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Retrospective Study

Magnetic resonance imaging predicts perianal fistula in Crohn's disease

Zhen-Peng Xu, Lu Li, Gui-Dong Sun, Yan-Yan Wu, Er-Wei Cai, Ke Wen, Wan-Jin Shao, Yu-Gen Chen

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Abstract

BACKGROUND

Due to the unique pathogenesis of perianal fistula in Crohn's disease (PFCD), transmural inflammation and active proctitis are characteristic features observed on magnetic resonance imaging (MRI). These features may help predict Crohn's disease when anal fistula is the first manifestation.

AIM

To assess the value of MRI in predicting PFCD.

METHODS

In this retrospective study, 251 inpatients and 168 inpatients with anal fistula who had undergone MRI at two hospitals were included in the discovery and external validation cohorts, respectively. Images were classified based on the presence of transmural inflammation or active proctitis. A diagnostic predictive model was developed and its performance was assessed using the area under the curve, with both internal and external validations performed.

RESULTS

Of the 69 patients with PFCD in the discovery cohort, 57 had transmural inflammation or active proctitis: (1) 21 (30.4) had both features; (2) 11 (15.9) had transmural inflammation only; and (3) 25 (36.2) had active proctitis only. In contrast, among the 182 patients with cryptoglandular anal fistula, only 35 (19.2) had these features. Using transmural inflammation or active proctitis to predict PFCD yielded a sensitivity of 82.6% and a specificity of 80.8%, with an area under the curve of 0.818 (95%CI: 0.757-0.879; SE = 0.031), indicating the model's good discriminative ability, which was confirmed in the external validation cohort.

CONCLUSION

MRI can predict PFCD and distinguish it from cryptoglandular anal fistula with good accuracy.

Key Words: Magnetic resonance imaging; Perianal fistula in Crohn's disease; Cryptoglandular anal fistula; Transmural inflammation; Active proctitis

Core Tip: This study confirms the high value of magnetic resonance imaging (MRI) in predicting perianal fistula in Crohn's disease (PFCD) and distinguishing it from cryptoglandular anal fistula. Transmural inflammation or active proctitis on MRI are key PFCD features, with the predictive model showing 82.6% of sensitivity and 80.8% of specificity in the discovery cohort, and even better performance in external validation. Therefore, MRI serves as a reliable non-invasive tool for early PFCD diagnosis, guiding rational treatment and helping to avoid unnecessary harm to patients.

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory bowel disease that can involve any part of the gastrointestinal tract[1], with fistulas occurring in up to 50% of patients[2]. Notably, 17.2% of patients develop anal fistula more than six months before diagnosis, which can be the first manifestation of CD[3]. Compared with cryptoglandular anal fistula (CAF), perianal fistula in CD (PFCD) carries higher surgical risk and is often associated with serious complications, including unhealed wounds or recurrence, perianal abscess, sphincter injury, and fecal incontinence[4]. Additionally, medical treatment plays an important role in PFCD management[5]. Therefore, early diagnosis of CD when anal fistula is the first manifestation is critical before initiating treatment[6], as an accurate diagnosis can guide standardized management and improve patient outcomes.

Magnetic resonance imaging (MRI) provides high soft-tissue resolution and enables accurate visualization of the anal sphincter, pelvic floor muscles, fistula tracts, and abscesses[7]. It can also be used to assess fistula activity and evaluate treatment efficacy and prognosis, and is currently considered the gold standard modality for evaluating anorectal fistulas [8].

Given the different pathogenesis of PFCD and CAF, transmural inflammation – where the fistula originates from the mucosal layer, penetrates the submucosa and internal anal sphincter to the intersphincteric space, and may penetrate the external sphincter complex (Figure 1A) – and active proctitis – characterized by multiple submucosal and internal anal sphincter inflammation or rectal wall thickening; (Figure 1B-D) – are important MRI features of PFCD. In contrast, CAF originates from the intersphincteric space and rarely involves the submucosa and internal sphincter (Figure 1E),

