orphanaesthesia

# Anaesthesia recommendations for

# Marfan syndrome

**Disease name:** Marfan syndrome

**ICD 10:** Q87.4

**Synonyms:** Marfan's syndrome

**Disease summary:** Marfan syndrome is an autosomal dominant, multisystem disease with a reported incidence of 1 in 3,000 to 5,000 individuals. There is a broad range of clinical severity associated with Marfan syndrome, ranging from isolated features to neonatal presentation of severe and rapidly progressive disease. Classic manifestations involve ocular (lens dislocation, myopia), cardiovascular (aortic root dilatation with aortic regurgitation, mitral valve prolapse with mitral regurgitation), and musculoskeletal abnormalities (long bone overgrowth, scoliosis, kyphosis, joint hypermobility), however involvement of the lung (pneumothorax), skin (striae), and central nervous system (dural ectasia) is also common in Marfan syndrome. It is an autosomal dominant inheritance mutation in the FBN1 gene located on chromosome 15 that encodes the extracellular matrix protein, fibrillin-1, which causes the classic Marfan syndrome. However, up to 30% of cases have neither parent affected and represent de novo mutations. Prophylactic treatment with beta-blockers is considered standard care in adults (unless contraindicated) and has been shown to reduce the rate of aortic dilatation. There is no definitive recommendation for either general or regional anaesthesia. Regardless of anaesthetic technique, care should be taken to prevent a sudden increase in myocardial contractility, producing an increase in aortic wall tension, which could lead to aortic dissection.

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Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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## Typical surgery

The literature review is limited to case reports/case series of patients presenting for surgical treatment of scoliosis, retinal detachment, orthodontic surgery, caesarean delivery, aortic root replacement, elective repair of thoracic aortic aneurism, and emergency repair of aortic dissection. Patients with Marfan syndrome have increased incidence of inguinal, femoral and umbilical hernia, recurrent pneumothoraces, requiring surgical treatment, as well as arthropathies, severe pectus deformities, necessitating orthopaedic correction. Bentall and De Bono were pioneers in the "Bentall" procedure to replace the dilated aortic root in 1968, improving patients' life expectancy.

## Type of anaesthesia

There is no definitive recommendation for either general or regional anaesthesia. A distinct advantage of general anaesthesia is that, if acute dissection should occur, the airway is protected and immediate cardiac surgery is possible. Disadvantages of general anaesthesia include the risk of hypertensive response to intubation, which could predispose to aortic dissection, if not prevented pharmacologically. There are no contraindications for sedation in these patients, however, in patients with significant pulmonary disease (emphysema, restrictive lung disease due to scoliosis) this technique should be considered with caution.

## Necessary additional pre-operative testing (beside standard care)

Cardiovascular complications are recognized to be the major cause of morbidity and mortality in patients with this disease. Cardiac investigations such as echocardiography or cardiac magnetic resonance imaging (MRI) should be ordered pre-operatively to rule out cardiac or aortic pathology. Left ventricular dilation may predispose to alterations of repolarization and fatal ventricular arrhythmias and could be identified on echocardiogram.

Patients with significant dilatation of aortic root should be referred to a cardiothoracic surgeon for evaluation of aortic root replacement before elective surgery. There have been case reports of caesarean delivery followed by repair of aortic dissection in parturients, therefore women with aortic dilatation >4cm, measured at the level of Valsalva sinuses, or history of aortic dissection should deliver in a centre where cardiovascular surgery is available.

The 2010 ACC/AHA/AATS guidelines recommend an elective operation for patients with Marfan syndrome at an external diameter of ≥5 cm to avoid acute dissection or rupture. Indications for repair at an external diameter less than 5 cm include rapid growth (>5 mm/y), family history of aortic dissection at a diameter less than 5 cm or presence of progressive aortic regurgitation. Prophylaxis against infective endocarditis in the presence of valvular abnormality is not required unless the patient has a mechanical valve. Pulmonary blebs may be present with a history of spontaneous pneumothoraces, therefore chest X-ray should be ordered pre-operatively.

