Chapter 50

Marfan Syndrome

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Case Scenario

A 16-year-old male, weighing 52 kg and 182 cm tall, presents for repair of pectus excavatum via Nuss procedure. The pectus deformity is severe, with a Haller index of 4.7, causing cardiac displacement and compression of the right atrium and right ventricle. Symptoms include worsening shortness of breath and chest discomfort during exertion. His medical history is also significant for Marfan syndrome, stable mild thoracolumbar scoliosis with 20-degree Cobb angle, mild ectopia lentis, and attention-deficit/hyperactivity disorder. The patient had a spontaneous left pneumothorax 2 years earlier that resolved with conservative treatment. Current medications include atenolol 25 mg and losartan 25 mg taken by mouth twice daily, and guanfacine ER 4 mg given once daily. Recent preoperative diagnostic studies include chest magnetic resonance imaging, chest computed tomography, pulmonary function studies, electrocardiogram, and an echocardiogram. Pulmonary function tests show moderate restrictive and mild obstructive pulmonary function. One small apical bleb in the left lung is seen on magnetic resonance imaging. Current vital signs are heart rate 62 beats/minute, blood pressure 106/71, SpO_2 98% on room air, respiratory rate 16 breaths/minute, and temperature 36.5°C. The surgeon is expecting to place two Nuss bars for correction of the pectus deformity.

A recent transthoracic echocardiogram reveals the following:

- *Stable aortic root dilatation measuring 3.7 cm (Z-score 3.8)*
- *Mild-moderate aortic insufficiency*
- *Mitral valve prolapse with mild mitral regurgitation*
- *Right atrial and ventricular compression with normal biventricular function*

Key Objectives

- Identify characteristic findings of Marfan syndrome.
- Define significant aortic root dilatation and the significance of the "*Z*-score."
- Describe medications used for management of cardiovascular pathology.
- Formulate anesthetic plans along with postoperative pain management strategies.
- Discuss the unique challenges of cardiopulmonary resuscitation in a patient with a pectus bar.

Pathophysiology

What is Marfan syndrome?

Marfan syndrome (MFS) is an autosomal dominant connective tissue disorder caused by *FBN1* gene mutations on chromosome 15, resulting in defective fibrillin-1 matrix glycoproteins manifesting as tissue abnormalities. Fibrillin-1, besides forming important structural tissue components, also impacts regulation of transforming growth factor β (TGF-β) which results in increased proteolytic activity and extracellular matrix degeneration. The aberrant protein expressions increase and worsen with age and are most notoriously manifested in the musculoskeletal, cardiovascular, and ophthalmic systems. Cardinal clinical features include aortic root dilatation and ectopia lentis. Other clinical manifestations may include pectus excavatum or carinatum, scoliosis, dural ectasia, pulmonary involvement (emphysema, lung cysts, spontaneous pneumothorax), retrognathia, malar hypoplasia, and joint abnormalities.

What cardiovascular abnormalities are commonly associated with MFS?

The most concerning cardiovascular abnormality is aortic root dilatation with progression to dissection and rupture. Aortic root dilatation is seen in approximately 50% of young children with MFS, with the risk of aortic rupture increasing during the teenage years. Aortic root rupture

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accounts for 50% of deaths by age 40 years in untreated patients with MFS. Dilatation can also involve the thoracic and abdominal aortic segments, the main pulmonary artery, and the carotid arteries. Other described cardiac findings are aortic valve insufficiency, mitral valve prolapse (MVP) and mitral valve insufficiency, ventricular arrhythmias, and dilated cardiomyopathy.

Clinical Pearl

Aortic root dilatation is seen in approximately 50% of young children with MFS, with the risk of aortic rupture increasing during the teenage years.

When aortic root dilatation is considered significant and what is the *Z*-score?

