

Perianal Fistulizing Crohn's disease: imaging modalities and therapeutic challenges

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SUMMARY

Perianal involvement in Crohn's disease is not infrequent. Risk factors for the development of fistulas include a high activity of CD, a fibrostenotic phenotype, genetic markers such as the HLA-DRB1 allele and certain mutations of the genes including NOD2. In perianal CD the treatment should be multidisciplinary. The best outcomes have been achieved when medical and surgical therapies-if needed- are used in conjunction. Therapy of perianal fistulizing CD traditionally includes the use of immunosuppressants and has been significantly modified after the introduction of biologicals.

Key words: magnetic resonance imaging, infliximab, perianal fistula, fistulizing Crohn's disease, inflammatory bowel disease, fistula healing.

1. PERIANAL FISTULIZING CD

Epidemiology and clinical characteristics

The incidence of perianal involvement in Crohn's disease (CD) has been reported to be as low as 3.8 per cent and as high as 80 per cent.¹ Risk factors for the development of fistulas include a high activity of CD, a fibrostenotic phenotype, genetic markers such as the HLA-DRB1 allele and certain mutations of the genes encoding TNF- α , tumor necrosis factor receptor superfamily member 1B and NOD2.²

It seems that the incidence of perianal disease increases the more distal the involvement of the gastrointestinal

tract. Thus, rectal disease increases the incidence of fistula with a predisposition to high anal fistula. In addition, it has been shown that the time elapsing between intestinal disease and perianal involvement was shorter for colonic than for ileal disease.

The trans-sphincteric is the commonest type of fistula while rectovaginal fistulas have been reported to occur in 5.2-10 per cent of patients and most are low or even anovaginal. Fistulas after ileal pouch surgery tend to occur in patients who originally had their pouch formed for indeterminate colitis.¹

Natural history

One particular problem in the management of perianal CD is that its natural history is difficult to predict. Fistulas rarely heal spontaneously and often relapse after surgical therapy. As a generalization, complex anal fistulas, deep cavitating ulcers and dense anorectal strictures tend to carry a poor prognosis. Perianal CD in the absence of rectal inflammation has a better outcome than disease associated with rectal inflammation.¹

A prospective evaluation of the clinical course of perianal fistulas in 90 patients showed that the risks of recurrent fistula activity were 48%, at 1 year and 59% at 2 years. Fistulas were healed in 51% of patients after 2 years but reopened in 44% of them within 18 months of healing.³

Another characteristic feature of perianal CD is that

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Abbreviations:

CD=Crohn's disease
CT=computer tomography
EUS=endoscopic ultrasound
EAUS=endoanal ultrasound
EUA=examination under anaesthesia
IFX=infliximab
MRI=magnetic resonance imaging
PAUS=perianal ultrasound

several abnormalities may coexist. The more complex the fistula tract, the higher the incidence of abscess formation. Finally, the overall incidence of carcinoma arising from fistulous tracts has been reported up to 0.7 per cent in CD patients.¹

2. CLASSIFICATION SYSTEMS IN PERIANAL DISEASE

The simplest system is to divide fistulas into either low or high, depending on their relationship to the dentate line. Patients may also be stratified into one of three groups: simple fistulas and no proctitis, simple fistulas and concomitant proctitis and complex fistulas.⁴

The most anatomically precise fistula classification system is Parks' classification.⁵ This system uses the external sphincter as a central point of reference and describes five types of perianal fistula: inter-sphincteric, trans-sphincteric, supra-sphincteric, extra-sphincteric, and superficial. Although Parks' system is the most accurate method of describing fistula anatomy it has several limitations including the failure to identify other perianal manifestations such as skin tags, anal strictures or abscesses. In addition, connections with vagina and bladder, although important, are not part of this classification.

The American Gastroenterological Association technical review on perianal CD⁶ proposes a more clinically relevant approach to the classification of perianal manifestations. This classification recommended the division of fistulas into either simple or complex. A *simple fistula* is a low one (superficial, low inter- or trans-sphincteric) with only one external opening, and it is neither associated with an abscess nor connected to an adjacent structure, while there is no active rectal inflammation on endoscopy. In contrast a *complex fistula* is characterized by at least one of the following features: location above the dentate line (high inter- or trans-sphincteric, extrasphincteric & suprasphincteric fistula), multiple external openings, association with a perianal abscess, concomitant active rectal inflammation and connection to an adjacent structure such as the vagina or bladder. This is a clinically important distinction because several studies have shown better outcomes for patients with "simple" fistula types.

