General surgical manifestations of Marfan's syndrome

Marfan's syndrome can manifest as various general surgical pathologies (herniae, diverticulosis, bowel obstruction and abdominal vasculature aneurysms). These pathologies often have abnormal presentations, and in some cases can be life-threatening.

Marfan's syndrome was first described in 1896 by a French paediatrician called Antoine Marfan (Aburawi et al, 2001). Marfan's syndrome is a connective tissue disorder. It is inherited as an autosomal dominant disorder and affects approximately 1 in 20 000 of the population. It is caused by mutations in the FBN1 gene on chromosome 15 (Lee et al, 1991). This chromosome is responsible for encoding fibrillin-1, which is the major constituent of elastin-associated microfibrils (Dietz et al, 1991). Fibrillin microfibrils are widely distributed extracellular matrix assemblies that endow elastic and non-elastic connective tissues with long range elasticity (Kielty et al, 2005). The diverse clinical features of this condition reflect the widespread distribution of fibrillin (Russell et al, 2000). The most important, and more common, clinical features of Marfan's syndrome involve the musculoskeletal, cardiovascular and ocular systems.

Cardiovascular catastrophes (aortic rupture and dissection) are responsible for death in the majority of patients with Marfan's syndrome (Srinvasan et al, 1990). Specifically, the mean life expectancy of untreated Marfan's syndrome is 32 years, with aortic dissection, aortic rupture and cardiac failure as a result of mitral or aortic regurgitation as the main cause of death in over 90% of cases (Von Kodolitsch et al, 1998).

Despite the fact that the gene responsible for Marfan's syndrome has been identified, chromosome analysis is still not practical for the diagnosis of Marfan's syndrome. Therefore the diagnosis of Marfan's syndrome depends on the presence of various major and minor diagnostic criteria, most of which involve various clinical features. It is recommended that there are major criteria in at least two different systems and involvement of a third organ system to make the diagnosis (Aburawi et al, 2001).

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Method

This is a review of the available literature, in English, of the rare general surgical manifestations of Marfan's syndrome. A systematic search was performed on Medline/Pubmed using the words 'Marfan's syndrome, hernia, diverticula, wound healing, scar, bleeding, colon, bowel, aneurysm, screening and gastrointestinal'. The related articles and the relevant MESH headings were then searched.

This search produced a wide range of case reports, each highlighting the various general surgical aspects of Marfan's syndrome. The case reports were mostly describing single cases (only two multi-case series were found). These correspond to level III evidence on the hierarchy of research design, or the lowest level (Harris et al, 2001). No reports were found of the actual incidence of these general surgical complications in this patient population. There was no literature about the possibility of screening for these complications.

The clinical features of Marfan's syndrome

There are multiple orthopaedic, proximal cardiovascular and ophthalmic features of Marfan's syndrome, all of which are well documented (Russell et al, 2000). Many of these features are listed in *Tables 1* and *2*. The clinical features of Marfan's syndrome are all a result of the effects on the body's connective tissue structure.

When assessing a Marfan's syndrome patient one must be aware of the various general surgical complications that may occur as a result of their disease.

The general surgical manifestations of Marfan's syndrome include abdominal vasculature aneurysms, bowel obstruction, diverticulae of abdominal viscera, diaphragmatic hernias and abdominal wall hernias, which are now discussed in more detail (*Table 3*).

Abdominal vasculature aneurysms

The defective elastin present in Marfan's syndrome can lead to a reduction in strength of the blood vessel wall (Lehmann, 1995). This can predispose to aortic aneurysm formation. The histology of the affected aorta typically shows cystic medial necrosis with irregular and disorganized elastic fibres (Sarkar et al, 1991).

The high incidence of proximal cardiovascular complications (e.g. aortic root disease and thoracic aorta dissec-

Table 1. Major diagnostic criteria

Skeletal	Pectus carinatum
	Pectus excavatum
	Reduced upper/lower segment ratio or arm span:height ratio >1.05
	Scoliosis (>20°)
	Pes planus
	Reduced elbow extension (<170°)
	Protrusio acetabulum
	Various wrist and thumb signs
Central nervous system	Lumbosacral ductal ectasia
Cardiovascular system	Dilatation of ascending aorta
	Dissection of ascending aorta
Ocular	Ectopia lentis
Family history	First degree relative
	Presence of mutation in fibrillin-1-gene
	Haplotype around fibrillin-1-gene

From Aburawi et al (2001)

Table 2. Minor criteria for organ system involvement

Skeletal	Joint hypermobility
	Characteristic faces
	Pectus excavatum
	High arched palate with teeth crowding
Cardiovascular system	Mitral valve prolapse+/- mitral regurgitation
	Dilatation or dissection of descending aorta <50 years old
	Dilatation of main pulmonary artery <40 years old
	Calcification of mitral valve annulus <40 years old
Ocular	Flat cornea
	Increased axial length of globe
	Reduced meiosis
Pulmonary	Apical blebs on chest X-ray
	Spontaneous pneumothorax
Skin	Striae atrophicae
	Recurrent incisional hernia

