of morbidity and mortality.

Effects of Pregnancy-Related Hemodynamic Changes

There is an increased risk of accelerated aortic root dilatation and aortic dissection during pregnancy, likely a result of the combined effects of pregnancy-related increases in cardiac output and alterations in aortic wall structure related to altered hormonal milieu. (see Cardiovascular Changes During Pregnancy) The risk of aortic dissection or rupture appears to increase as gestation advances and persists for some months post-partum. Increased risk of dissection or rapid aortic root dilation has been noted in women with aortic root dimensions >40-45 mm. Dissection or dilatation in distal regions of the aorta has been reported in women with a history of previous aortic root surgery, though frequency of this complication is unknown. Surgical repair may be offered prior to conception if the aortic root diameter is > 44 mm, although this is unlikely to fully normalize the risk of dissection.

Maternal Cardiac Complications

Based on a review of studies published between 1995 and 2006 involving more than 350 unselected pregnancies in women with Marfan syndrome, the overall rate of dissection in pregnancy was found to be ~ 3% overall. Estimated risk of dissection is thought to be ~1% in women with an aortic diameter < 40 mm and ~10% in women who are deemed to be high risk (i.e., aortic root diameter > 40 mm, rapid dilation of aortic dimensions and/or previous dissection of the ascending aorta). In Marfan syndrome, aortic dissection has been reported as a complication of pregnancy, rarely, notwithstanding normal aortic dimensions. During pregnancy, it is important to identify cardiac symptoms including chest and/or back pain, presyncope or syncope. Risk of dissection is highest in the last trimester and in the first 6 post-partum months. In addition women with Marfan syndrome and dilating aortic roots may manifest severe aortic regurgitation, which may result in ventricular dilation and dysfunction leading to heart failure or ventricular arrhythmia.

Other cardiac characteristics can have an impact on outcomes (see General Considerations).

Fetal Complications

Risk of transmission to the fetus of an affected parent is 50% due to the autosomal dominant pattern of inheritance. Severe expression of the syndrome can occur in offspring of a mother with relatively mild disease. Premature delivery is more frequent in women with Marfan syndrome and may confer increased mortality risk to the child. Should a mother develop an aortic dissection during pregnancy, there is a substantial risk of fetal hypoperfusion with consequent compromise of fetal wellbeing.

Management Strategies

Preconception Counseling/Contraceptive Methods

Ideally, management for women with Marfan syndrome begins preconceptionally. Risk of morbidity and mortality related to pregnancy should be reviewed with the prospective mother. Cardiac imaging should be arranged for detailed study of the aorta so that risk stratification can occur and should include echocardiography and optimally also cardiac magnetic resonance imaging (MRI) (note that the safety of MRI *during* pregnancy has not been determined). MRI is preferred over cardiac computed tomography (CT) due to the ionizing radiation associated with the latter.

Despite thorough screening methods, ~ 10% of the genetic mutations that cause Marfan syndrome are not identified despite testing. Prenatal diagnosis can be accomplished by chorionic villus sampling or amniocentesis, and preimplantation diagnosis can be achieved through sampling a cell at the 8 cell blastocyst stage using techniques of in-vitro fertilization. Such testing is only useful, however, if the genetic abnormality in the affected parent has been previously determined.

Risk of pregnancy is relatively low in women with minimal cardiac involvement and an aortic root diameter < 40 mm, though pregnancy risk does exceed baseline risk in any woman with Marfan syndrome, even with an apparently normal aorta. As pregnancy is contraindicated in women with enlarged aortic roots, contraception should be used at least until more definitive management can be obtained.

A discussion about contraceptive methods is appropriate in all women with Marfan syndrome. Given evidence to suggest that there is a hormonally mediated decrease in aortic wall integrity (amount of mucopolysaccharides and loss of elastic fibres), estrogen-containing oral contraceptives should be avoided. (see Contraception)

In women with prior aortic valve replacement with a mechanical prosthesis, complexity and risk of anticoagulation during pregnancy should be highlighted antenatally. In any patients using anticoagulants, estrogen-containing contraceptive products should be avoided because they increase thrombosis risk.

Beta-blockers have been shown to slow growth of the aorta and decrease cardiovascular morbidity and mortality related to Marfan syndrome outside of pregnancy. By extension, they should therefore be used throughout pregnancy and for at least six months postpartum in patients not previously using them. It should be emphasized that many guidelines and expert recommendations call for universal use of beta blockers from the time the diagnosis of Marfan syndrome is made, independent of pregnancy. Risks and benefits should be discussed with the patient although there is a consensus that the β_1 -selective agent, metoprolol, is well-tolerated by mother and fetus during pregnancy.

As certain cardiac medications and anticoagulants are contraindicated in pregnancy, medication use should be reviewed if a woman is contemplating pregnancy or is pregnant. The MOTHERISK website (<http://www.motherisk.org>) is an excellent resource.

Ante-partum Care

If a woman with Marfan syndrome is pregnant, care should be coordinated between a cardiologist and high-risk obstetrician.

Meticulous blood pressure control should be maintained throughout antenatal, perinatal, and postpartum periods to attenuate shear stress on the aorta.

Serial echocardiography should be performed at 6-8 week intervals during pregnancy and until the 6th post-partum month.

Beta-blockade should be maintained throughout pregnancy, as described above, and probably indefinitely thereafter.

If there is a need for ongoing anticoagulation, a hematologist should be involved to discuss risk and benefits of various strategies involving use of warfarin or low-molecular heparin throughout pregnancy.

Women may be offered fetal echocardiography at approximately 20 weeks gestation.

Labour and Delivery

Labor and delivery must be planned carefully with a multidisciplinary team well in advance of the proposed due date. The plan should be communicated to the patient and all potentially involved healthcare teams. Because a majority of patients with Marfan syndrome have lumbosacral dural ectasia, an anesthetist should be consulted well in advance of labour in order to assess the feasibility of early and continuous epidural anesthesia, the preferred method of analgesia during labour when it can be applied.

Planned Cesarean delivery rather than labour and vaginal delivery is advised if the aortic root exceeds a diameter of 40-45 mm, if there has been a history of previous dissection, or if there is evidence of progressive dilation of the aorta during pregnancy. This is one of the rare indications for cesarean delivery for cardiac reasons only. If vaginal delivery is planned, forceps or vacuum delivery is often utilized to decrease maternal expulsive efforts during the second stage of labour. To decrease potential harmful complications from difficult mid cavity-assisted delivery, uterine contractions are often utilized to facilitate the initial descent of the presenting part.

Particular attention should be paid to avoidance of hypertension, which can be achieved with use of epidural anaesthesia and β -blockers, with or without vasodilating agents.

In general, endocarditis prophylaxis at the time of labour and delivery is not recommended in women with Marfan syndrome. However, some experts continue to administer antibiotics because they feel that the risks of adverse reactions to antibiotics are small and the risk of developing endocarditis has major health consequences.

Post-partum care

Risk of aortic dilatation and dissection extends into the post-partum period. Pregnancy-related cardiovascular changes do not fully return to baseline until about 6 month's post-partum. For this reason, follow up at a frequency thought to be appropriate by the coordinating physicians should take place until 6 months post-partum, and should include serial echocardiography.

Most beta-blocking agents are excreted in breast milk in low concentrations, but can be used in nursing mothers when required.

References

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