Patients with severe scoliosis should undergo pulmonary function testing to evaluate the extent of restrictive lung disease. Due to the high prevalence (70% incidence in the lumbosacral area) of dural ectasia (increased diameter of the dural sac) in this patient population, MRI of the spine should be ordered before planning any neuraxial procedure, even in the absence of the symptoms (low back pain, headache, proximal leg pain, weakness and numbness above and below the knee, and genital/rectal pain).

In patients suffering from Marfan syndrome, caudal epidural anaesthesia should only be performed after a radiological diagnostic examination. The absence of symptoms does not exclude meningeal abnormalities.

## Particular preparation for airway management

Pre-operative examination of the airway is critical because the presence of prognathism and high arched palate with crowded teeth may make visualization of the larynx during direct laryngoscopy difficult. Clinically symptomatic cases of atlantoaxial dislocation in these patients are rarely reported in the literature and screening radiographs of the cervical spine for patients with Marfan syndrome undergoing general anaesthesia are not routinely recommended.

It is recommended that before endotracheal intubation, a fibre-optic bronchoscope should be used to inspect the airways to avoid compression of the aneurysm. There is one case-report of tracheomalacia in a patient with Marfan syndrome manifested by increased airway pressures and difficulty with ventilation during anaesthesia in a prone position. Obstructive sleep apnoea has been reported in patients with Marfan syndrome, although there are no case reports describing difficulties managing the airway due to this comorbidity.

Patients are at increased risk of developing pneumothorax, which should be kept in mind during positive pressure ventilation. Although there is a possibility of temporomandibular joint dysfunction, this condition has not been reported to cause difficulty with laryngoscopy. Excessive traction on laryngoscopy should be avoided to prevent temporomandibular joint dislocation. Cardiovascular response during laryngoscopy should be blunted pharmacologically. The haemodynamic goal is to reduce the stress imposed upon the wall of the aneurysm.

## Particular preparation for transfusion or administration of blood products

There is no evidence from the literature that patients with Marfan syndrome have pre-existing coagulation abnormalities associated with a higher risk of blood transfusion. Patients requiring anticoagulation due to prosthetic valve or aortic root should be offered a bridging therapy before elective surgery.

## Particular preparation for anticoagulation

There is no information suggesting the need for particular anticoagulation, except in patients following valve or aortic root replacement.

## Particular precautions for positioning, transportation and mobilisation

Patients must be carefully positioned and handled on the operating table and stretchers to avoid joint dislocations and injuries secondary to joint laxity.

## Interactions of chronic disease and anaesthesia medications

Patients might be taking beta-blockers, angiotensin receptor blockers (ARB) for blood pressure control to minimize shear forces and wall stress in the aorta, diuretics (history of heart failure), and anticoagulants, if they had valve or aortic root replacement in the past. Beta-blockers should be continued peri-operatively.

One of the populations that could potentially benefit the most from treatment with β-blockers is the paediatric population, and the rationale is that treatment with β-blockers may allow surgery to be delayed and, therefore, the eventual implantation of a larger graft, which may, in turn, avoid the need for re-intervention at a later time. Potential adverse effects of perioperative β-blockade include bradycardia and hypotension. Continuing ARBs up to the time of surgery increases peri-operative hypotension. Omitting diuretics in the morning of the surgery minimizes hypovolaemia and electrolyte disturbance.

## Anaesthetic procedure

Patients with Marfan syndrome require special considerations regarding the anaesthetic technique to avoid extreme hypotension and hypertension, conserve coronary perfusion, and prevent the development of an increase in the aortic wall and dissecting aneurysm. Labetalol and nitroglycerin should be available to treat hypertensive episodes, and haemodynamically stable induction should be performed. This could be achieved by using short-acting opioids like Remifentanil under target-controlled infusion regimen. Volatile anaesthetics have the potential to decrease the force of cardiac ejection, therefore decreasing the risk of aortic dissection. Phenylephrine is a vasopressor of choice, because ephedrine may induce tachy-cardia via its β-adrenergic effect. Avoidance of excessive endogenous catecholamine production through control of pain and anxiety is essential.

Volatile agents or neuromuscular blocking agents are generally avoided if somatosensory evoked potentials or motor evoked potentials monitoring is necessary. In this case, anaesthesia will rely on a propofol infusion (50-100 µg/kg/min) to provide anaesthetic maintenance.

