Aorto-enteric fistulas: A physiopathological approach and computed tomography diagnosis

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\textbf{Abstract}  Infection of an abdominal aortic prosthesis with an enteroprosthetic fistula is a very serious, life-threatening complication, leading sometimes to severe functional consequences, the most serious being amputation. Since the symptoms, if there are any, are often rather non-specific, diagnosis is frequently difficult and has always to be based on a whole series of justifications. Early diagnosis is essential and this fistula should be the first possibility considered in a patient with an abdominal aortic prosthesis who is presenting rectorrhagia or melaena (even if only to a slight degree), sepsis and/or abdominal pain. Although rare, the clinical existence of hypertrophic osteoarthrophy may assist diagnosis. A CT scan is the examination of choice, the criteria providing evidence of a fistula being the presence of gaseous images in a periprosthetic fluid collection, thickening and/or retraction of the intestinal walls in contact, the existence of a false aneurysm, and finally, very rarely, extravasation of contrast agent into the intestinal lumen. The differential diagnoses that may mimic a fistula need to be well known, and can include retroperitoneal fibrosis, an infectious aneurysm, inflammatory or infectious aortitis, and above all, a ‘simple’ prosthesis infection without fistulisation.

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An aorto-enteric fistula may be primary or secondary. In the vast majority of cases, a primary fistula, the rarer (only 250 cases described in the literature [1]), complicates a pre-existing aneurysm. Secondary fistulas are far more common. They occur as a sequel to surgery for an abdominal aortic aneurysm with or without implantation of a prosthesis, more commonly during open surgery than when an endoprosthesis is implanted by the endovascular route. Infection of a synthetic prosthesis with an aorto-enteric (or entero-prosthetic) fistula is a serious complication. Its seriousness is related to the life-threatening consequences (mortality near 50%, and up to 100% if not treated), the functional

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consequences (amputation in 30% of cases), and to the underlying infection, itself correlated with the degree of involvement of the prosthesis and the anastomoses. These secondary fistulas may appear 2 weeks to more than 10 years after the surgery. The existence of an abdominal aortic prosthesis infection is sometimes even revealed by clinical signs of hypertrophic osteopathy, which need to be recognised. It must therefore be remembered from the outset that diagnosing an aorto-enteric fistula is difficult, but should always be the first possibility envisaged in a patient with an abdominal aortic prosthesis who presents even the slightest rectorrhagia or melaena, abdominal pain and/or sepsis.

Basic clinical facts

Infection of a vascular prosthesis is rare, involving between 0 and 6% of prostheses. Its frequency depends on the site of implantation: for a strictly intra-abdominal prosthesis, this is 0.4 to 0.7%. The risk increases as the femoral triangle is approached, and is greatest for axillofemoral bypasses, at 5 to 8%, firstly because some of the subjacent terrain has often been weakened, and secondly because this type of bypass is still one of the methods of treating aortic prosthesis infections. Early infections (less than 4 months after implantation) must be clearly distinguished, by their strange physiopathology, from late infections, which occur more commonly (70 to 85% of cases).

The clinical presentation of aorto-intestinal fistulas is very variable, with acute or chronic, massive or slight intestinal haemorrhage, and this diagnosis should also be considered when confronted with prolonged fever or abdominal or lumbar pain in a patient with an aorto-iliac or aortofemoral prosthesis. Brutal, massive haemorrhage is often preceded by more restricted episodes of bleeding (herald bleeds).

Therapeutic management needs to combine antibiotic therapy with a surgical procedure. Specific features are required of the antibiotic therapy, which may otherwise not be very effective due to the mass of fibrin and platelets, the poorly vascularised environment and the high bacterial inoculum protected by a biofilm (cf. Basic physiopathological facts): it is essential to associate two or three high dose antibiotics; in the case of an aorto-enteric fistula, it is necessary to cover anaerobic organisms; the length of treatment is at least 6 weeks IV, then 6 months oral administration (even for life, according to certain authors). Surgical treatment must observe the following rules:

• the extent of the infection must be precisely determined by dedicated imaging and, if necessary, by surgical exploration;
• the causal micro-organism must be identified;
• if one of the anastomoses is involved the infected prosthesis must be totally ablated.

Various surgical options can then be offered:

• total ablation of the prosthesis with implantation of an extra-anatomical bypass (in the same procedure or at a later time);
• simple ablation of the prosthesis with no revascularisation;
• replacement of the prosthesis in situ (using a polyester prosthesis impregnated with rifampicin, an allograft or autograft);
• retaining the prosthesis;
• finally, and extremely exceptionally, endovascular treatment [2–7].