From Aburawi et al (2001)

tion) in Marfan's syndrome is well known (Russell et al, 2000). There also seems to be an increase in disease of the abdominal aorta and its branches. Currently, patients with Marfan's syndrome undergo routine echocardiography to assess the proximal aorta and mitral valve. Pregnant Marfan's syndrome patients have a far greater chance of aortic dissection, aneurysm and rupture during their pregnancy. An aortic root diameter greater than 40 mm is a contraindication to pregnancy (Klipple, 1989).

In a normal subject paediatric aortic aneurysms are extremely rare, while those with Marfan's syndrome can often develop associated aortic aneurysms (Sarkar et al, 1991). These are usually in the ascending aorta rather than the abdominal aorta; this is thought to be because of the higher proportion of elastic fibres in the ascending part, and also the greater pressures which are experienced there (Van Ooijen, 1988).

Table 3. Results of literature search for general surgical manifestations of Marfan's syndrome

Marfan's-related complication	Single case report series	Multiple case report series
Abdominal aneurysms	6	0
Bowel obstruction	2+1*	0
Diverticulae	2+1*	1 (3 cases)
Diaphragmatic herniae	2+1*	0
Abdominal wall herniae	1	1*

*This relates to the de Silva et al (1996) case report, which described a brother and sister with Marfan's syndrome. The brother developed bowel obstruction, visceral diverticulae and abdominal wall hernia. The sister developed recurrent abdominal wall herniae and diaphragmatic herniae.

A case report by Lafferty et al (1987) described a 32-year-old man with known Marfan's syndrome who presented with severe abdominal and lumbar pain. Ultrasound showed an 11cm infra-renal aortic aneurysm, with no proximal extension. This patient underwent a successful open repair using a Dacron graft, and subsequently made an uneventful recovery.

Van Ooijen (1988) described a 43-year-old woman with no known past medical history who presented with severe abdominal pain. Following multiple investigations, an infra-renal aortic aneurysm was demonstrated on ultrasound and arteriography. This was successfully repaired with a Dacron graft, from which she made a full recovery. She was formally diagnosed with Marfan's syndrome later on. However, the rest of her aorta was not investigated, and 5 months later she was readmitted with a thoracic aortic dissection, from which she subsequently died.

Ugwu et al (2003) described a 16-year-old patient with Marfan's syndrome who presented with back pain and an upper abdominal mass. After a significant delay and uncertainty about the underlying diagnosis, the patient deteriorated further and went for a laparotomy. During this procedure, he was found to have a leaking large abdominal aortic aneurysm. This was repaired, but the patient died shortly after the procedure.

A 16-patient case series by Grego et al (2003) showed that aneurysms of the splanchnic arteries are very rare, and they have a high mortality rate in emergency surgery. However, if diagnosed early, in an elective setting, surgery and endovascular treatment can offer successful management with few complications.

Srinvasan et al (1990) describe a 32-year-old patient with Marfan's syndrome who presented with acute abdominal pain and a clinical picture of hypovolaemic shock. An abdominal computed tomography scan showed a mass in front of the pancreas, the cause of which could not be explained. The patient underwent a laparotomy, during which he was found to have a ruptured middle colic artery aneurysm. He underwent a transverse colectomy with primary end–end anastomosis. He survived and had an uneventful postoperative recovery.

Goffi et al (2000) described an aneurysm of the jejunal branch of the superior mesenteric artery in a Marfan's syndrome patient. The patient had suffered blunt abdominal trauma which had caused a pre-existing aneurysm to rupture.

Santiago-Delpin et al (1972) described a 48-year-old Marfan's syndrome patient who presented with haematemesis and right upper abdominal pain. A subsequent angiogram revealed multiple intra-abdominal aneurysms. These were of the distal aorta, both renal arteries, hepatic artery, gastroduodenal artery and the superior and inferior mesenteric arteries. Following an unsuccessful graft repair, this patient died. This report was the first to describe multiple intra-abdominal aneurysms in relation to Marfan's syndrome.

These examples show the increased incidence of abdominal vasculature aneurysms in Marfan's syndrome. One should always consider the presence of an aneurysm in any Marfan's syndrome patient (or even one who is suspected to have Marfan's syndrome) who presents with abdominal symptoms, even in the young. Rapid treatment in these cases is often necessary to prevent the high mortality associated with ruptured intra-abdominal aneurysms. Certainly some form of cardiovascular screening would appear to be necessary for Marfan's syndrome patients, ultrasound and magnetic resonance imaging allows accurate images of the descending aorta, while echo studies of the aortic root are also vital (Lehmann, 1995).