Hypothermic circulatory arrest (HCA) for the repair of the adult aortic arch has become a standard technique in thoracic aortic surgery. But a prolonged deep HCA greater than 30 minutes is associated with the occurrence of severe neurological damage. Three major neuroprotective techniques in HCA for the repair of the adult aortic arch have been championed in the contemporary era: profound hypothermia alone, retrograde cerebral perfusion, and ante-grade cerebral perfusion. To ensure optimal anaesthesia management, close communication between the anaesthesia team, surgical team, perfusionist, operating room nurses, and staff in the intensive care unit is necessary.

Antibiotic prophylaxis: According to the latest AHA guidelines, patients with isolated valvular abnormality do not require antibiotic prophylaxis against infective endocarditis. If the patient has a history of a prosthetic cardiac valve or a history of infective endocarditis in the past, preoperative antibiotic prophylaxis should be administered according to AHA guidelines.

Antibiotic prophylaxis is recommended for all dental procedures that involve manipulation of gingival tissues or periapical region of teeth or perforation of the oral mucosa, procedures on respiratory tract or infected skin, skin structures, or musculoskeletal tissue. The regimen for antibiotic administration in those cases might be either oral using Amoxicillin 2 g or intra-venous with Ampicillin 2 IM/IV or Cefazolin or Ceftriaxone 1 g IM/IV. Patients allergic to penicillin or ampicillin could receive oral Cephalexin (or any other 1st or 2nd generation

cephalosporin) 2 g, Clindamycin 600 mg, or Azithromycin or Clarithromycin 500 mg. Alternatively, parenteral Cefazolin or Ceftriaxone 1 g IM/IV or Clindamycin 600 mg IM/IV could be used in patients with an anaphylactic reaction to penicillin and ampicillin and unable to take oral medications. Procedures, requiring antibiotic prophylaxis for surgical wound infection prevention should utilize antibiotics effective against suspected pathogens. Antibiotic prophylaxis solely to prevent IE is not recommended for GU or GI tract procedures, as well as is not recommended for vaginal deliveries.

## Particular or additional monitoring

For temperature monitoring, it is recommended that two different sites be used. A temperature probe is placed into the oesophagus for core temperature measurement as well as another visceral monitoring site. For monitoring of central nervous system oxygenation and function cerebral oximetry, monitoring probes are attached to the patient's forehead. An arterial line should be used intra-operatively to monitor for sudden changes in the blood pressure. The use of intraoperative transoesophageal echocardiography to monitor aortic root diameter has been reported in several case reports. Central line placement is not necessary unless significant valvular dysfunction is present.

## Possible complications

Patients with Marfan syndrome and left ventricular dilatation are at risk of ventricular arrhythmias. Aortic root diameter greater than 4 cm carries a risk of aortic dissection. Type 2 aortic dissections as classified by De Bakey is the commonest type seen in patients with Marfan syndrome. Spontaneous coronary artery dissection has been also reported in the literature.

## Post-operative care

The degree of postoperative monitoring depends on the surgical procedure and the preoperative condition of the patient, particularly the size of the aortic root and left ventricle. Intensive care is not mandatory.

## Disease-related acute problems and effect on anaesthesia and recovery

Due to high mortality associated, anaesthetic management of patients with severe aortic root dilation is a challenging situation. Elastic fibre degeneration, lacking smooth muscle cells in aorta and mucopolysaccharide deposition in between the cells of the media are the main features of aorta in Marfan syndrome.

Aortic dissection in patients with Marfan syndrome can be precipitated by major haemodynamic changes under anaesthesia. Haemodynamic instability can be minimised with adequate monitoring and preparation during intubation, intraoperative fluid resuscitation, planned extubation, and adequate analgesia. These goals can prevent this life-threatening event.

## Ambulatory anaesthesia

There are no reported experiences in patients with Marfan syndrome in the ambulatory anaesthesia setting. The author's opinion is that low risk, minimally invasive surgery could be performed on patients with Marfan syndrome in the ambulatory setting, in the absence of significant involvement of cardiovascular and respiratory systems.

## Obstetrical anaesthesia

All women with genetically proven Marfan syndrome should have counselling on the risk of dissection and the recurrence risk and have a complete multidisciplinary evaluation including imaging of the entire aorta before pregnancy. Pregnancy should be discouraged in women with previous aortic dissection because of the high risk for aortic complications.