Basic physiopathological facts

Abdominal aortic prosthesis infections

Intestinal commensal micro-organisms (anaerobic enterococci) are responsible for a major proportion of intra-abdominal infections. Staphylococcus epidermidis (and more and more frequently Staphylococcus aureus) is the prime offender as concerns aortofemoral reconstruction. Pseudomonas and other Gram negative bacilli are increasingly emerging. The time to appearance and the clinical aspects of prosthesis infection depends on the microorganism:

• in the event of early infection (< 4 months), the bacteria incriminated, such as S. aureus are very virulent. General and local signs of infection are considerable and cultures often positive. Gram negative bacilli (Pseudomonas and Proteus) may more rarely be the cause;
• later infections on the other hand are caused by much less virulent micro-organisms, capable of producing a biofilm (slime) protecting them against the body’s defences and antibiotics. They are nearly always caused by S. epidermidis. The biofilm is an organised system of layers of microbial cells and extracellular polymers on a surface. These micro-organisms therefore stay quiescent for a long time, and the infection develops gradually, possibly becoming symptomatic only months (or even years) after implantation. Enterobacteria can also cause late onset infections, in particular when there is an aorto-intestinal fistula or blood borne contamination [3].

Primary aorto-enteric fistula

A primary aorto-enteric fistula is a communication between the native aorta and an adjacent intestinal segment in a patient who has never undergone surgery or suffered prior trauma. It is usually a complication developing from an atheromatous aneurysm of the abdominal aorta. Much more rarely, it may be related to an infectious (‘mycotic’) aneurysm, vasculitis, tuberculosis or lastly, and historically, syphilitic aortitis [1,9–11].

Secondary aorto-enteric fistula

A secondary aorto-enteric fistula is a communication between the aorta and an adjacent intestinal segment in a patient who has previously had aortic surgery, with or without insertion of a prosthesis. It is generally the ultimate complication developing from a chronic aortic prostheses or endoprosthesis infection, which explains why abdominal prosthesis infections and aorto-enteric fistulas share many radiological signs and appearances and are often quite difficult to detect. In 80% of cases, the fistula
involves the third or fourth sections of the duodenum [12].

**Key points of imaging diagnosis**

Irrespective of the slice imaging method used, it should be remembered that the lack of a periprosthetic fluid collection or gas bubble does not mean there is no infection.

Oesophagogastroduodenoscopy is essential in all patients with an aorto-iliac or aortofemoral prosthesis presenting high intestinal haemorrhage for attempting to detect any erosion of the intestinal wall onto the prosthesis (which unfortunately is only very rarely seen, even with an endoscopic video-capsule), but especially for eliminating any other cause of bleeding (in particular a gastroduodenal (stress) ulcer or rupture of oesophageal varices). Colonoscopy may be useful in certain patients for the same reasons [13].

Ultrasoundography is not indicated in the detection of an aorto-enteric fistula, mainly because of the difficulty in identifying the presence of gas or a periprosthetic collection owing to the depth of exploration and the frequent parietal artefacts (obesity, ileus).

MRI does not reliably detect the presence of aortic extraluminal gas.

The CT scan is currently the most effective examination, therefore, with very variable sensitivity and specificity depending on the series (sensitivity of 40 to 90% and specificity of 33 to 100% for Vu et al. [14]), the rather low figures being probably partly related to poor recognition of the ‘finer’ signs of this pathology. The abdominal aortic acquisition protocol proposed consists of spiral scanning without contrast injection (collimation 0.625, thickness 2.5 mm, interval 2 mm), followed by acquisition in the arterial phase for bolus detection, then acquisition 80 seconds after injection (collimation 0.625, thickness 1.25 mm, interval 0.9 mm). Oral opacification is not recommended on a routine basis because it could mask slight extravasation of contrast agent from the aortic lumen towards the intestines.

The generalisation of early postoperative CT scans means it is necessary to be aware of certain physiological time periods: the time anticipated for a postoperative periprosthetic haematoma to disappear is 2 to 3 months, and for a periprosthetic gas bubble, 3 to 4 weeks. The radiologist should pay particular attention to the possible presence of surgical haemostatic gauze in the periprosthetic region (e.g. SURGICEL®), which, due to its very ‘aerated’ structural conformation, can mimic a fluid/gas collection in the CT scan; a simple consultation between radiologist and surgeon will dispel any doubts (Figs. 1–3).

