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Transperineal ultrasonography: first level exam in IBD patients with perianal disease

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Abstract

**Background:** A pelvic MRI represents the front-line method for evaluating perianal disease in patients with IBD. Recently, transperineal ultrasonography (TPUS) has been proposed as a simple, safe, time-sparing and useful diagnostic technique to assess different pathological conditions of the pelvic floor.

**Aim:** The aim of this prospective single centre study was to evaluate the accuracy of TPUS versus MRI for the detection and classification of perineal disease in IBD patients.

**Methods:** From November 2013 to November 2014, 28 IBD patients underwent either TPUS or MRI. Fistulae and abscesses were classified according to Parks’ and AGA’s classification methods. A concordance was assessed by k statistics.

**Results:** Overall, 33 fistulae and 8 abscesses were recognized by TPUS (30 and 7 by MRI, respectively). The agreement between TPUS and MRI was 75% according to Parks’ classification (k = 0.67) and 86% according to AGA classification (k = 0.83), while it was 36% (k = 0.34) for classifying abscesses.

**Conclusions:** TPUS proved to be as accurate as MRI for detecting superficial and small abscesses and for classifying perianal disease. Both examinations may be performed at the initial presentation of the patient, but TPUS is a cheaper, time-sparing procedure. The optimal use of TPUS might be in follow-up patients.

**Keyword:** transperineal ultrasound; perineal disease; inflammatory bowel disease
Introduction

Inflammatory bowel diseases (IBDs) are chronic inflammatory disorders of the gastrointestinal tract and are mainly constituted of Crohn's disease (CD) and ulcerative colitis (UC). Currently, their incidence is increasing\(^1\). Although the precise pathogenetic mechanisms underlying the development of IBD have not yet been fully elucidated, it is widely accepted that the two conditions stem from an inappropriate response of the gastrointestinal mucosal immune system to antigens that are normally present in the intestinal lumen and more specifically, to antigens derived from either ingested food or intestinal bacteria\(^2\).

Perianal disease is generally found in association with CD and represents one of the classic criteria originally outlined by Lennard-Jones as capable of differentiating CD from UC\(^3\). The reported incidence of perianal CD varies from 25 to 80\(^%\)\(^4\). The disparity in prevalence rates is, in part, because of differences in definition. Some series include only patients who have been surgically treated; others include all patients with perianal manifestations, such as skin tags, haemorrhoids, and anal fissures\(^5, 6\). To date, we know very little about perianal disease associated with UC. The true incidence of perianal disease in patients with UC is not available; in the original study, a prevalence ranging from 20 to 25\(^%\) was reported\(^7\), whereas a recent study claims a rate lower than 5\(^%\)\(^8\).

A thorough assessment of the perianal pathology is the cornerstone for a successful outcome in disease treatment. Several classification systems for perianal fistulae have been described; the most established one is Parks' classification system\(^9\). Parks classified fistulae in relation to the external anal sphincter; four fistula types were described including intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric. However, this classification takes into account neither superficial fistulae nor rectovaginal fistulae and is difficult to use in clinical practice. For this reason, a new classification was proposed in 2003 by the AGA Technical Review Panel\(^10\); the system provides a simplified, more
clinically relevant approach to perianal fistulae that were classified as either simple or complex. A simple fistula is low (superficial, or with a low intersphincteric or transsphincteric origin of the fistula tract), has a single external opening, and has no undrained perianal abscess. Conversely, a complex fistula is high (with a high intersphincteric or transsphincteric or extrasphincteric or suprasphincteric origin of the fistula tract), may have multiple external openings, may be associated with a perianal abscess, may be associated with fistulae to adjacent organs, may be associated with the presence of an anorectal stricture, and may be associated with the presence of active rectal disease. This classification also proved to have a high prognostic value because patients with simple fistulae may be treated less aggressively and may have a better outcome than those with complex tracts\textsuperscript{11}.