With the widespread use of MRI in clinical practice it became necessary that an MRI-based scoring system should be integrated into currently used clinical classification systems. An MRI-based score of perianal CD severity has been developed (Table 1) using both criteria of local extension of fistulas (complexity, supralelevatoric extension, relation to the sphincters) and of active inflam-

Table 1. MRI-based score for severity of perianal Crohn's disease according to Van Assche et al (Am J Gastroenterol 2003; 98:332-9).

SCORE PARAMETERS	SCORING (max=22)
Number of fistula tracts	
None	0
Single, unbranched	1
Single, branched	2
Multiple	3
Location	
Extra- or intersphincteric	1
Transsphincteric	2
Suprasphincteric	3
Extension	
Infralevatoric	1
Supralelevatoric	2
Hyperintensity on T2-weighted images	
Absent	0
Mild	4
Pronounced	8
Collections (cavities>3mm diameter)	
Absent	0
Present	4
Rectal wall involvement	
Normal	0
Thickened	2

mation (T2 hypersensitivity in MRI images, presence of cavities/abscesses, and rectal wall involvement). The MRI score was reliable in assessing the fistula tracts with a good inter-observer concordance.⁷

Another interesting MRI-based classification is the Freiburg University Hospital MR-classification of anal fistulas and abscesses which refers to both Parks and St James University Hospital classification.⁸

3. THERAPEUTIC CHALLENGES IN PERIANAL FISTULIZING CD

Several studies in CD have demonstrated that failure to recognize occult lesions such as abscesses or fistula branches can result in recurrent fistulas or abscesses and/or can convert a simple fistula into a complex fistulizing process. The cornerstone of this approach is to fully define disease extension and behavior before any kind of therapy. Thus, perianal disease process should first be fully delineated with endoscopy and a radiological technique before treatment is begun.⁴

In perianal CD the treatment should be multidisciplinary. The best outcomes have been achieved when med-

ical and surgical therapies-if needed- are used in conjunction. Several observational studies have highlighted the benefit of this type of multidisciplinary approach. Treatment of perianal fistulizing CD must be individualized for each patient on the basis of the type of fistula present (simple or complex), the degree of rectal inflammation present and the severity of symptoms.

Therapy of perianal fistulizing CD traditionally includes the use of immunosuppressants (azathioprine, methotrexate) and has been significantly modified after the introduction of Infliximab.

Surgery has usually been limited to laying open low inter-sphincteric fistula and drainage of abscesses. The recent trend in surgery has been to be more aggressive in the management of abscesses and fistula than was previously recommended. This includes long term drainage with loop catheters and seton drainage as well as fistulotomy.⁹ Prior examination with anesthesia with placement of non-cutting or draining seton sutures in fistula tracts may be also a useful adjunct in many patients. More aggressive surgery may however, result in more fistulas or in damage to the anal sphincter and unacceptable incontinence. Severe unremitting disease can in extremis be improved only by stomas or abdomino-perineal excision.¹⁰

4. EFFECTS OF IFX IN PERIANAL CD

Currently immunosuppressives combined or not with IFX represent one of the best treatment options for fistulizing CD with 20-70% healing rates¹¹⁻²⁸ also including pediatric cases.²⁹

Although the clinical efficacy of IFX as measured by closure of fistulas in Crohn's disease has been widely demonstrated, its influence on the inflammatory changes in the fistula tracks is less clear.

The main message of the imaging studies is that even though fistulas clinically may have healed in the short term with IFX, they may persist radiographically and long term IFX treatment may be required to completely heal fistulous tracts as assessed by ultrasound or MRI. The radiographic persistence of fistulas might explain early relapse after induction IFX therapy alone.³⁰

Examination under anesthesia (EUA) with selective seton placement and maintenance immunosuppressives is one of the traditional methods to treat perianal fistulas.³¹ A study with 32 perianal fistulizing CD who had at least 3 month follow-up after the third dose of IFX showed that patients who underwent an EUA and seton placement before IFX treatment had a better initial response (100% vs