Aortic root size and rate of dilatation should be serially monitored. Per the 2010 Revised Ghent criteria for MFS, aortic root dilatation is significant when the aortic diameter (at the sinus of Valsalva) *Z*-score is 2 or greater. The ***Z-score*** conveys the deviation of a measurement from the population mean specific for body size and other factors, thus becoming a valuable tool for serial monitoring of a patient's aortic root diameter over time. Imaging modalities used for aortic root diameter measurement and correlation include echocardiography, computed tomography (CT), and/or magnetic resonance imaging (MRI). Yearly monitoring is recommended for stable rates of progression and more frequently for concerning findings. Risk factors for aortic dissection in MFS include aortic diameter 5 cm or greater, rapid rate of aortic dilatation, aortic dilatation progressing past the sinus of Valsalva, and family history of aortic dissection. Medical therapy aims to slow down the rate of aortic dilatation and delay surgical intervention. Delaying surgery until an adult-sized graft and valve can be utilized is highly beneficial for the pediatric patient; it also potentially lessens total lifetime replacements. Surgical therapy aims to improve survival via elective aortic root replacement for patients at high risk of rupture.

Clinical Pearl

The Z-score conveys the deviation of a measurement from the population mean specific for body size and other factors, thus becoming a valuable tool for serial monitoring of a patient's aortic root diameter over time.

What are the recommended treatment modalities for MFS?

Early therapy with β-blockers is the currently recommended treatment for all patients with MFS if tolerated. Dosage is adjusted to maintain a submaximal exercise heart rate of 110 bpm or less in children and 100 bpm or less in adults. It is thought that β-blockers' antihypertensive effect, reduction of myocardial contractility, pulse pressure, and aortic wall tension may delay the progression of aortic root dilatation. Atenolol is usually the drug of choice due to its long half-life and relative cardioselectivity. In patients intolerant to β-blockade, second-line therapy with an angiotensin receptor blocker (ARB) such as losartan is recommended. Currently, ARBs are the subject of ongoing research due to their action on reducing TGF-β activity, which is also implicated in tissue degeneration in MFS. Aortic root surgery is reserved for those patients at high risk of dissection and rupture; common approaches include use of a composite valve-graft or valve sparing aortic root replacement. Improved aortic root monitoring and elective aortic root surgery have decreased the rate of sudden death from aortic dissection, yielding improved life expectancies for patients with MFS. Careful monitoring of the aorta distal to the repair should continue after aortic root surgery because dilatation of the distal aorta continues to occur. Concomitant repair of MVP or replacement of the mitral valve is performed for those with severe mitral regurgitation.

What are the indications and possible surgical approaches for surgical correction of pectus excavatum?

The ***Haller index*** is the intrathoracic transverse diameter divided by the smallest anteroposterior diameter in a chest CT axial slice. Intrathoracic structures are commonly affected by the mechanical compression of the pectus deformity, leading to reduced thoracic volume with restrictive/obstructive lung disease, cardiac impingement or displacement, potential conduction abnormalities, and valvular disease. With chronically reduced chest compliance, cardiopulmonary function and symptoms may worsen with age. Surgical correction for pectus excavatum is indicated in the presence of cardiopulmonary symptoms, severity of deformity (defined by Haller index of 3.2 or greater), rapid progression of the malformation, cardiopulmonary compression or displacement, restrictive or obstructive pattern in pulmonary function tests (PFTs), and psychological disorders related to the chest deformity.

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The Nuss procedure, a minimally invasive approach involving the placement of a retrosternal bar to correct the depressed anterior chest wall, has become the technique of choice for correction of pectus excavatum deformity. Compared to the open approaches, which are modifications of the original Ravitch procedure involving cartilage or sternal resection, the Nuss procedure is associated with shorter intraoperative times, significantly less blood loss, *increased* postoperative pain levels, and improved cosmetic results.

Anesthetic Implications

What are the primary goals of the preanesthesia visit?

Since this operation is elective, goals of the preoperative evaluation include a complete systemic review including anesthesia history, coexisting diseases, pertinent diagnostic studies and laboratory values, physical examination, preparation and optimization for this surgery along with discussion of anesthetic plans with the patient and family. Special attention is placed on the organ systems impacted by MFS and pectus excavatum, with careful documentation of symptoms and physical examination findings pertaining to the cardiopulmonary and musculoskeletal systems. A thorough airway examination should be performed. If the ophthalmologic history shows concerning deterioration, a consult may be warranted to rule out retinal involvement. Review of pertinent recent diagnostic studies with special consideration to the cardiopulmonary system is crucial. Discussion of specific anesthetic risks including the risk of aortic rupture and death, invasive monitoring, and plans for postoperative pain management should ensue with the patient and family. Emphasis on continuation of current medications is important.

What diagnostic studies are indicated in preparation for this surgery?