For this reason, it becomes very important to accurately classify perianal disease. The latest ECCO guidelines recommend performing surgical exploration under general anaesthesia (EUA). Among the non-invasive tests, pelvic MRI and endoscopic rectal ultrasound (EUS) play a pivotal role\textsuperscript{12}. Although MRI and EUS provide the treating physician with a precise definition about the nature of the perianal disease, allowing correct classification of the fistula and appropriate management decisions, both methods require experienced and dedicated staff and are not always available. Moreover, MRI is contraindicated in patients with cardiac pacemakers or claustrophobia, while EUS is difficult to perform in patients with anal stenosis or tenderness in the involved areas. Finally, both methods are cumbersome in paediatric patients who generally require the examination to occur under general anaesthesia.

TPUS has been developed over the past years as an alternative to conventional radiological and endoscopic techniques for evaluating various pathological conditions of the pelvic floor, including perianal disease\textsuperscript{13-15}. TPUS is a simple, painless, and cheap method that compares favourably to MRI, computed tomography (CT) and EUS\textsuperscript{16,17}. The
Technique is well accepted by patients and is carried out with conventional ultrasound systems that require a relatively short amount of training for the operators to be proficient. Moreover, as a real-time method, a TPUS examination might be particularly useful in patient follow up because it may provide physicians with relevant information about completeness of perianal abscesses and/or the correct positioning of a surgically positioned drain. Finally, TPUS could allow the clinician to monitor the response to medical therapy during periodic follow-up visits\textsuperscript{13, 18, 19}.

To date, the usefulness of this technique in IBD patients with perianal disease is still unclear\textsuperscript{13, 14, 16-25}. The aim of this study was to evaluate whether TPUS is accurate in detecting and classifying perianal disease.

**Patients and Methods**

All IBD patients with a firm diagnosis or clinical suspicion of perianal fistulae or abscesses who were consecutively referred to our Institution from November 2013 to December 2014 were included in the study. Patients with previous (less than six months) MRI or EUS examinations or recent (less than 1 month) surgery for perianal disease were excluded. However, in the present study, only patients with perianal fistulae and abscesses were enrolled because physical examination with visual inspection or anoscopy is generally able to recognize skin tags, haemorrhoids, and anal fissures.

All patients underwent MRI and TPUS. During the elapsed time between the MRI and TPUS, no medical treatment (except antibiotics for abscess) was started to avoid any interference with the analysis of the results. All MRI exams were performed by an expert radiologist (> 200 pelvic MRI in the last two years), while all TPUS exams were performed by an expert sonographer (> 500 TPUS examinations in the last two years), in a double blind fashion. The two methods were performed within 30 days (median: 9.5; mean: 11.4; SD: 9.4; range: 0 – 30 days); in patients with abscesses, the methods were performed
within seven days.

The MRI was performed with an external magnet placed on the pelvis using specific sequences. The imaging acquisition protocol started with T2-weighted sequences on a sagittal plane to allow anatomic orientation along the anal canal and identification of any free fluid pelvic and/or presacral collections. Scans on the axial and coronal planes as well as scans perpendicular and parallel to the longitudinal axis of the anal canal were performed. High-resolution T2-weighted images were also carried out to obtain important information on the regional anatomy of the sphincters and adipose spaces. T2-weighted images with fat suppression were performed to allow for comprehensive assessment of the perianal disease. A standard dose of contrast paramagnetic agent (0.2 ml/kg of gadopentetate dimeglumine or 0.1 mL/kg gadobutrol) was administered to either enhance the visualization of fistulae and abscesses or to evaluate the inflammatory activity.

TPUS was performed without specific preparation using a transabdominal ultrasonographic microconvex probe (4–8 MHz transducer with a maximum penetration of 6-7 cm of the beam ultrasound) before the MRI examination. The examination was performed with the patient laying in the left lateral position with knees brought to the chest to improve the exposition of the perineal region to the probe. This region was investigated by appropriate longitudinal and transverse scans to search for fistulae and abscesses. Fistulae were visualized as tubular hypoechoic structures with or without hyperechoic spots corresponding to air bubbles (Figure 1 A and 1B); abscesses appeared as anechoic areas (Figure 1 C and 1D). All lesions were also analysed by using colour- and power-Doppler modules. The presence of hypervascularity peripheral to the lesions was considered as a sign of active benign disease.

