

R E V I E W

MRI of perianal fistulas in Crohn's disease

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Summary. Perianal fistulas represent one of the most critical complications of Crohn's disease (CD). Management and treatment need a multidisciplinary approach with an accurate description of imaging findings. *Aim.* This study aspires to assess the significative role of Magnetic Resonance Imaging (MRI) in the study of perianal fistulas, secondary extensions, and abscess in patients with CD. Therefore it is essential to standardize an appropriate protocol of sequences that allow the correct evaluation of disease activity and complications. *Methods:* We selected and reviewed ten recent studies among the most recent ones present in literature exclusively about pelvic MRI imaging and features in CD. We excluded studies that weren't in the English language. *Conclusions:* MRI has a crucial role in the evaluation and detection of CD perianal fistulas because, thanks to its panoramic and multiplanar view, it gives excellent anatomic detail of the anal sphincters. Today MRI is the gold standard imaging technique for the evaluation of perianal fistulas, mainly because this technique shows higher concordance with surgical findings than does any other imaging evaluation. Surgical treatment is often required in the management of perianal fistula in patients with CD, which often have complex perineal findings. (www.actabiomedica.it)

Keywords: Magnetic Resonance Imaging, Crohn, Fistula in ano, Perianal disease.

Introduction

Perineal manifestation in patients with CD includes skin tags, hemorrhoids, anal fissures, rectal ulcers, perianal fistulas and abscesses (1).

The cumulative incidence of perianal fistulas in patients with Crohn's disease range is from 13% to 27% (2-4). The significant risk factors are the inflammatory colonic CD and the active rectal involvement (2-6). Still, the type of fistulas (simple or complicated) (Fig 1) and the presence of an abscess may influence the course of the disease. Complicated fistula is more often seen in CD (1), having one or more secondary tracts and abscess. The patient frequently refers peri-

anal swelling, fever, drainage of pus, or blood, and in a long time, also fecal incontinence may occur. For those reasons, it can be possible to develop also psychiatric diseases like anxiety and depression (7). The treatment is the same as the other CD locations and usually requires a combined surgical and medical approach.

Pathogenesis & Pathology

Currently, the central hypothesis about the origin of CD is represented by a disorder of the mucosal barrier that activates innate immunity in people with genetic predisposition and alteration of the microbiota

(8). After the initial trigger, there is massive recruitment of leukocyte and inappropriate stimulation of the immune system. Fistulas originate by an epithelial defect caused by inflammation whose repair is impaired because of the migratory potential of colonic lamina propria fibroblasts (9). Another hypothesis is represented by the migration of the intestinal epithelial cells and the transformation, lead by the TGF-Beta, into myofibroblasts. This process is called epithelial-to-mesenchymal transition. Another critical factor in the pathogenesis of CD is the up-regulation of the matrix metalloproteinases (MMP) such as MMP-9 and MMP-3.

Another hypothesis consists in the “cryptoglandular hypothesis”: anomalous drainage of the anal glands located within the intersphincteric space may start the inflammatory process, passing through a perianal

abscess acutely and a fistulous tract in a second time (87% of patients with an abscess may develop a fistula) (Fig 2) (10).

Available data indicate that CD-associated fistulas start from an epithelial defect that may be caused by ongoing inflammation. Often CD fistulas penetrate the gut wall surrounded by acute and chronic cells. Perianal fistulas in CD have a high grade of recurrence. In this regards, MRI has assumed a primary role over CT in the study of various district and pathologies, thanks to its high contrast resolution its excellent soft tissue contrast and multiplanar capability (11-16).

MRI imaging is the gold standard for the evaluation of perianal disease and allows us to classify fistula correctly to choose the type of treatment (9).

Classification of perianal fistulas

Incorrect classification and/or determination of extent increases the risk of incomplete healing, recurrent fistula, and inadvertent sphincter injury.