Bowel obstruction

Various instances of bowel obstruction secondary to Marfan's syndrome have been described.

A case report by Atta et al (1999) described a 15-year-old man with Marfan's syndrome who presented with large bowel obstruction. During laparotomy he was found to have no hepatic suspensory ligaments with recurrent displacement of the liver to the left upper quadrant, and a mal-positioned transverse colon that was sited directly under the right hemi-diaphragm. There was also a congenital band across the distal transverse colon, contributing to his bowel obstruction. During the initial laparotomy the liver was replaced in its correct position and the band was divided. Several weeks later the patient developed an obstructed distal transverse colon. He underwent resection on the right colon, with the formation of an ileostomy. A subsequent ileo-colonic anastomosis was carried out. The patient had no further gastrointestinal complaints.

The case report from Clunie and Mason (1962) showed a 27-year-old man with Marfan's syndrome who presented with acute bowel obstruction. This was found to be secondary to a failure of rotation of the mid-gut loop, and a volvulus had developed. This volvulus was reduced at laparotomy, and the patient made an uneventful recovery

de Silva et al's (1996) case report showed a Marfan's syndrome patient who developed acute bowel obstruction at the age of 5 years. The cause of this was found to be secondary to a volvulus of the stomach. This volvulus was sucessfully reduced at laparotomy and the child made an uneventful recovery.

As mentioned later on, McLean et al (1985) stated that the Marfan's syndrome patient in their case report had markedly long caecal and sigmoid mesenteries. This abnormality causes hypermobility of bowel, which leads to an increased likelihood of developing acute bowel obstruction.

These cases all seem to indicate an increased incidence of bowel obstruction in Marfan's syndrome. There is a wide variation of causes, but the one thing that most have in common is an abnormal anatomical arrangement.

Abdominal visceral diverticulae

Diverticulosis is usually rare before the age of 30 years, but is seen in around one-third of those over 60 years old. In the Marfan's patient, these are far more common in patients in their 20s and 30s (U.S. Navy Aeromedical Reference and Waiver Guide, 2007).

Colonic diverticulae typically form in parallel rows between the taenia coli, because of weakness of the muscle wall at the sites of penetration of the vasa recta supplying the mucosa. In western populations these diverticula arise mostly in the left colon, with 90% of these patients having sigmoid involvement. Several factors are responsible for the formation of diverticulae; these are colonic wall resistance (hence early development of diverticulae in connective tissue disorders, such as Marfan's syndrome), disordered motility and lack of dietary fibre (Stollman and Raskin, 2004).

An Israeli case report described a woman aged 38 years who had Marfan's syndrome and presented with a thoracic aortic aneurysm. This aneurysm ruptured and the patient died. At post-mortem she was found to have extensive diverticulosis throughout her entire colon, which had appeared to be asymptomatic (Suster et al, 1984).

An interesting case report from the UK described three brothers, all of whom had Marfan's syndrome. They all presented with abdominal pain in their 20s that was related to either bowel obstruction or recurrent bilateral inguinal hernias. At laparotomy they were all

found to have incidental extensive diverticular disease involving the entire colon, and some of the jejunum and ileum. One of the brothers had also developed a distended bladder with multiple vesical diverticulae (with no causative urinary obstructive lesion seen) (Clunie and Mason, 1962).

A Sri Lankan case report described a 10-year-old boy with Marfan's syndrome who had presented with a lump in his right buttock that was reducible, and was accompanied by an urge to micturate. Following a pelvic ultrasound scan and then a cystogram, he was found to have a large bladder diverticulum that had herniated through the pelvic floor into the buttock. This was successfully repaired (de Silva et al, 1996).

An American case report described a 41-year-old man with Marfan's syndrome who presented with abdominal pain, and loose stools (with a background of hiatus hernia, and previous bilateral inguinal and femoral herniae repairs). After several investigations, an exploratory laparotomy was performed. He was found to have multiple large diverticulae throughout his jejunum, and a dilated and flaccid small and large bowel. The mesenteries were seen to be long and very mobile. He was diagnosed with bowel malabsorption as a result of bacterial overgrowth, secondary to the large jejunal diverticulae and hypotonic bowel. The patient was readmitted the following year with further abdominal pain. He went into hypovolaemic shock and died. At post-mortem he was found to have an infarcted ileum, secondary to torsion of the over-long small bowel mesentery (McLean et al, 1985).

These cases all highlight the increased incidence of visceral diverticulae in Marfan's syndrome. In a young Marfan's syndrome patient presenting with abdominal pain, one should always consider the presence of bowel diverticulosis and its possible complications as a cause of the presentation. There do not appear to be any guidelines for the follow up for diverticular disease in these patients.