Fistulae identified on MRI and TPUS were classified according to Parks' criteria as superficial, intersphincteric, transssphincteric, suprasphincteric, or extrasphincteric. Anovulvar and rectovaginal fistulae were also considered, although not as part of Parks’
original classification. Moreover, perianal disease was classified as simple or complex according to AGA classification\textsuperscript{10}. Briefly, a simple fistula is low (superficial or low intersphincteric or low transsphincteric origin of the fistula tract), has a single external opening, has no pain or fluctuation to suggest perianal abscess, has no evidence of a rectovaginal fistula or of anorectal stricture. A complex fistula is high (high intersphincteric or high transsphincteric or extrasphincteric or suprasphincteric origin of the fistula tract), may have multiple external openings, may be associated with the presence of pain or fluctuation to suggest perianal abscess, may be associated with the presence of a rectovaginal fistula or an anorectal stricture, and may be associated with the presence of active rectal disease in endoscopy.

The study was approved by the Institutional Review Board of the IRCCS “Casa Sollievo della Sofferenza” Hospital in San Giovanni Rotondo, Italy, and informed consent was obtained from all patients.

**Statistical Analysis**

The agreement between MRI and TPUS in the classification of perianal disease according to Parks’ and AGA criteria was assessed using K statistics, considering a k above 0.81 as excellent, 0.61 to 0.80 as good, 0.41 to 0.60 as moderate, 0.21 to 0.40 as modest, 0.01 to 0.20 as poor and < 0.01 as nothing.

**Results**

Demographic and pathological features of the patient population are reported in Table 1. Of the 28 examined patients, 23 (75\%) were suffering from CD [four ileal (33.3\%), eight colonic (16.7\%), nine ileocolonic (50\%)] and seven patients (25\%) were suffering from UC [six pancolitis (75\%) and one proctitis (25\%)]. Five patients (31.2\%), two with UC and three with CD, underwent surgery after MRI and TPUS examinations; one ileal resection, two
total colectomies with ileo-pouch-ano-anastomosis (IPAA), one rectal resection with nerve sparing technique and preservation of the anal canal, and one total colectomy with ileal resection and IPAA were carried out.

The results for fistula and abscess detection with both methods are given in Tables 2 and 3. Overall, 30 fistulae (seven superficial, 11 intersphincteric, eight transsphincteric, no suprasphincteric, one extrasphincteric, three rectovaginal) and seven abscesses (one superficial and six deep) were recognized in the MRIs for 28 patients. Two patients had no perianal disease. In two patients with rectovaginal fistulae, one patient with intersphincteric fistulae, one patient with transsphincteric fistulae, and four patients with superficial and small abscesses on TPUS, no abnormality was detected during the MRI.

Conversely, TPUS identified 33 fistulae (four superficial, 13 intersphincteric, eight transsphincteric, no suprasphincteric, two extrasphincteric and six rectovaginal) in 28 patients. In agreement with MRI findings, two patients had no perianal disease. Eight abscesses were found during TPUS examination (five superficial and three deep). In one patient with an intersphincteric fistula and in three patients with deep abscesses observed during MRI, no abnormality was detected on TPUS.

Table 4 shows fistulae distribution, per patient, according to AGA classification: eight patients had simple fistulas, 14 patients suffered from complex fistulas, and six patients had no pathological alteration during MRI examination. In contrast, seven patients had simple fistulas, 18 patients had complex fistulas, and three patients had no pathological alteration during TPUS examinations (see Figure 2A, 2B, 2C, 2D).

The degree of correlation between MRI and TPUS for fistula classification according to Parks' criteria was good ($k = 0.67$), the degree of correlation for fistula classification according to AGA's criteria was excellent ($k = 0.83$) and the degree of correlation for the detection of abscesses was modest ($k = 0.34$).
Discussion

Perianal disease usually denotes a more aggressive phenotype of IBD. Beaugerie and colleagues found that patients with CD and perianal disease at diagnosis had a significant risk of developing a "debilitating disease" characterized by chronic disabling symptoms, long-course treatments of steroids and immunosuppressive drugs, development of steroid dependence or resistance, and need for frequent hospitalizations and surgical resection\(^8\), \(^26\), \(^27\).