It is very difficult in imaging—but crucial—to distinguish a simple prosthesis infection from an authentic fistula, because these two entities are intimately related. The criteria highly indicative of a fistula are: the presence of images of gas bubbles in a periprosthetic collection; thickening and/or retraction of the intestinal walls in contact (subject to sufficient distension of the lumen); the existence of a false aneurysm; extravasation of contrast agent into the intestinal lumen, which is extremely rare and pathognomonic of fistula, but lack of it must never be a reason for challenging the diagnosis of an aorto-enteric fistula [15–17] (Figs. 4–7).

Isotopic methods can sometimes help detect small amounts of occult intestinal bleeding [18]. Their principle is based on extravasation and accumulation of the tracer at the site of bleeding. Scintigraphy can be performed using two different tracers: technetium-labelled colloids and Tc-labelled red blood cells. Tc-labelled colloid scintigraphy is of limited use if the patient is bleeding intermittently, because less than 10% of the dose injected remains in the vascular compartment for more than 7 minutes. Moreover, rapid accumulation of technetium in the reticulo-endothelial system of the liver and spleen masks haemorrhages in the upper abdomen, and sometimes therefore of the abdominal aorta. For this reason it is preferable to use technetium-labelled red blood cells which have the advantage of remaining in the vascular compartment for longer. Consequently it is possible to obtain repeat images for up to 24 hours following injection, which increases the likelihood of detecting intestinal bleeding even if it is intermittent [19].

Red blood cells are labelled with technetium in the presence of stannous ions, which act as reducing agents, fixing the pertechnetate ion within the cell. The activity of the technetium injected is approximately 750 MBq. Initial dynamic acquisition is followed by delayed images every 30 or 60 minutes on the day of injection, and sometimes by late images for up to 24 hours. It is not necessary for the patient to be fasting. Active bleeding is seen by the appearance of a focus in an abnormal location, which moves over time. The site and appearance of the initial focus, its displacement, as well as the use of hybrid SPECT/CT techniques or oblique acquisitions, all help locate the bleeding. This localisation is approximate, especially in the small intestine, because the tracer is rapidly diffused due to intestinal peristalsis. The major disadvantage is that this examination is only positive in a period of bleeding. Scintigraphy must not be considered as a first-line examination, nor as an examination of last resort after repeating explorations that have all proved negative. It is an alternative to repeating the usual examinations and may guide other explorations or a surgical procedure towards the site of bleeding. Depending on the series, the sensitivity of scintigraphy ranges from 60 to 100% for intestinal haemorrhage [14] and the percentage of false localisations varies from 3 to 50% for old series [20,21]. Sensitivity depends on the intensity of the bleeding, which needs to be at least 0.5 mL/min for the examination to be clearly positive. This examination delivers an average whole body dose of 5 mSv [18,22,23].

A PET scan may also assist diagnosis [24], but there are a large number of false-positives, and the PET data always have to be considered in conjunction with the other biological and clinical parameters.

Finally, if in doubt, ultrasound or CT-guided aspiration of a periprosthetic fluid collection can confirm the infection and indicate the causal micro-organism.

**A special entity: hypertrophic osteoarthropathy**

The existence of hypertrophic osteoarthropathy (HOA) is sometimes an argument for infection of an aortic prosthesis and therefore for possible aorto-enteric fistulisation. It
Figure 1. Voluminous retroperitoneal collection on D2 of an aortobifemoral bypass. The presence of hyperdense areas within it (right arrow) indicates its being of blood; the gas bubbles (curved arrow) are unremarkable. All should disappear in a few weeks. Note the partial left renal infarction (arrowhead) secondary to reimplantation of the left renal artery on the prosthesis: a, b: axial contrast-enhanced CT scan slices; c: frontal oblique reformation.

Figure 2. Unenhanced CT scan. Periprosthetic aortic collection on postoperative D8. With purposely "pinched" windowing, the spontaneously hyperdense nature (arrow) of the collection confirms that it is just of blood.

Figure 3. Enhanced CT scan on postoperative D2. Considering the recent surgery, the presence of this periprosthetic collection (right arrow) and of gas bubbles within it (curved arrow) looks perfectly normal; there is no need to worry unless it has not disappeared in later follow-up examinations.
Figure 4. 70-year-old male patient, with no history of aortic surgery, admitted for rectorrhagia. Oesophagogastrroduodenoscopy shows ulceration of the 2nd section of the duodenum, with a purulent discharge but not of blood, initially treated with proton pump inhibitors. The CT scan has fortunately 'corrected' the diagnosis by revealing the existence of a typical primary aorto-enteric fistula, associating infiltration with a periaortic collection (arrowhead), containing small gas bubbles (right arrow), a false aneurysm (curved arrow), joining and retraction of the neighbouring 3rd section of the duodenum (asterisk). Drug treatment alone was naturally not sufficient.