Recent evaluations of aortic and cardiopulmonary status for manifestations of MFS and pectus excavatum are needed for planning this elective procedure and should include the following:

- ***Transthoracic echocardiogram*** for assessing aortic root dimensions, evaluating valvular function, diastolic filling, and cardiac compression
- ***Electrocardiogram (ECG)*** for detecting the presence of conduction abnormalities due to MFS or cardiac compression
- ***Magnetic resonance and CT imaging*** to demonstrate the effects of the pectus excavatum on the intrathoracic structures (including delineation of aortic size, morphology, and presence of dissection), lung parenchymal integrity, and to calculate the Haller index
- ***Pulmonary function studies*** for evaluating the degree of preoperative pulmonary impairment resulting from MFS, pectus excavatum, and kyphoscoliosis

In patients with MFS, if aortic root surgery seems impending, a multidisciplinary discussion is needed to determine the optimal timing of pectus correction and cardiac surgery.

What medications should be continued on the day of surgery?

It is very important to continue β-blocker therapy on the day of surgery to lower aortic wall stress and the risk of dissection throughout the case. The ARB can be held due to reports of hypotension under general anesthesia. Guanfacine, a central alpha-2 agonist, can be continued for treatment of attention deficit/hyperactivity disorder (ADHD) and for its concurrent effect of maintaining blood pressure control.

Clinical Pearl

β-Blocker therapy should be continued throughout the perioperative period to minimize the risk of aortic root dissection.

What postoperative pain strategies should be discussed for this patient?

The Nuss procedure is associated with significant levels of postoperative pain, reported to be much greater than pain from the open Ravitch procedure. No pain management technique has been demonstrated to be superior but varied multimodal techniques have been described as effective for postoperative pain management. The elevation of the sternum, new geometric chest wall configuration, and sternal pressure of the bars generate high-intensity pain in the patient's chest and spine. Many patients with MFS require more than one bar for correction of the pectus deformity. Pain management should start in the preoperative period. Continuous thoracic epidurals or bilateral paravertebral catheter infusions have been successfully utilized, and decision making regarding the use of regional techniques is institution dependent. Other components of postoperative analgesia management include intercostal nerve blocks, narcotic patient-controlled analgesia, subcutaneous infusion catheters of local anesthetic, nonsteroidal antiinflammatory drugs, intravenously administered acetaminophen,

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benzodiazepines for muscle spasms and anxiety, other muscle relaxants such as methocarbamol, and agents for neuropathic pain such as gabapentin. Postoperatively, the patient is mobilized early with physical therapy and encouraged to ambulate, which may acutely increase pain levels but is beneficial for long-term pain resolution. Preoperative education of the family and patient regarding expected pain levels is critical to create reasonable expectations and diminish anxiety.

Are there special concerns regarding regional or epidural anesthesia in this patient?

Dural ectasia, usually asymptomatic, has been associated with MFS. It results from the dilatation of the dural sac owing to pressure from the cerebrospinal fluid (CSF). Dural ectasia is most prominent in the lumbosacral area where the CSF also exerts the highest pressure. In general, neuraxial techniques have been described as potentially more challenging and less reliable in patients with MFS. Epidural catheter placement over the areas of degenerated dural sac may be associated with increased risks for dural puncture. Additionally, the dilated dura sac may hold an increased volume of CSF that would make appropriate dosing of spinal anesthesia more challenging. The presence of scoliosis in the patient with MFS may further complicate epidural catheter placement. Bilateral paravertebral catheters have been successfully used in patients with MFS. Placement under ultrasound guidance allows visualization of the pleura and may improve successful catheter placement. In the event of epidural placement in the postoperative period, the lateral decubitus position is contraindicated after surgery for fear of dislodging the recently placed Nuss bar.

Should premedication be utilized in this patient?

The patient's history of ADHD as well as the goal of avoiding a sympathetic surge leading to hypertension would favor the administration of premedication for anxiety with minimal risk.

What associated characteristics of MFS can cause airway concerns?

Patients with MFS have associated characteristics such as high-arched palate, retrognathia, and ligamentous hyperlaxity that can lead to joint subluxation during intubation maneuvers. The anesthesiology team should be prepared for a potentially difficult intubation owing to those factors.

What are the perioperative hemodynamic goals?