The ability to diagnose and characterize perianal disease has improved in recent decades because of the development of new imaging technologies, such as pelvic MRI, anorectal EUS, endoanal ultrasound, fistulography and CT. However, EUA is recommended to be performed by an expert surgeon before any diagnostic imaging study\(^12\).

MRI is currently regarded as the best non-invasive technique for perianal disease classification and management. However, the procedure is expensive, time-consuming, and not readily available in all medical centers\(^13\). Conversely, TPUS is a simple method that is safe, painless, easily repeatable, inexpensive, and time sparing; additionally, TPUS allows physicians to study perianal disease in both static and dynamic conditions. TPUS, in experienced hands, allows obtaining an accurate diagnosis within approximately 10-15 minutes without discomfort for the patient and without waiting for the examination because it is able to be executed during the course of the same visit. In contrast, MRI requires longer times for image acquisition (approximately 90 minutes); additionally, accessing the examination requires a considerable waiting time.

Our study shows that the diagnostic accuracy of TPUS in IBD patients with perianal involvement is very high when compared to MRI findings. The degree of concordance of both methods in diagnosing and classifying perianal fistulae, according to Parks’ and AGA’s criteria, is high with a k-value ranging from 0.67 to 0.83. Conversely, MRI is less sensitive than TPUS in the evaluation of superficial abscesses, but this might be related to
the small size of abscesses detected in our patients. In addition, when TPUS is performed together with colour/power Doppler modules, it proved to be as accurate as contrast-enhanced MRI in differentiating active from non-active disease, thus providing relevant information for the clinical management of patients.

TPUS also has the advantage of studying the vascularization of the lesions by means of colour and power Doppler modules. Sonographers are generally able to distinguish peripheral hypervascularity, which is a distinctive feature of active inflammatory lesions, from the central hypervascularity that characterizes proliferative lesions. In this regard, it should be outlined that neoplastic degeneration of perianal disease in IBD patients, although rare, has been reported\textsuperscript{14, 19, 20}.

Moreover, in doubtful cases whenever it proves difficult to identify strongly suspected lesions, it is possible to inject hydrogen peroxide into an external fistula orifice. The literature has debated the use of this contrast agent for this purpose because it allows detection of the suspected lesion but generates a series of artefacts that may further impair detailing the area\textsuperscript{13, 16, 21}. In this respect, we would suggest the use of intravenous second-generation ultrasound contrast agent SonoVue, which would show lesions that are particularly active, to enable judgement of disease activity and differentiation of phlegmons from abscesses\textsuperscript{13}.

Another potential application of TPUS in characterizing perianal disease could be the ability to differentiate IBD-related from non-IBD-related fistulae. In two recent studies, Zawadzki et al.\textsuperscript{28} and Blom et al.\textsuperscript{29} described some ultrasonographic features of fistulae that were identified by endoanal ultrasound that make it possible to distinguish the forms of perianal diseases related to IBD from those that are non-IBD related (cryptoglandular), such as a hypochoic fistula track surrounded by a well-defined hyperechoic area with extension in the perianal tissue with a thin regular hypoechoic edge, bifurcation or secondary extension, cross-sectional width $\geq 3$ mm, and hyperechoic secretions content.
However, these studies suffer from important limitations because they do not take into account other factors, such as disease duration and treatment performed before endoanal examination. Further studies are needed to elucidate this problem.