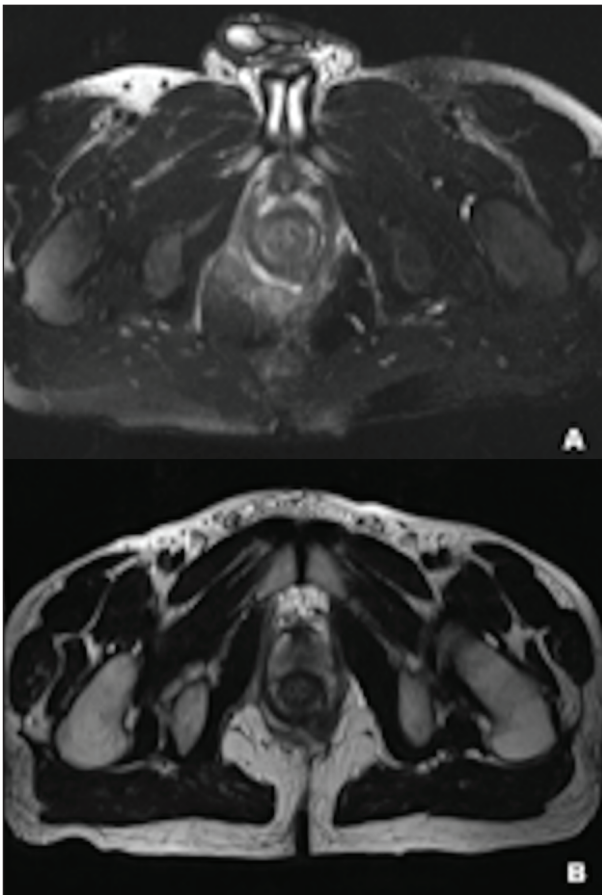


Figure 1 An oblique axial T2w fat-sat (a) and T2w (b) images show a complex transsphincteric fistulous tract with an “horseshoe” feature

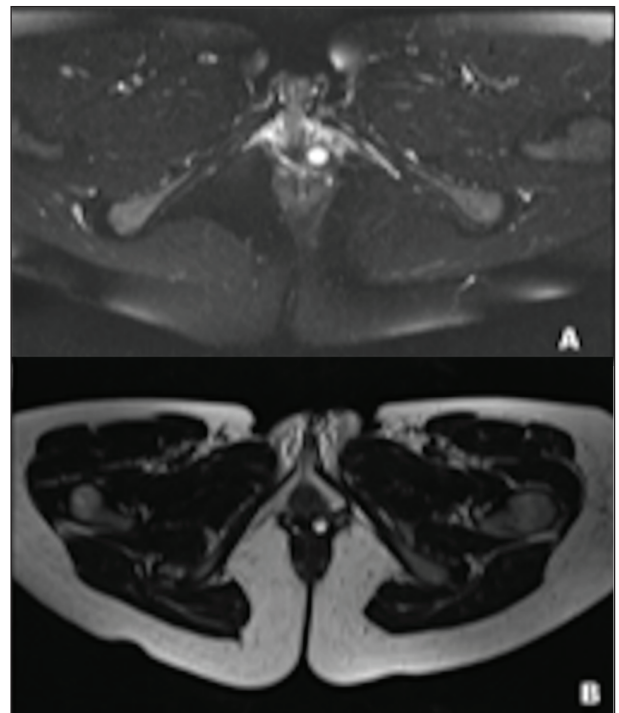


Figure 2 An oblique axial T2w fat sat (a) and T2w (b) images show an inflammatory collection at the level of the external anal sphincter

There are two main classification systems for perianal fistulas: Parks classification and St.James's University Hospital classification. Both are based on the relationship between the primary track and the sphincter muscles.

Parks classification gives central importance to the external sphincter and proposes a division into four groups:

- Intersphincteric fistulas involve only in the intersphincteric space and may reach the perianal skin through or medial to the subcutaneous external sphincter.
- Transsphincteric fistulas pass through the external sphincter into the ischio-rectal fossa.
- Suprasphincteric fistulas travel upward into the intersphincteric space, passes over the top of the puborectalis muscle, then descends through the levator plate to the ischio-rectal fossa and then to the skin.
- Extrasphincteric fistula travel outside the external sphincter space without touching the anal canal.