Figure 5. The signs are sometimes more subtle: 70-year-old male patient with a history of aortobifemoral bypass, presenting rectorrhagia. A proximal anastomotic false aneurysm (curved arrow) can be seen associated with infiltration of the peripheral fat and joining of the jejunum (right arrow). The absence of gas bubbles does not rule out infection: a: axial contrast-enhanced CT scan slice; b: sagittal oblique reformation.
was described for the first time in 1889 by the German chemist Eugen von Bamberger and the French neurologist Pierre Marie, and combines clubbing of the digits, painful oedema of the limb affected, arthralgia and arthritis, and periostitis of the long bones.

Two categories are usually differentiated: primary HOA (hereditary or idiopathic, accounting for only 3 to 5% of cases), also known as pachydermoperiostosis, and more frequently occurring secondary HOA (secondary to a primary or secondary pulmonary tumour lesion, chronic pulmonary suppuration, a pleural tumour, a blood disease, a cyanotic congenital heart disease, inflammatory bowel disease, a chronic hepatic disease (primary biliary cirrhosis and other chronic active hepatic diseases), more rarely a carcinoma of the ENT region). In these cases, involvement is generally diffuse, bilateral and symmetrical.

Secondary forms of HOA confined to the lower extremities are very rare, and the major feature of the condition in this case is periostitis, clubbing of the digits being less common. These forms are described in patients presenting a patent ductus arteriosus with flow reversal, venous insufficiency or an aortic prosthesis infection (this is not related to the prosthetic material used [Dacron®, PTFE or other]). There are two theories as to the cause:

- the neurogenic theory, incriminating the autonomic nervous system (postulated because of a decrease in the symptoms after vagotomy);
- the humoral theory, currently favoured, based on observation of improvement in the clinical symptoms when the infected prosthesis is removed or blood flow within it interrupted. The chronic infection produces release by the platelet aggregates of platelet-derived growth factor (PDGF) into the arterial circulation distally of the infected prosthesis (if only one limb is affected, the unilateral distribution indicates the site of infection right from the ‘clinical’ stage as involving a particular prosthesis). PDGF is then metabolised in the extremities or in the pulmonary capillary bed; it stimulates mesenchymal cells, increases capillary permeability, and takes part in the inflammatory reaction with chemotaxis of monocytes and neutrophils. This ‘platelet’ theory does not, on the other hand, explain why bone involvement is limited to the periosteum. Other authors incriminate vascular endothelial growth factor (VEGF), which induces vascular hyperplasia, capillary hyperpermeability and new bone formation, and probably TGFβ.

The interval between implanting the prosthesis and the first clinical symptoms of HOA varies from a few months
to 10 years, which explains the frequent problems of diagnosis. The signs of infection may remain occult for a long time.

Imaging (standard X-ray, 99mTc-MDP bone scintigraphy, CT scan, MRI) shows the same signs as for the other forms of HOA (usually unilamellar, thin, diaphyseal/metaphyseal periostal apposition sparing the epiphysis, inflammation of soft tissues, joint effusion), but in HOA on a prosthesis infection the abnormalities are characteristically strictly confined to the anatomical region distal to the site of infection. Most often, only one limb is affected (Figs. 8 and 9).

The most commonly observed differential diagnoses of unilateral periostosis must always be contemplated: thyroid acropathy, inflammatory rheumatic disease, chronic osteomyelitis, a bone tumour lesion, bone infarction, chronic venous stasis, polyarteritis nodosa or Takayasu arteritis [25–27].

**Main differential diagnoses of aorto-enteric fistulas**

**Retroperitoneal fibrosis (RPF)**

Retroperitoneal fibrosis (RPF) causes retroperitoneal inflammatory and/or fibrous infiltration often sheathing the aorta, the inferior vena cava, the iliac axes and sometimes the ureters. It is generally a chronic process evolving in sudden outbreaks. It is sometimes idiopathic, but more often secondary, when there is then a large number and variety of aetiologies: malignant RPF, peripheral to an aortic aneurysm, associated with post-radiation, infectious, drug-induced (rye ergot derivative) vasculitis, etc. Unlike with an aorto-enteric fistula, this never causes periaortic gas, and as a rule, there is no anterior displacement of the aorta relative to the spine (Fig. 10).