Maintenance of hemodynamic control and avoidance of hypertension both deserve special attention in order to minimize the risk of developing aortic dissection. β-blocker therapy should be continued until the day of surgery. In addition to adequate baseline levels of anesthesia and analgesia, various techniques are employed to blunt the hemodynamic response ahead of highly stimulating events such as laryngoscopy, intubation, and surgical maneuvers such as sternum elevation. Pharmacologic agents used to attenuate the hypertensive responses include short-acting opioid infusions and vasoactive agents such esmolol and nicardipine. Maneuvers or drugs that may lead to tachycardia or hypertension should be avoided.

Clinical Pearl

Maintenance of hemodynamic control with avoidance of hypertension deserves special attention during the entire perioperative period to minimize the risk of developing aortic dissection. Maneuvers or drugs that may lead to tachycardia or hypertension should be avoided.

What monitoring is appropriate for this patient?

In addition to the standard American Society of Anesthesiologists recommended monitoring for general anesthesia using a 5-lead ECG, invasive arterial blood pressure monitoring can be utilized for close monitoring and blood pressure management. The Nuss procedure is generally associated with minimal blood loss unless cardiac laceration occurs, an extremely rare complication (0.1% or less) with modern surgical techniques including thoracoscopy and sternum elevation for dissection. Although the risk of aortic dissection and rupture is present in this patient with MFS, the exact risk is unknown but presumed to be low in the setting of appropriate hemodynamic control. Transesophageal echocardiography can provide additional monitoring as needed to visualize the aortic root and cardiac status if unexplained or sudden changes in hemodynamics occur.

Clinical Pearl

In addition to invasive arterial blood pressure monitoring, transesophageal echocardiography can provide additional monitoring as needed to visualize the aortic root and cardiac status during unexplained sudden changes in hemodynamics.

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If this patient had a prior history of mitral valve repair, how might that affect the anesthetic plan?

Previous surgeries (or inflammatory processes) in the intrathoracic cavity place the patient at a higher risk for cardiovascular or lung injury. Adhesions can obscure visualization of important mediastinal structures and make surgical dissection challenging. The risks of cardiovascular injury and bleeding are also increased in this setting. Some centers make this factor a contraindication for the closed chest approach. If the surgeon determines that the minimally invasive approach is feasible after thoracoscopic exploration, adequate blood availability with the cardiac team on standby until safe passage of the bars occurs should be arranged. The anesthesia team must prepare for and be able to respond quickly to adequately resuscitate the patient should catastrophic bleeding occur.

What anesthetic induction methods are appropriate?

Placement of a preinduction peripheral intravenous line allows the administration of pharmacologic agents for titrated induction and rapid control of hemodynamics. There is no superior anesthetic induction agent or technique as long as hemodynamic control is maintained during the process of induction and intubation. Significant hypotension during induction has been reported for patients with cardiac compression. Hypertension and tachycardia can occur during laryngoscopy and intubation. Blunting of sympathetic stimulation (i.e., use of lidocaine and opioids) and dose titration of induction agents with administration of short-acting vasoactive agents as needed can prevent detrimental hemodynamic swings while the airway is secured. If airway management proves difficult, having a separate person designated to monitor and control hemodynamics while the primary anesthesiologist's attention is placed on securing the airway is recommended.

What positioning concerns exist for this patient?

Proper positioning and support must be ensured, considering the scoliosis and joint hyperlaxity of patients with MFS. The arms are normally positioned 90° to the side to allow surgical access to both sides of the chest. The arms should not be hyperextended at the level of the brachial plexus, and proper support should be available at the elbows and wrists. Patients with MFS may have asymptomatic protrusio acetabuli (migration of the femoral heads into the pelvic cavity); there are no existing specific recommendations for positioning apart from the usual proper support of the hips, knees, and heels.

Does this patient need subacute bacterial endocarditis prophylaxis?

Per the current 2007 American Heart Association recommendations, this patient does not meet the current criteria to require prophylaxis for bacterial endocarditis. Antimicrobial prophylaxis for surgical site infection should be given per institutional guidelines.

What additional concerns exist during anesthetic maintenance?