St.James's University Hospital classification has been composed of radiologists, giving an essential role to MRI imaging, especially to landmarks that can be seen in the axial plane. The classification is composed five grade for the fistulas:

- Grade 1: Simple linear intersphincteric fistula.
- Grade 2: Intersphincteric fistula with an abscess or secondary track.
- Grade 3: Transsphincteric fistula
- Grade 4: Transsphincteric fistula with an abscess or secondary track in the ischio-rectal or ischio-anal fossa.
- Grade 5: Supralevator and Translevator Disease (17).

MRI technique

Today MRI is the gold standard imaging technique for the evaluation of perianal fistulas, mainly because it shows higher concordance with surgical findings than does any other imaging evaluation (18).

It has a high-resolution contrast and, thanks to its panoramic and multiplanar view, it gives excellent anatomic detail of the anal sphincters. It has to be performed with body or phased-array coils and not require special preparation.

The imaging plans have to be oriented perpendicular (for the axial acquisition) and parallel (for the coronal acquisition) to the long axis of the anal canal to evaluate the source of the fistulous tract including all the levator plate and the entire perineum to identify areas of sepsis and infected tract that may lead to recurrence.

For transverse image, it's better to use FOV that should extend from L5 to the anus, and for the sagittal plane, it should include both acetabula (19).

First, the operator has to perform a TSE T2w in the sagittal plane, providing an overview of the pelvis and the anal canal. After that, the appropriate protocol consists in:

1. Oblique Axial T1w FSE
2. Oblique Axial T2w FSE
3. Oblique Axial and oblique coronal fat-suppressed T1w FSE with gadolinium-based contrast material.

The saturation of fat may be obtained either with short time inversion-recovery (STIR) or frequency-selective fat saturated T2-weighted FSE.

Three-dimension (3D) T2w TSE sequences can provide source data for post-processing reformation in any plane (17). Another new tool for the diagnosis of fistulas is the MR fistulography: it is based on the presence of the wall enhancement after the injection of contrast material with digital subtraction MR (17). It is a 3D T1w gradient-echo sequence with digital subtraction, and it appears useful in the diagnosis of fistulas.

Diffusion Imaging sequence DWI/ADC is used for the study of CD fistulas, particularly in patients unable to receive intravenous contrast material.

Dynamic contrast-enhanced MR imaging with 2D T1w sequences permit to create a time-signal intensity curve and the misuration of the volume of enhancing pixels (17).

Intravenous injection of gadolinium could be performed, especially in the first MR imaging assessment of perianal CD or in case of doubts in the precontrast sequences (20).

The last development of pelvic MRI consists of the possibility of use in clinical practice higher-field-strength MR with the 3.0 T imaging. A better signal-to-noise ratio can be used to allow decreasing imaging time and maximize spatial resolution with

a better chance of characterization of perianal fistulas (1). Therefore few papers are published about the use of 3T MRI for studying patients affected by CD. Some studies are focused on pediatric patients showing more accuracy for diagnosing IBD in children and can detect perianal disease (PAD) with high specificity and moderate sensitivity (21).

MRI findings

Three pelvic spaces are present at the level of the rectum: the peritoneal space, the supra levator, and the infralevator space, divided by the levator ani muscle. Perirectal fascia splits the supralevator space in perirectal (medial, containing fat) and pararectal (lateral, including connective tissue and ureters). The levator ani has a V-shaped aspect on the coronal plane and a linear hypointensity on the sagittal one (19).

The first sequences of the protocol have to be an unenhanced T1w image for an anatomy overview of the pelvis. We can identify the ischiorectal fossa, the levator plate, the sphincter complex. If there is a fistula, the T1w image shows the fistulous tract as an area of low/intermediate signal similar to the typical anatomical structures of the pelvis. An advantage of using T1W sequences is in the postoperative assessment because it's possible to see hemorrhage as areas with high signal intensity.

T2w before and after contrast-enhancement signal within the fistula correlate directly with the state of flogosis (22). Therefore T2w imaging, especially with fat suppression sequences, shows the active fistula and abscesses as areas with high signal instead of chronic fistulous tract, which have low signal both in T1w and T2w.

T1w imaging after the injection of gadolinium-based contrast material help to identify small lesion and secondary tracts, particularly in recent surgical intervention. With fat suppression, we can obtain a better visualization of the fistulous track both in T1w and T2w imaging and, in T1w images, the extensions and the relationship to the anal canal mainly to the external sphincter (1). Abscesses show a central area of low signal intensity due to pus and/or air that is surrounded by intense ring enhancement. In order to

avoid post-operative incontinence is helpful to establish a relationship between the primary track and the sphincter complex before treatment planning (22-24).