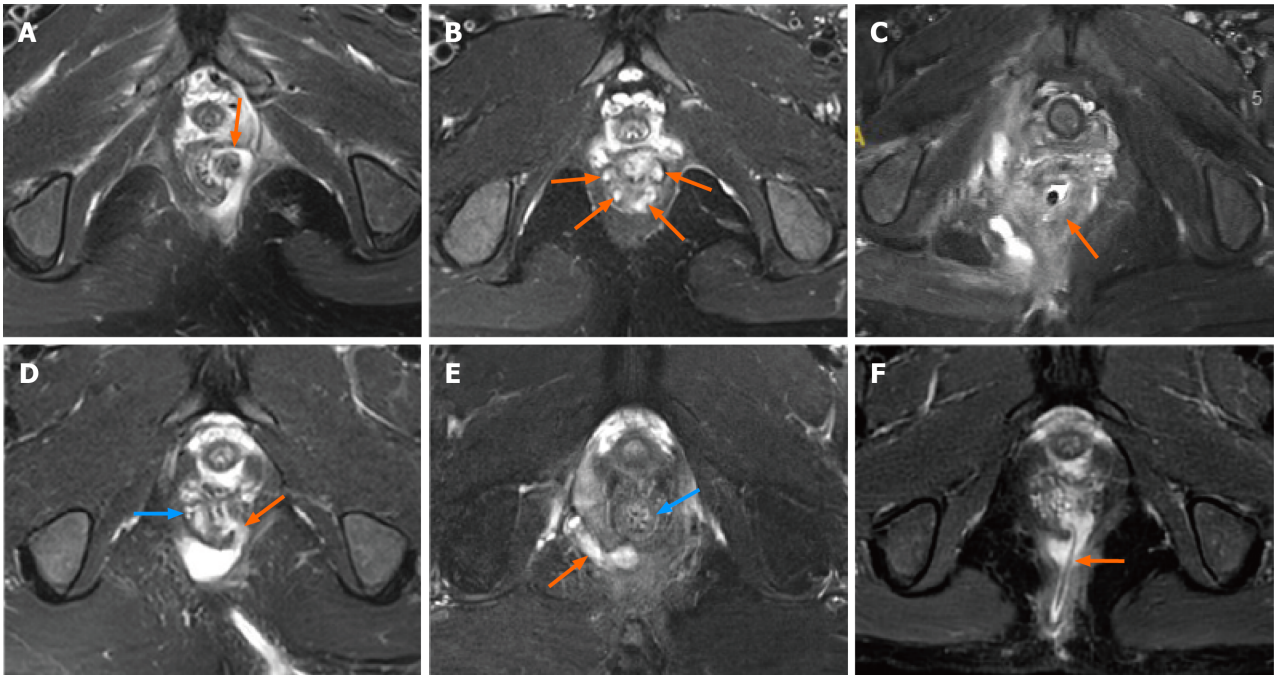

Figure 1 Magnetic resonance imaging T2-weighted fat saturation of perianal fistula in Crohn's disease and cryptoglandular anal fistula. A: Transmural inflammation, the fistula originates from the mucosal layer, penetrates the submucosal and internal anal sphincters (orange arrow) to the intersphincter space or external sphincter complex; B: Active proctitis, multiple submucosal and internal anal sphincter inflammation (orange arrows); C: Thickened rectal wall (at 10.0 mm); D: Transmural inflammation (orange arrow) and submucosal and internal anal sphincter inflammation (blue arrow); E: High transsphincteric cryptoglandular anal fistula (orange arrow), the source of infection is located in the intersphincter space at the 6 o'clock position, and the submucosal and internal anal sphincters are not involoved (blue arrow); F: The presence of a seton drainage at the time of magnetic resonance imaging shows a transmural appearance (orange arrow).

facilitating differentiation between the two conditions.

To our knowledge, data linking these imaging features to PFCD diagnosis are limited. Therefore, this study aimed to predict PFCD based on MRI features, thereby improving diagnostic accuracy before treatment.