Airway pressures during positive pressure ventilation must be kept as low as possible to reduce the risk of pneumothorax, especially if this patient has sustained a previous spontaneous pneumothorax and is known to have a current apical bleb. Pneumothorax must be kept high in the differential diagnosis if increased airway pressures or hemodynamic deterioration is noted. Although they are not routinely placed for uneventful Nuss procedures, chest tube(s) are often left in place for patients with MFS at risk of postoperative pneumothorax. Regarding the maintenance of anesthesia, since there is no anesthetic technique that has proven to be superior, anesthetic maintenance techniques are left to the discretion of the anesthesiologist while continuing to meet the hemodynamic goals for this patient.

Clinical Pearl

Airway pressures during positive pressure ventilation should be kept as low as possible to reduce the risk of pneumothorax.

New onset ectopy is observed during passage of the surgical introducer tool: what are the likely etiologies?

If the patient is otherwise stable and the arrhythmia coincides with surgical maneuvering of a tool inside the chest cavity, this is potentially a sign of contact with the myocardium and irritation of the conduction system. The surgeon needs to stop the maneuver and reassess the working distance to the heart. If the arrhythmia does not resolve or there are signs of hemodynamic instability, a detrimental cardiovascular event is occurring, and it must be quickly assessed and managed.

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Ventricular fibrillation occurs during the placement of the pectus bar: what should the surgeon be asked to do?

If ventricular fibrillation (VF) occurs during placement of the pectus bar, the surgeon should immediately pull the pectus bar out of the thorax under direct thoracoscopic visualization while confirming again the absence of obvious structural injury. Removing the pectus bar will allow for improved chest compression and defibrillation efforts.

Clinical Pearl

If ventricular fibrillation occurs during the placement of the pectus bar, the surgeon must remove the pectus bar to allow for improved chest compression and defibrillation efforts.

What changes in chest compression strategy during cardiopulmonary resuscitation are recommended for patients with uncorrected pectus excavatum?

When performing cardiopulmonary resuscitation (CPR), patients with uncorrected pectus excavatum might benefit from compression at the level of the lower half of the sternum, with less compression depth required than for subjects with normal thoracic architecture. Evidence exists that standard compression depths might increase the risk of myocardial injury or other intrathoracic organ damage in these patients. Arterial tracings and end-tidal carbon dioxide waveforms are helpful to guide the effectiveness of chest compressions.

Clinical Pearl

If CPR is needed for patients with uncorrected pectus excavatum, compression at the lower half of the sternum with less compression depth than normally expected may decrease the risk of cardiac injury. Use arterial blood pressure tracings and end-tidal carbon dioxide waveforms to guide the effectiveness of chest compressions.

Should VF occur postoperatively, what changes during performance of CPR and positioning of defibrillating pads are recommended for patients with a sternal Nuss bar in place?

Stronger than usual chest compressions are recommended to achieve effective results when the sternal bar is in place. Front-to-back defibrillation pad placement is recommended so that the electric current will better reach the heart and not be dissipated via the Nuss bar. At the time of hospital discharge patients should be given a medical alert bracelet about the Nuss bar to alert emergency medical and other healthcare providers about the recommended adjustments for resuscitative efforts should they ever be necessary.

Clinical Pearl

If CPR is needed on a patient with a pectus bar in place, stronger than usual chest compressions are recommended to achieve effective results. Front-to-back defibrillation pad placement is preferred, so that the electric current will better reach the heart and not be dissipated via the Nuss bar.

What are the anesthetic considerations for emergence and extubation?

Avoidance of agitation and coughing is highly desirable to minimize the risks of displacement of newly placed bars, to avoid hypertension placing stress on the aortic root and to minimize the risk of spontaneous pneumothorax.

What postoperative concerns are present during the early recovery period?

Adequate pain control can remain challenging once the patient regains consciousness despite the use of preemptive and continuing multimodal pain management strategies. Emphasis on adequate monitoring for blood pressure and heart rate thresholds needs to be clearly communicated to the healthcare team. Recommendations exist to maintain a heart rate of 110 bpm or less and blood pressure within 20% above baseline to reduce the risk of aortic dissection. In addition to aggressive pain management, continuation of preoperative β-blockade and ARB therapy is also important for control of hypertension during the entire postoperative period. Resumption of guanfacine, a central alpha-2 agonist, may be helpful both for treatment of ADHD and for its effects on modulation of blood pressure. The patient may benefit from admission to the intensive care unit for close monitoring. Follow-up transthoracic echocardiography can be performed postoperatively to assess for improvement in cardiopulmonary compression and assessment of aortic root status.

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Suggested Reading

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