**An infectious aneurysm**

An infectious aneurysm (formerly wrongly called ‘mycotic’) is also seen on a CT scan as an infiltration of the periaortic fat, possibly with the presence of a fluid or fluid/gas collection, associated with a generally sacciform aneurysm. There are sometimes signs of spondylitis, spondyloodiscitis or discitis of the adjacent vertebral segments. Only 50% of blood cultures are positive. Characteristically these infectious aneurysms generally show very rapid growth even on successive images that are only a few days apart. In these cases, all the CT data (at least the thoraco-abdominopelvic data) need to be meticulously analysed to look for precious aetiological signs (spondylitis or tuberculous spondyloodiscitis, septic visceral emboli due to infective endocarditis), but, as always, very special importance must
be attached above all to the patient’s medical history (Fig. 11).

**Inflammatory or infectious aortitis**

Inflammatory (in the case of major vessel vasculitis) or infectious (bacterial, viral or fungal) aortitis is only distinguished from the previous entity in that the aorta retains its normal, regular calibre. The CT signs are moreover identical. In inflammatory aortitis, they are often limited to subtle thickening of the aortic wall (sometimes associated with infiltration of the periaortic fat); it is then difficult to differentiate it from a simple non-calcified circumferential atheroma (Fig. 12). An 18-FDG PET scan may in this case greatly contribute to the diagnosis, by showing hypermetabolism of the aortic wall indicating aortitis, with good sensitivity and specificity (60 and 99.8% respectively), correlated with the rise in blood concentration of C reactive protein [28].
Figure 9. Pain in the right knee. History of aortobifemoral bypass 4 years previously. The standard X-rays show unilamellar periosteal apposition of the distal extremity of the two leg bones (a). 99mTc-MDP bone scintigraphy shows diffuse unilateral pericortical hyperfixation in the right leg (b). MRI shows periosteal apposition of the distal end of the right femur (c, black arrowheads) with knee-joint effusion. Hypertrophic osteoarthropathy secondary to infection of the abdominal prosthesis needed to be considered here, and was shown by the contrast-enhanced CT scan (d) as a periprosthetic fluid/gas collection, fistulated to the right psoas muscle: a: standard frontal X-ray of the right ankle; b: 99mTc-MDP bone scintigraphy, anterior surface; c: axial MRI of the distal extremity of the right femur; d: axial contrast-enhanced abdominopelvic CT scan.
Figure 10. Idiopathic retroperitoneal fibrosis. Periaortic retroperitoneal hypodense tissue infiltration (a, b, c, curved arrows), extending along the primary iliac arteries. Note that there is no anterior displacement of the aorta (a, right arrow). There is, of course, never any gas bubble in this infiltration. Favourable evolution after 1 month of corticosteroid therapy (d): a, b: axial contrast-enhanced CT scan slices; c: frontal oblique reformation; d: follow-up axial contrast-enhanced CT scan slice after 1 month of corticosteroid therapy.
Figure 11. Sacciform infectious false aneurysm of the abdominal aorta (right arrow) with small peripheral collection (arrowhead). Here, the presence of a left psoas-iliac muscle collection (curved arrow) and spondylodiscitis (asterisk) is characteristic of the tuberculous origin: a, c: axial contrast-enhanced CT scan slices; b: frontal oblique reformation; d: frontal oblique reformation centred on the spine.

Figure 12. Inflammatory aortitis in Takayasu arteritis. Uniform circumferential thickening, taking up contrast, of the wall of the thoracic (right arrow) and abdominal (curved arrow) aorta, which maintains its regular calibre. Differential diagnosis with a diffuse non-calcified atheroma is sometimes difficult; an 18-FDG PET scan should then be performed to help show possible hypermetabolism of the wall of the aorta in the case of aortitis: a: axial contrast-enhanced thoracic CT scan; b: axial contrast-enhanced abdominal CT scan.
Conclusion

It is quite difficult (and sometimes impossible) to differentiate between a 'simple' prosthesis infection and an authentic enteroprosthetic fistula. No sign, no additional examination taken in isolation is totally specific. Diagnosis of a fistula is sometimes easy if the clinical context suggests it (abundant rectorrhagia in a patient with an aortic prosthesis) and is associated with CT signs, which are complete and typical: a periprosthetic fluid/gas collection, thickening of the neighbouring intestinal wall, a false aneurysm. Elsewhere, the signs are confined to simple periprosthetic infiltration. The final diagnosis will almost always, therefore, be based on a series of justifications, and it is essential for all radiologists to be fully acquainted with the subtle signs of these, so as to be able to convince the sceptic vascular surgeon, who is often too optimistic when faced with the images.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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