MATERIALS AND METHODS

Study design and participants

Data from patients with anal fistula treated in the colorectal surgery department of two hospitals in China between January 2021 and December 2022 were retrospectively analyzed. Inclusion criteria were as follows: (1) Anal fistula diagnosed on admission; (2) Rectal MRI with clear and complete images; and (3) Anal fistula confirmed on MRI. Exclusion criteria were as follows: (1) Secondary anal fistula associated with presacral cyst, malignancy, trauma, tuberculosis, sexually transmitted disease, or radiation; and (2) Presence of seton drainage at the time of MRI, as this could produce a transmural appearance on the images (Figure 1F). The diagnostic criteria for PFCD was based on the 2014 World Gastroenterology Organization global consensus on the classification, diagnosis, and multidisciplinary treatment of perianal fistulizing CD[9]. Patients with CAF were those in whom PFCD were excluded. A colorectal surgeon with 10 years of clinical experience served as study coordinator and performed a computerized search of medical workstations and imaging databases to confirm patient eligibility.

The clinical and MRI data from patients (n = 251) at the Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine were collected as the discovery cohort to assess the association between the MRI features and PFCD diagnosis. The discovery cohort was subsequently divided into two groups according to the study timeline for internal validation. Data from patients at Suzhou TCM Hospital Affiliated to Nanjing University of Chinese Medicine (n = 168) were used as the external validation cohort. The Institutional Review Board of the Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine and Institutional Review Board of Suzhou TCM Hospital Affiliated to Nanjing University of Chinese Medicine approved this study and waived the requirement for informed consent.

Data collection

The following data were collected: (1) Age; (2) Sex; (3) Duration of anal fistula; (4) Duration of CD; (5) History of surgery; and (6) History of biological agent use [*e.g.*, anti-tumor necrosis factor (anti-TNF)] in patients with PFCD. Rehospitalization for failed anal fistula treatment was considered a new record.

MRI analysis

The MRI examinations were performed using clinical 1.5-T or 3.0-T systems. The images were reviewed through consensus by two anorectal surgeons (both with > 10 years of experience in anorectal MRI interpretation), who were blinded to clinical data. The scans were assessed for transmural inflammation (fistula originating from the mucosal layer, penetrating the submucosa and internal anal sphincter to the intersphincteric space, and even penetrating the external sphincter complex) and active proctitis (multiple submucosal and internal anal sphincter inflammation or rectal wall thickening). The patients were classified into four categories based on MRI features: (1) Neither transmural inflammation nor active proctitis; (2) Transmural inflammation only; (3) Active proctitis only; and (4) Both transmural inflammation and active proctitis. Predictive models for PFCD were developed based on these imaging features and validated internally and externally.

Statistical analysis

Data were analyzed using SPSS version 26.0 (IBM Corporation, Chicago, IL, United States). Quantitative data are expressed as mean ± SD and analyzed using the independent samples *t*-test. Qualitative data were expressed as counts and proportions and were analyzed using the χ^2 test. Receiver-operating characteristic (ROC) curve analysis was performed for the predictive models. The area under the curve (AUC) was determined between 0 and 1, with values closer to 1.0 indicating higher diagnostic performance, whereas a value of 0.5 indicates no diagnostic utility.

RESULTS

After screening 284 patients with developed anal fistula who underwent MRI during the study period at the Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine, 33 were excluded for not meeting the study criteria (Figure 2). A total of 251 patients were included, including 17 readmissions after treatment failure, which were considered separate records. The MRI scans of these 251 patients were analyzed to develop and determine the optimal predictive model. The final population included 69 PFCD (male/female: 50/19; mean age: 26.03 years) and 182 CAF (male/female: 158/24; mean age: 42.70 years) patients. Among the 69 PFCD patients, 32 (46.4%) had previously undergone anal fistula surgery, and 24 (34.8%) patients were receiving biological agents (*e.g.*, anti-TNF) at the time of MRI. Among the 182 CAF patients, 94 (51.6%) had undergone anal fistula surgery.

Result of MRI analysis

MRI analysis (Table 1) showed that among the 69 patients with PFCD, 12 (17.4%) had neither transmural inflammation nor active proctitis, 11 (15.9%) had transmural inflammation only, 25 (36.2%) had active proctitis only, and 21 (30.4%) had both transmural inflammation and active proctitis. Among the 182 patients with CAF, 147 (80.7%) had neither transmural inflammation nor active proctitis, 16 (8.8%) had transmural inflammation only, 16 (8.8%) had active proctitis only, and 3 (1.6%) had both transmural inflammation and active proctitis.