82.6), lower recurrence rate (44% vs 79%) and longer time to recurrence (13.5 months vs 3.6 months) compared with those receiving IFX alone. The seton was usually removed 2-4 weeks after the second infusion of IFX. However, according to the authors it remains obscure which patients would benefit from an EUA and seton and what the results would be in the setting of maintenance IFX therapy.³²

Finally, the successful use of IFX for the closure of pouch vaginal fistulas has been also suggested. However there is no large prospective trial on the use of IFX in chronic pouchitis.³³

5. DIAGNOSING PERIANAL FISTULIZING CD: WHICH ARE OUR OPTIONS?

The initial assessment with clinical inspection followed by digital examination is not always accurate because perianal CD leads to pain, induration and scarring, and thus, manual examination even by experienced physicians is not always the best descriptive method of the perianal involvement. Examination under anesthesia has been regarded as a gold standard for perianal CD evaluation; however it still has limitations such as missing many abscesses and mislocating fistula tracts. Perioperative assessment seems the ultimate modality to assess perianal disease extension but it is more than obvious that no surgeon dares to operate a patient with pelvic CD blindly, without a previous imaging technique.³⁴

Endoscopic examination, contrast liquid enemas, catheterization of a fistula tract with thin catheters, fistulography with methylene blue or fistulography with contrast materials (gastrographin or barium) are classical and widely accepted traditional methods of fistula detection and identification.

The role of cross-sectional imaging in the diagnosis of pelvic CD has expanded with recent technologic advances helping to characterize altered bowel segments as well as luminal lesions.³⁵ Virtual endoscopy based on CT scans of the bowel is feasible based on high resolution CT but still is on a rather investigational level.³⁶

MRI imaging

MRI allows the evaluation of the whole pelvic region³⁷ and is useful for the demonstration and evaluation of pelvic and abdominal sinus tracts or fistulae associated with Crohn's disease.³⁸ Scans can involve use of body coils, phased-array multicoils or endoanal coil.³⁹

MRI can detect the most relevant findings in perianal CD with accuracy sometimes superior to that of conventional radiology.⁴⁰ Furthermore, MRI can identify clini-

cally silent sepsis as fistulas may persist despite clinical remission in many cases.¹¹ Additionally, MRI allows evaluation of anovaginal fistulas and additional abnormalities, such as abscesses within the rectovaginal septum, secondary perianal fistula tracts, and sphincter damage.⁴¹

In a case of an epidural abscess complicating CD in which a pelvic CT delineated the perirectal fistula tract but was unable to detect the abscess, MRI of the pelvis made the final diagnosis. According to the authors MRI of the pelvis must be considered when perirectal fistulization to the spine is suspected.⁴²

MRI preoperative evaluation may also reduce the risk of procedure-dependent complications. However, this can be reliably established only with a prospective randomized trial of patients who undergo surgery after undergoing preoperative MRI and those who undergo surgery without undergoing preoperative MR imaging.⁴¹

To summarize, the MRI examination in perianal CD allows the analysis of: 1. the location of the fistula tracts according to Parks' classification, 2. the location of the internal opening(s) 3. the location of the external opening(s), 4. the location of deep abscess(es), 5. the long distance extension(s), 6. the state of the ano-rectal wall and the perirectal spaces, and 7. the damages of the anal sphincter.⁴³

Ultrasound imaging

Endoanal ultrasound (EAUS)

EAUS has been suggested as a very reliable and cost effective method for perianal CD assessment. One general limitation of all ultrasound imaging protocols is the motion and the experience of the examiner.

A prospective study of 22 CD patients with EAUS, MRI and operative assessment showed that EAUS with linear probe was more accurate than MRI in detecting anorectal abscesses and complicated fistulas.⁴⁴ However, the use of a rigid endoanal ultrasound (EAUS) probe can

be painful or even impossible in patients with inflammatory perianal disease due to anal stenosis. Furthermore, EAUS does not allow the assessment of pathological changes extending to the gluteal region.³⁷

Perianal ultrasound (PAUS)

Perianal ultrasound (PAUS) combines the high resolution and real time capabilities of EAUS and the panoramic view generated by MRI. In addition PAUS requires no special preparation. PAUS is as effective as MRI in the detection of perianal fistulae and it has been suggested that the detection of air bubbles within a fistulous tract can clearly indicate active fistulae.³⁷ Additionally, anal wall thickness can be measured by PAUS, as it has been shown to be increased in patients with perineal CD and may reflect disease activity.⁹