These cases also show the presence of unusual abdominal viscera diverticulae, such as bladder diverticulae. This should be considered in the Marfan's syndrome patient presenting with urinary symptoms or unusual pelvic masses.

Diaphragmatic hernias and gastrointestinal symptoms

It is thought that hiatus hernias are more common in Marfan's syndrome, especially in children, although para-oesophageal hernias are much less common than sliding hiatus hernias (Parida et al, 1997). The increased incidence of diaphragmatic hernias is thought to be the result of the generalized connective tissue disorder weakening the diaphragmatic muscles (de Silva et al, 1996).

An American case report described a male infant with Marfan's syndrome, who presented with a upper gastrointestinal bleed secondary to severe gastro-oesophageal reflux. This was caused by a large hiatus and para-oesophageal hernia, with the para-oesophageal component positioned posteriorly and to the right of the gastro-oesophageal junction. The child also had bilateral inguinal hernias. These defects were all successfully repaired (Parida et al, 1997).

Diaphragmatic hernias in Marfan's syndrome can present later in life. Another American case report described a 22-year-old man with Marfan's syndrome, presenting with acute dyspnoea. This patient was also known to have aortic root dilatation, mitral valve prolapse, lens dislocation and scoliosis (all features of Marfan's syndrome). The initial chest radiograph was interpreted as a bacterial pneumonia. It was only after a repeat chest radiograph and a computed tomography scan of the thorax, that a large diaphragmatic defect was found. This defect had allowed bowel to herniate up into the thoracic cavity. This defect was closed uneventfully (Yetman et al, 2003).

An 11-year-old Sri Lankan girl with Marfan's syndrome developed acute bowel obstruction and dyspnoea. This was found to be secondary to a large left-sided diaphragmatic hernia. This was also associated with bilateral inguinal hernias. The patient died after attempted repair of the diaphragmatic hernia (de Silva et al, 1996).

These cases highlight the need to consider diaphragmatic hernias in the patient with Marfan's syndrome who presents with chest or abdominal symptoms (Yetman et al, 2003). There also appears to be some variability in the age range of these patients (from infancy to adulthood). These cases also show the possible co-existence of other general surgical problems, such as abdominal wall hernias, as well as the other features of Marfan's syndrome.

Abdominal wall hernias

Inguinal and incisional hernias are more common in Marfan's syndrome, and can be recurrent (Kashyap et al, 2004). How much more common is not clear. Recurrent incisional hernias are one of the minor diagnostic criteria, indicating organ system involvement (Aburawi et al, 2001). The increased incidence of these is likely to be the result of the generalized connective tissue weakness of Marfan's syndrome, affecting the integrity of the abdominal wall.

A French case report (Stoll, 2002) described a patient with a variant of Marfan's syndrome called Shprintzen–Goldberg Marfanoid syndrome. In this report the patient was found to have bilateral inguinal, and a diaphragmatic hernia, for which he was operated on twice as an infant. In this case there was no recurrence of the hernias after 24 years of follow up.

A Sri Lankan case report described a brother and sister who, among other clinical features of Marfan's syndrome, had bilateral inguinal hernias from infancy. The brother

underwent a successful repair, but the sister had recurrence of inguinal hernias. Following the initial repair when she was 2 years old, she required two further repairs during childhood (de Silva et al, 1996).

These cases highlight the need to consider the increased incidence of abdominal wall hernias in the Marfan's patient (even in the younger patient), and therefore also the increased likelihood of hernia-related complications (e.g. strangulated herniae). One must also consider the fact that there may well be multiple hernias present, and also that there is an increased likelihood of recurrence even after a seemingly successful repair.

Conclusions

This article highlights the broad range of rare, but potentially life-threatening general surgical complications that one must bear in mind when assessing a patient with Marfan's syndrome. It also shows how one must have a different list of differential diagnoses in mind when assessing the patient with Marfan's syndrome who has presented with abdominal pain. One must also remember the possibility of co-existing Marfan's syndrome-related pathology in other systems of the body. This highlights the need for more work into the incidence of these complications in the Marfan's syndrome patient.

This work also raises the question of whether a screening system to look for these general surgical complications would be of benefit to patients with Marfan's syndrome. Such a system would require an accurate, non-invasive imaging technique. Modern computed tomography angiography is a fast, high quality imaging modality able to detect the relevant aortic pathology (Yu et al, 2007). Magnetic resonance imaging and angiography can provide excellent visualization of affected vascular structures, while avoiding radiation exposure (Russo et al, 2006). BJHM

Conflict of interest: none.

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KEY POINTS

- Various general surgical pathologies can appear in patients with Marfan's syndrome.
- These would appear to often present atypically.
- One should have a broader range of differential diagnoses in mind when assessing a patient with Marfan's syndrome who has abdominal pain.
- More work is needed to assess the incidence of these pathologies, and to evaluate the use of a screening system to look for these problems.