Predictive model and ROC analysis

A predictive model for PFCD was established based on the MRI features, with transmural inflammation or active proctitis considered a positive predictor. The ROC curve analysis (Table 2) showed a sensitivity of 82.6% and a specificity of 80.7%, with an AUC of 0.818 (95%CI: 0.757-0.879; SE = 0.031), indicating excellent discriminative capacity (Figure 3).

Verification

Reliability was assessed by evaluating the consistency of model over time (test-retest correlation). Patients were divided into two groups according to the study timeline: (1) Group A (January-December 2021; n = 111); and (2) Group B (January-December 2022; n = 140). The ROC curve analysis results were similar between both periods (Table 3). External validation was performed using 168 patients with anal fistula from Suzhou TCM Hospital Affiliated to Nanjing University of Chinese Medicine, including 50 patients with PFCD and 118 patients with CAF. In this cohort, the model achieved a sensitivity of 88.0% and a specificity of 83.9%, with an AUC of 0.859 (95%CI: 0.795-0.924; SE = 0.033, Table 4).

DISCUSSION

CD causes inflammation of the digestive tract lining and can lead to serious complications[4]. Anal fistula is a common manifestation of CD. Although many studies have reported on the complications and treatment of CD[10], few have examined on the role of MRI in identifying specific features that may help to predict CD in such patients. Therefore, we describe MRI features of anal fistulas and correlate them with CD diagnosis[11]. Our results show that accurate interpretation of MRI features helps distinguish PFCD from CAF with good diagnostic performance and can effectively prevent patients with CD presenting initially with anal fistula from being misclassified as CAF cases indicated for surgical treatment, which may cause serious consequences, including prolonged wound healing, sphincter injury, and fecal incontinence.

This study's findings indicate that both PFCD and CAF are more common in men. A significant age difference was observed, with PFCD patients being younger. This is consistent with reports that CD onset typically occurs at 20-40 years,

Table 1 Characteristics and outcome of the patients with anal fistulas, mean ± SD/*n* (%)

Variables	Perianal fistula in CD (*n* = 69)	Cryptoglandular anal fistula (*n* = 182)	*P* value
Age	26.03 ± 7.75	42.70 ± 12.08	< 0.001
Male/female	50/19	158/24	0.007
Duration of anal fistula (month)	14.61 ± 22.09	25.51 ± 49.73	< 0.001
Duration of CD (month)	8.87 ± 18.29	-	-
Previous fistula surgery	32 (46.4)	94 (51.6)	> 0.05
Biological agents (such as anti-tumor necrosis factor)	24 (34.8)	-	-
magnetic resonance imaging feature			
Neither transmural inflammation nor active proctitis	12 (17.4)	147 (80.7)	< 0.001
Only transmural inflammation	11 (15.9)	16 (8.8)	< 0.001
Only active proctitis	25 (36.2)	16 (8.8)	< 0.001
Transmural inflammation and active proctitis	21 (30.4)	3 (1.6)	< 0.001

CD: Crohn's disease.

Table 2 Receiver-operating characteristic curve analysis of predictive model, *n* (%)

Predictive model	Perianal fistula in Crohn's disease (*n* = 69)	Cryptoglandular anal fistula (*n* = 182)	Area under the curve	Sensitivity (%)	Specificity (%)	Youden index
Positive	57 (82.6)	35 (19.3)	0.818	82.6	80.7	0.633
Negative	12 (17.4)	147 (80.7)				

Table 3 Receiver-operating characteristic analysis of predictive model in two periods, *n* (%)

Period	Perianal fistula in Crohn's disease	Cryptoglandular anal fistula	Area under the curve	Sensitivity (%)	Specificity (%)	Youden index
Patients in January 2021-December 2021						
Positive	23 (82.1)	17 (20.5)	0.808	82.1	79.5	0.616
Negative	5 (17.9)	66 (79.5)				
Patients in January 2022-December 2022						
Positive	34 (83.0)	18 (18.2)	0.824	83.0	81.8	0.648
Negative	7 (17.0)	81 (81.8)				