Dissection occurs most often in the last trimester of pregnancy (50%) or the early postpartum period (33%). In all women with the known aortic disease and/or an enlarged aortic root diameter, the risks of pregnancy should be discussed before conception. Aortic root diameter >4cm during pregnancy carries a higher risk of dissection (10% compared to 1% in patients with aortic root diameter <4 cm) and conception is not advised if the root diameter is >4.5 cm. Depending on the aortic diameter, patients with aortic pathology should be monitored by echocardiography at 4–12-week intervals throughout the pregnancy and 6 months post-partum because aortic root enlargement may be accelerated by pregnancy. Pregnancy should be supervised by a cardiologist and obstetrician who are alert to the possible complications. Instrumented vaginal delivery can be safely performed in patients with Marfan syndrome who have no cardiovascular involvement or stable minimal aortic dilatation (<4 cm). Epidural analgesia is strongly recommended to minimize the stress associated with labour pain. Caesarean delivery is indicated in patients with an aortic diameter >4.5 cm, aortic dissection, severe aortic regurgitation or heart failure. Caesarean delivery should also be considered in the presence of contraindications for epidural analgesia for vaginal delivery or epidural analgesia has failed, to avoid the stress on the dilated aortic root, caused by untreated labour pain. For patients with aortic root diameter 4.0-4.5 cm, the decision about the method of delivery should be individualized and involve a multidisciplinary team approach, including an obstetrician, anaesthesiologist and cardiologist. Family history of dissection, rapid growth during pregnancy should be taken into account. It is essential to continue β-blocker therapy during pregnancy, peripartum and postpartum period to prevent aortic dissection.

Management of anticoagulation during pregnancy:

Parturients with Marfan syndrome will only require anticoagulation if they have a mechanical valve. Women with well-functioning prosthetic valves tolerate pregnancy well from the haemodynamic point of view. Yet, the need for anticoagulation raises specific concerns because of an increased risk of valve thrombosis, of haemorrhagic complications, and offspring complications. According to the European Society of Cardiology guidelines, oral anticoagulants (OAC) could be continued during the 1st trimester if the required dose of warfarin is <5mg/day. If the dose is >5 mg, discontinuation of OAC between weeks 6 and 12 and replacement by adjusted-dose UFH (a PTT ≥2× control; in high-risk patients applied as intravenous infusion) or LMWH twice daily (with dose adjustment according to weight and target anti-Xa level 4-6 hours post-dose 0.8-1.2 U/mL) is recommended. If OAC is continued through the 2nd and 3rd trimester, at 36 weeks of gestation they should be replaced by either dose-adjusted UFH (a PTT ≥2× control) or adjusted-dose LMWH (target anti-Xa level 4-6 hours post-dose 0.8-1.2 U/mL). In pregnant women managed with LMWH, the post-dose anti-Xa level should be assessed weekly. LMWH should be replaced by intravenous UFH at

least 36 hours before planned delivery. UFH should be continued until 4-6 hours before planned delivery and restarted 4-6 hours after delivery if there are no bleeding complications. Normal aPTT after discontinuation of IVUFH should be confirmed before performing the neuraxial procedure.

Both regional and general anaesthesia have been used successfully in parturients undergoing caesarean delivery. Neuraxial anaesthesia may pose technical challenges due to kyphoscoliosis. The standard dose of local anaesthetic required for the spinal anaesthesia might be inadequate due to the presence of dural ectasia, therefore combined spinal-epidural anaesthesia might be a technique of choice for caesarean delivery. Local anaesthetic without epinephrine is preferable for epidural anaesthesia in case of accidental intravascular injection. Although dural ectasia is not an absolute contraindication for epidural anaesthesia, the theoretical risk of increased incidence of dural puncture or inadequate anaesthesia should be discussed with the patient. Structural changes in the ligamentum flavum have been suggested as a likely cause of accidental dural puncture. Ultrasound examination of the back before placing an epidural catheter may decrease the risk of puncture of the enlarged dural sac. Ascending and descending aortic dissection has been reported in the postpartum period in parturients with Marfan syndrome, therefore symptomatic women should undergo immediate investigations. Asymptomatic patients still need to undergo an echocardiographic examination before hospital discharge.

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