In another study it has been demonstrated that fistulae are more often present in patient with CD than in patients with hidradenitis suppurativa and they also communicate more often with anal sphincters. It is possible to make also a specific differential diagnosis searching features' predominance in perianal area, absence of rectal wall thickening and bilaterality of features that are more common in hidradenitis suppurativa (25).

It is also important to give information about the extension of fistulous tracts into the supralevator space because it may change the surgical treatment: if a fistula develops both under and above the levator ani muscle, it must be managed from both sides of it to be radical (19).

Medical Treatment

Patients suffering from Crohn's disease often experience perianal disease and have complex perianal sepsis requiring repeated treatments (11).

Today the treatment of perianal fistulas in patient with CD is based on combined medical and surgical therapy. First of all antibiotics, such as ciprofloxacin and/or metronidazole are used as first line. Remission and response with this antibiotics is reported in several studies. Antibiotics have also been studied as bridges or adjuvant therapy to immunomodulators or biologics. Recent European guidelines show that antibiotics therapy must be added both in medical and surgical treatment in order to avoid local sepsis and to maintain clinical response. Immunosuppressors such as 6-mercaptopurine and azathioprine are often proposed for treatment of luminal CD but they did not demonstrate significant efficacy in perianal disease (1).

Nowadays medical management of CD is based on anti-tumor necrosis factor alpha agents. The mechanism of action is unknown but it is proposed a probable down regulation of pro-inflammatory cytokine (26,27). The benefit of the treatment with infliximab, adalimumab and certolizumab pegol in the maintenance of remission is demonstrated in many studies.

Particularly, infliximab maintenance therapy prolongs the clinical response (1). According to the Italian group for the study of inflammatory bowel disease IG-IBD, anti-TNF should be used as the first choice of medical treatment in CD (28).

Surgical Treatment

Surgical treatment is often required in the management of perianal fistula.

Complex fistula need often a surgical approach. Initially, conservative sphincter-sparing techniques are preferred. However, because of the probable recurrence with these procedures these patients often need multiple interventions. Recurrence is usually due to infection that has gone undetected and untreated. In CD, the primary objective of initial surgery is the drainage of abscesses to control perianal sepsis in the least invasive way possible. The secondary aim of surgery performed at a later stage is to cure the fistula while preserving continence (1).

The placement of non-cutting setons combined with medical treatment is a right solution for the treatment of complex fistula or fistula involving a significant part of the anal sphincter. This approach has shown optimal results in several studies thanks to the closure of the external opening and the minimal risk of incontinence (1). Fistulotomy allow the healing by secondary intention. Still, this treatment is used for superficial intersphincteric or transphinteric fistula, so it is fit only for few patients with CD. Biomaterials like fibrin glue can be injected into the external opening of the fistula for the treatment of complex fistula to avoid fecal incontinence or recurrence. Ligation of the intersphincteric fistula tract (LIFT) is a new surgical approach that consists of a ligature of the intersphincteric tract close to the internal opening removing all the granulation tissue. Video-assisted anal fistula treatment is another minimally invasive sphincter-sparing technique, but it needs no perineal wound.

Other surgical options are represented by a rectal mucosal advancement flap or a curvilinear flap made with mucosa, submucosa, and sometimes the muscle may be considered when sphincter function could be lost by fistulotomy (1).

When conservative therapies are not possible, fecal diversion is required packing a loop ileostomy .

An Italian group studied the use of autologous bone marrow-derived mesenchymal stromal cells and report a feasible, safe, and beneficial therapy in refractory cases (29).

Conclusions

Today pelvic MRI is the gold standard for the evaluation and quantification of perianal disease in patients with CD. Classification systems such as Parks and St James ones help the choice of the best surgical treatment and the assessment of the activity of the fistula. Thanks to MRI imaging is possible to assess the timing of the surgery accurately. Radiologists have to be familiar with perianal CD findings and complications for the central role of MRI in the management of these patients.

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