Table 4 Receiver-operating characteristic analysis of predictive model in the external validation cohort, *n* (%)

Model 4 (patients in external validation cohort)	Perianal fistula in Crohn's disease (*n* = 50)	Cryptoglandular anal fistula (*n* = 118)	Area under the curve	Sensitivity (%)	Specificity (%)	Youden index
Positive	44 (88.0)	19 (16.1)	0.859	88.0	83.9	0.719
Negative	6 (12.0)	99 (83.9)				

younger than the age of onset of CAF[12].

The most common theory for the formation of perianal abscesses and anal fistulas is the cryptoglandular theory proposed by Parks in 1961, which involves the obstruction of anal glands and ducts. This hypothesis states that anal glands are primarily located in the intersphincteric space, cross the internal sphincter, and open into the anal crypts at the dentate line[13]. The primary pathology is gland infection rather than duct or opening infection; therefore, anal fistulas caused by a cryptoglandular infection rarely involves the submucosa and internal anal sphincter.

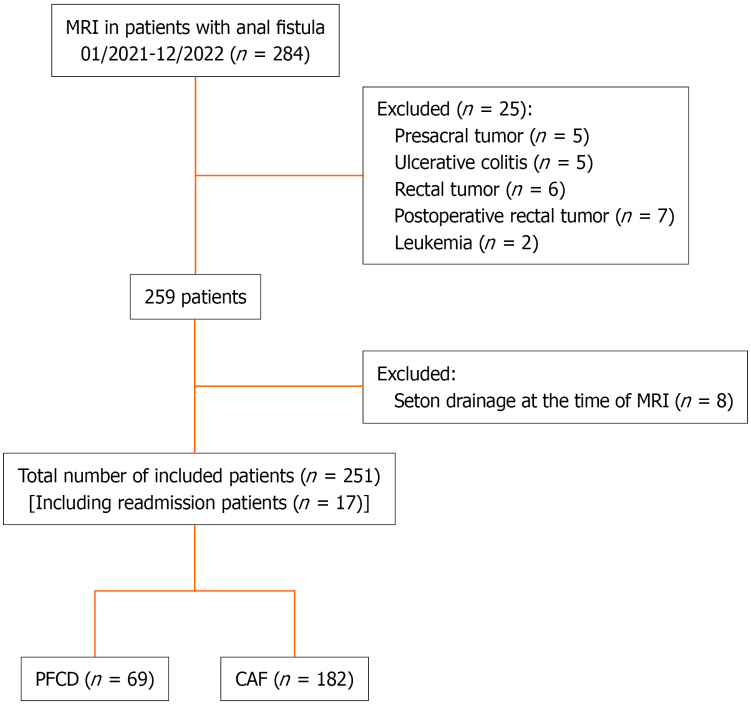

Figure 2 Flow chart of the study population. CAF: Cryptoglandular anal fistula; MRI: Magnetic resonance imaging; PFCD: Perianal fistula in Crohn's disease.