Although relatively simple and accurate, TPUS is not without shortcomings. Some artefacts, such as the shadow cones generated by air inside fistulae and/or abscesses, may compromise the identification of deeper lesions. These limitations are to be taken into account in IBD patients with perianal disease because the exclusion of abscesses is of paramount importance for any therapeutic decision\textsuperscript{30}. In this regard, TPUS showed a low sensitivity in the evaluation of suprasphincteric and extrasphincteric fistulae. This is most likely because of the frequency of the probe, which allows a more detailed study of the superficial layers of the perineum at the expense of image resolution at deeper levels. Surprisingly, in our study, the diagnostic performance of TPUS in anovulvar and rectovaginal fistulae was higher than the MRI findings, confirming previous reports\textsuperscript{13}. In our series, six rectovaginal fistulae, confirmed by gynaecological and proctologic examination, were found on TPUS, while MRI was able to only detect three. Certainly, the lack of use of an MRI endoanal dedicated coil increases the distance of the detector from the affected area and also reduces the sensitivity of the method in detecting small lesions that are expressed in a reduced space. In contrast, the TPUS probe is very close to the above anatomical region and allows searching for suspicious lesions with appropriate scans. For the same reason, TPUS found more superficial abscesses than MRI, but this finding is most likely related to three of the four abscesses being less than < 15 mm in diameter; TPUS lost three small deep abscesses that were visualized on MRI because of the low resolution power of the probe into the deep layers.

The biggest limitation of our study is represented by the time between the execution of the two exams in some patients, thus producing less comparability between the results of the two methods. Moreover, the lack of a comparison with a surgical visit in most patients and
/ or a follow-up over time represents further limitations. The low sample size (though collected in a single year) could represent an additional limitation. The main strength of our study is the presence of patients who had not undergone a previous surgery for perianal disease.

The excellent correlation between the two methods, especially considering the AGA classification, allows the clinician to have a powerful tool that allows quick selection of different treatment types depending on whether the perianal disease is simple or complex. However, the results of our study support the use of TPUS as a complementary technique to MRI. As a real-time, easily available, repeatable, inexpensive and time-sparing method, it could be proposed along with MRI to determine the best therapeutic strategy in IBD patients with perianal disease. Moreover, because it is easily transportable, TPUS could be used in the operating room to assess correct positioning and complete abscess drainage. Furthermore, because of the lack of pain and radiation risks, it could play a pivotal role in the study of perianal disease in a paediatric population. Finally, because TPUS is as accurate as MRI in monitoring the response to either medical or surgical therapies, it could be more cost-effective than MRI because of the need for more follow-up visits to check on the outcome of the treatment.

In conclusion, TPUS, as an inexpensive, time-sparing and non-invasive procedure, and might be recommended in patient follow up to check for perianal lesion healing.

**Abbreviations:** American Gastroenterological Association (AGA), Crohn's disease (CD), computed tomography (CT), exploration under general anaesthesia (EUA), endoscopic ultrasound (EUS), inflammatory bowel disease (IBD), magnetic resonance imaging (MRI), transperineal ultrasound (TPUS), ulcerative colitis (UC)
Figure Legends

Figure 1: Intersphincteric fistula (arrows) visualized as tubular hypoechoic structures without hyperechoic spots (A); Recto-vaginal fistula (arrows) visualized as tubular hypoechoic structures with hyperechoic spots (arrowhead) that correspond to air bubbles (B).

Abscesses appeared on TPUS as anechoic areas. Horseshoe-shaped abscess (stars) (C); large abscess (D).

Figure 2: Intersphincteric fistulae (arrows) on TPUS (A) and MRI (arrows) (B); Rectovaginal fistula (arrow) on TPUS (A), not shown on MRI (B).

References


2010; 4:63-101


Table 1: Characteristics of the patients enrolled in the study

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<tr>
<td>Mean Age ± SD</td>
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<td>37.6 ± 16</td>
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Table 2: Distribution of fistulae: Park’s classification TPUS vs MRI

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Table 3: Distribution of abscesses TPUS vs MRI

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<td>Deep</td>
<td>No abscesses</td>
<td></td>
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<tr>
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<td>(1)</td>
<td>(6)</td>
<td>(4)</td>
<td></td>
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<tr>
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<td>0</td>
<td>4</td>
<td></td>
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<tr>
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Table 4: Distribution of fistulae per patient: AGA classification TPUS vs MRI

<table>
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<th>Complex (14)</th>
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