6. COMPARING IMAGING MODALITIES IN PERIANAL FISTULIZING CD (TABLE 2)

The major advantages of MRI over EAUS are the multi-planar capacity which allows examination in surgically relevant planes and the high inherent contrast resolution, which highlights tracks and abscesses. Furthermore, MRI has not field limitations and can depict certain areas which are not sufficiently shown during EAUS or during clinical examination.¹¹

MRI findings also prompted useful changes in classifications and permitted supposed supralevator extensions to be drained when other type of imaging established them as ischio-rectal.⁴⁵

There is still debate regarding the role of EAUS and MRI in the assessment of fistulae. However, most of studies suggest that MRI is the investigation of choice at least for complex perianal disease, despite its higher cost.¹ Furthermore, it can be used as a predictor of success following fistula surgery and can predict recurrence of fistu-

Table 2. Comparison between pelvic magnetic resonance imaging and endoanal/perianal ultrasound.

Parameter	MRI	EAUS/PAUS
Cost	More	less
Real time	No	Yes
Extended pelvic area inspection	Yes	No
Dental line differentiation	No	Yes
Detection of fistulization to spine	Yes	No
Detection of short perianal fistula	Less probable	More probable
Detection of activity of fistula	probable	probable
Concomitant bowel information	More probable	Less probable
High detective power	Less probable	More probable

la. In pediatric perianal CD cases MRI can be extremely helpful.⁴⁶

According to one study⁴⁷ MRI is superior to ultrasound in the localization of affected bowel segments and in recognizing stenoses and abscesses in pelvic area. Authors suggest that MRI of the pelvis should be obtained to clarify discrepant clinical and sonographic patients and despite its higher cost, MRI of the pelvis is justified in patients in whom CD lesions are located highly in the pelvis.

MRI has some limitations. It lacks the real time capacity of ultrasound and the

high resolution of high frequency linear ultrasound probes.⁴⁷ MRI cannot identify the dental line as a discrete anatomical structure. In that case suprasphincteric fistulas may be classified on MRI as extrasphincteric, for example. MRI also has problems with some superficial, epithelialized, or well drained tracks or short perianal fistulae which are obvious on clinical inspection.⁴⁸

7. WHICH IS THE GOLD STANDARD DIAGNOSTIC MODALITY FOR PELVIC CD?

Studies comparing new techniques for investigation of perianal fistulas have used surgical exploration or examination under anesthesia (EUA) as the gold standard. However, it became apparent that surgery or EUA miss some fistulas. In fact, in a study of 36 patients with a clinical diagnosis of anal fistula or abscesses which were scheduled for surgical exploration and were preoperatively imaged with high resolution MR-fistulography, MRI was generally more efficacious compared to surgery in abscess and fistula detection. In detail, six fistulas were described in MRI and only one fistula was seen in surgery while a total of 27 abscesses were detected with MRI compared to 22 during surgery. Complete agreement between MRI and surgery occurred in 89% of patients. The 11% of patients in whom procedures disagreed had complex sepsis with multiple fistulas and/or abscesses.⁸

Examination under anesthesia (EUA) can misclassify up to 10% of patients with perianal fistulas leading to poor outcomes. This accuracy can be improved up to 100% with the addition of either MRI or EAUS. A study in 34 patients with suspected Crohn's perianal fistulas which blindly compared the accuracy of MRI, EAUS and examination under anesthesia, showed that all three methods demonstrated good agreement. Furthermore, a combination of any of the imaging modalities with EUA provided 100% accuracy.³⁴

In 16 patients with perianal CD, flexible sigmoidoscopy and examination under anesthesia (EUA) showed close correlation with MRI findings. There was only one false examination in a patient with colovesical fistula.⁴⁹

It seems that it is nowadays recommended that either EAUS or MRI should be performed in addition to EUA for patients with pain, fluctuation, or stricture on digital examination because EUA misclassifies fistulas in a small percentage of patients, and an inadvertent fistulotomy for a high fistula might result in fecal incontinence.³⁰

The benefits of image-guided surgery are now self-evident and patients must decide for themselves whether to accept a small risk of unnecessary exploration in exchange of a much better chance of cure.