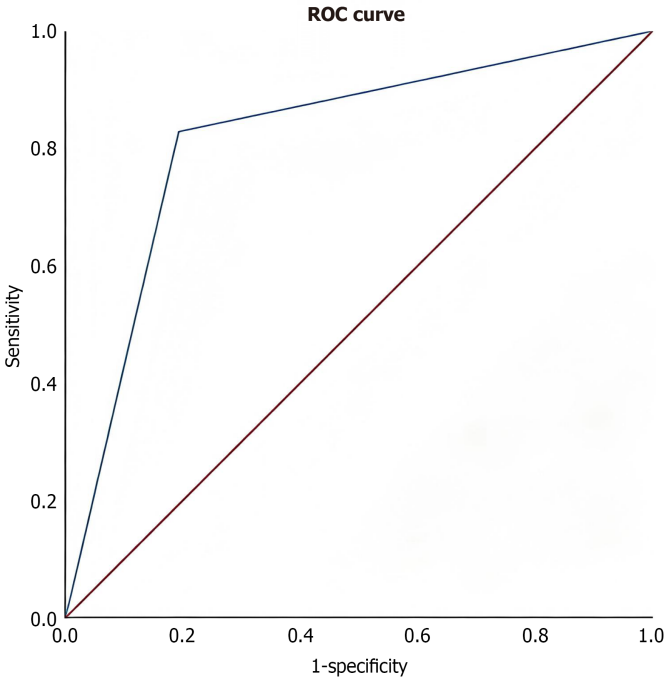

Figure 3 Receiver-operating characteristic curve showing the area under the curve of the predictive model. The area under the curve of the receiver-operating characteristic was 0.818 (95%CI: 0.757-0.879; SE = 0.031). ROC: Receiver-operating characteristic.

Anal fistula as the first manifestation may to be a risk factor for disabling CD (*e.g.*, repeated recurrence, medical refractoriness, need for immunosuppressive therapy, hospitalization, and surgery)[11]. The prevalence of anal fistula varies by CD location, with rates of 12%, 41%, and 92% in isolated ileal disease, colonic disease with rectal involvement, and disease with rectal involvement, respectively[14]. The mechanism of PFCD formation differs from that of CAF and is mainly related to epithelial-to-mesenchymal transition and matrix remodeling enzymes[15]. Compared with CAF, CD-associated fistulas are often more complex, carry higher surgical risk, and are more prone to complications, including prolonged wound healing, recurrence, perianal abscess, sphincter injury, and fecal incontinence. Fiber colonoscopy remains the most important method for definitive CD diagnosis. However, the incidence of anal fistula is approximately 1.69/10000[16], with CAF accounting for 90%-95% of cases[17], and PFCD for only 4.55%. Routine fiber colonoscopy for

all patients with anal fistulas is therefore not aligned with the principles of social health and economy. If non-invasive MRI can be used to identify PFCD before treatment, clinical assessment would be more efficient and patient benefit improved.

Imaging is essential for assessing fistula anatomy and extent, planning treatment, and evaluating treatment response [11]. A meta-analysis by Giles *et al*[18] reported that MRI enterography has a sensitivity of 84% and specificity of 97% for detecting active terminal ileal CD, indicating high diagnostic performance, particularly in children. Cavusoglu *et al*[19] found that diffusion-weighted imaging combined with conventional sequences was significantly more valuable in the diagnosis of perianal fistula than T2-weighted imaging alone. The van Rijn *et al*[20] showed that MRI fibrosis degree and the MAGNIFI-CD index are associated with long-term clinical closure of Crohn's perianal fistula. MRI is therefore considered the optimal imaging modality for the preoperative evaluation of patients with anal fistulas[21]. However, MRI characteristics of PFCD remain insufficiently described, and large-scale studies are lacking. As noted, PFCD and CAF differ in pathogenesis: PFCD involves epithelial-to-mesenchymal transition and deeper tissue spread, manifesting as transmural inflammation and active proctitis, whereas CAF originates from infection of anal glands in the intersphincteric space and rarely involves the submucosa and internal anal sphincter. Accordingly, their MRI features differ substantially. To date, no studies have examined the association between transmural inflammation or active proctitis on MRI and PFCD diagnosis.

Our results indicate that, compared with CAF, PFCD more frequently exhibits transmural inflammation or active proctitis on MRI, which is an intuitive finding. Interestingly, we also found that these features were independent of biological agent use (*e.g.*, anti-TNF) and surgical history. When such features are present, patients with anal fistula may be considered high risk for CD and should undergo further endoscopic and related examinations. This approach may help avoid misclassification and unnecessary surgical treatment, thereby reducing potential physical and mental harm, as well as the broader social and economic burden associated with indiscriminate colonoscopy.

This study has several limitations. First, it is retrospective. Second, large-scale endoscopic confirmation was not performed for patients diagnosed with CAF; CD exclusion relied on medical history, clinical manifestations, and laboratory findings. However, the relatively large sample size may help minimize measurement bias. In addition, both internal and external validation were conducted, supporting the credibility of findings.

CONCLUSION

In summary, MRI can help distinguish PFCD from CAF; however, these findings require validation in prospective studies.

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