It should be here, however emphasized that in perianal CD a good clinical inspection combined with digital examination when feasible as well as classical fistulography are of great importance for patient initial assessment and further investigational planning. MRI seems a promising diagnostic modality⁵⁰⁻⁵⁵ complementary to EAUS and classical radiologic methods such as fistulography. We believe that a strategic planning including all imaging modalities available in each center is of great importance in the treatment of perianal fistulizing Crohn's disease.

A common language for radiologists, gastroenterologists and surgeons must guarantee the greatest benefit for CD patients with perianal complications.

8. OUR EXPERIENCE WITH PERIANAL FISTULIZING CROHN'S DISEASE

In our Department we have been evaluating patients with perianal involvement of CD with a combination of traditional and modern imaging methods. Each patient with a clinical suspicion of perianal sepsis first undergoes a thorough perianal inspection, palpation and digital examination in order to acquire a general clinical orientation. In the case of an obvious external orifice, we normally schedule flexible sigmoidoscopy and a fluoroscopic fistulography. During the first procedure we assess the degree of mucosal inflammation and use H₂O₂ instillation through a 23G plastic I.V. catheter via the external opening to detect a possible rectal opening. During the latter procedure (Figure 1) we slowly instill up to 15 ml of a diluted iodine-based contrast through a 23G cannula, tightly supported by a gauge in order to avoid leakage artifacts and take posteroanterior and profile radiographs. In the case of obvious superficial fluctuation of the gluteal region we initiate antibiotic therapy followed by local in-



Figure 1. Fluoroscopic fistulography in a male patient 26 years old with an anterior complex fistula with 2 branching secondary tracts.

cision and drainage.

During the last 9 years we have incorporated body coil pelvic MRI in the evaluation of our patients, usually implementing a combination of the following sequences: T1-weighted, T1-Spir with gadolinium enhancement, T2-TSE with fat suppression, in the transverse, coronal and sagittal planes. Different sequences provide different and complementary clinical data (anatomic delineation of the sphincter complex, inflammatory activity of the fistulous tract, suppurative collection enhancement).

During the last 4 years we have introduced the advent of EAUS and rectal EUS in the evaluation of our patients. We use a BK Medical 7,5-10 MHz mechanically rotating transducer and all the examinations are performed by AP. Patients are usually prepared with a Fleet enema and examined in the left lateral position, using H₂O₂ whenever feasible. We have found this method extremely useful as it is readily accessible, quick (mean time 15 minutes), reproducible whenever needed for a proper follow-up, cheap and with immediate results. From our experience EAUS is generally well tolerated with the exception of large perianal abscesses and few patients with pouch-associated sepsis, while EUS could be less well tolerated in cases of stenosis or active anorectal inflammation. The provided information proved valuable, involving anatomic sepsis classification, recognition of blind, accessory and clinically unexpected tracts, evaluation of inter-

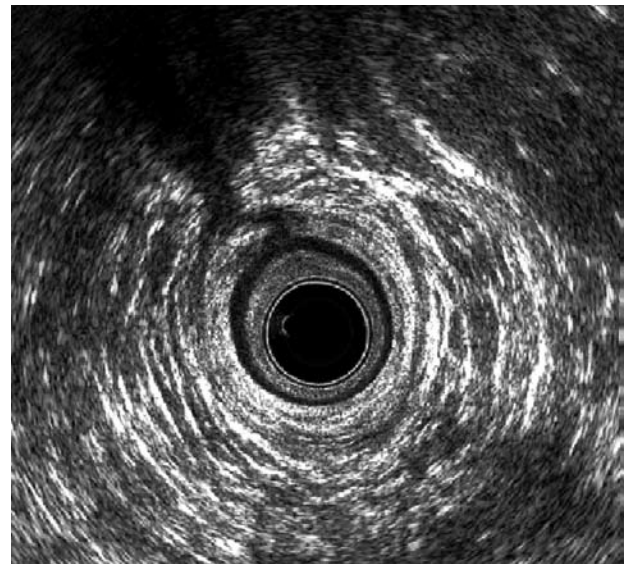


Figure 2. Ischiorectal collection and transsphincteric fistula (11 o'clock) in a young male patient with recurrent perianal sepsis due to CD

nal anal oss, evaluation of therapy response and sphincter integrity (Figure 2).

All the abovementioned modalities supplemented by the directed use of modern biological therapies and a good feedback with the local surgical department (collection drainage and loose seton placement) have provided our patients with a more rational and efficient care standard.

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