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RESEARCH

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The additive value of diffusion tensor imaging in the determination of perianal fistula activity

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Abstract

Background Although the activity of the perianal fistula has been evaluated before by MRI in the literature, limited diffusion tensor magnetic resonance imaging (DT-MRI) studies are reported to date. Our study aimed to elucidate the role of DT-MRI in evaluating the activity state of the perianal fistula and the prediction of postoperative complications. We reviewed the data of 30 patients diagnosed with perianal fistula and referred them for an MRI diffusion study before the surgical intervention. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) were calculated for the fistulous area and the normal surrounding puborectalis as a control area.

Results According to the presence of pus intraoperatively, patients were allocated into two groups: the active group (10 patients) and the inactive group (20 patients). FA and ADC measurements showed a significant decrease in association with the active disease when measured at the fistula site, and this was not observed in the normal surrounding tissues. The area under the curve (AUC) was 0.985 and 0.730 for the ADC and FA, respectively, when cutoff values of 1×10^{-3} mm^2/s and 0.621 were applied, respectively. Adding the FA to the ADC increased the DT-MRI specificity to 95% in the determination of the active fistula. The combination between both FA and ADC increased the AUC to 0.785 with a sensitivity of 73.7% and specificity of 63.6% in the detection of postoperative complications.

Conclusions DT-MRI could be used as a reliable diagnostic tool to differentiate patients with active perianal fistula disease from inactive ones and to predict the postoperative outcome.

Keywords Diffusion tensor imaging, Perianal fistula, Activity

Background

The perianal fistula is an epithelium-lined tract that connects the anal canal to the perianal skin [1]. This entity is commonly encountered in daily general surgical practice, as it is one of the most common anorectal disorders [2, 3]. It is more encountered in men compared to women, with a prevalence of 12.3 and 5.6 cases per 100,000 individuals, respectively [4]. Even after surgical intervention, this disease has a high recurrence rate owing to the potential infections that are usually ignored during surgery [5]. Preoperative identification of these infections and their proper management are crucial to decrease the recurrence rates [6]. Accurate assessment of the fistula activity is a crucial decision, as it will affect the number and types of commenced drugs, the time of surgical intervention, and the type of surgical intervention itself [5]. In recent decades, magnetic resonance imaging (MRI) has been widely used for the assessment of such

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patients, as it could accurately delineate the primary fistulous tract with the surrounding related abscesses [7–9]. Moreover, MRI could be applied to evaluate the activity of these fistulae, which helps in deciding the optimum management plan [5, 9, 10]. Although many studies have evaluated the efficacy of diffusion-weighted imaging (DWI) in the assessment of perianal fistula and its activity, given the fact that ADC value is reduced in the case of active fistula due to the presence of pus, protein, and thick fluid content. [10–13], limited studies have evaluated the role of diffusion tensor imaging (DTI) in the same pathology. DTI is a new sequence added to evaluate the feasibility of detection of perianal fistula activity by analysis and quantitative assessment of FA value. The FA demonstrates the microstructure of tissue and its orientation as regards water diffusion along this orientation while MD carries the same ADC concept as it expresses the motion of water molecules that is variable according to tissue cellularity and size of extracellular spaces [14]. Therefore, decreased FA value means that the examined part is disorganized and filled with inflammatory cells [15]. Similarly, when the perianal muscles are destroyed by the fistula, the direction of water molecule diffusion is expected to be distorted, leading to a noticeable drop in the FA value.

Hence, we conducted the current investigation to elucidate the role of DT-MRI in evaluating the activity state of the perianal fistula and its effect on the postoperative outcome.

Methods

Patient population

This prospective study was conducted at the Radiology Department (MRI unit), Mansoura University Hospitals. We collected the data of adult patients who were diagnosed with perianal fistula or chronic perianal pain and referred them for an MRI examination to identify the anatomy and activity of the perianal fistula. We included a total of 30 consecutive patients during the period between January and December 2021. The inclusion and exclusion criteria are detailed in Fig. 1.

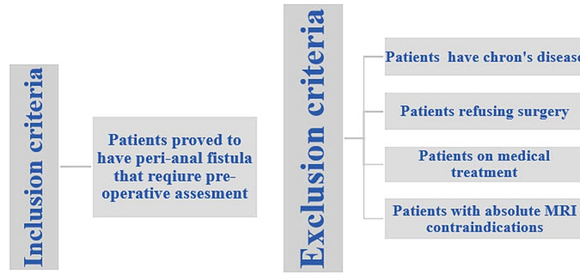

Fig. 1 The inclusion and exclusion criteria of our patients

Clinical assessment

All patients were subjected to detailed clinical history, including general and local examinations. Surgical intervention was decided if the patients had purulent discharge, swollen reddish skin, severe perianal pain, restriction of daily or sexual activity, and/or increased serum C reactive protein > 5 mg/l. The surgery was scheduled after the routine preoperative laboratory and radiological investigations (including MRI). All patients were ordered to fast for six hours and to evacuate their urinary bladders just before the MRI procedure.

MRI procedure

We used a 1.5 T MRI device with a 16-channel coil (Ingenia, Philips, Netherlands). With individuals in a supine position with parallel and lightly flexed legs, the coil was utilized to cover the whole pelvic area. Our MR scanning protocol included a fat-suppressed non and post-contrast-enhanced T1-weighted sequence, Short Tau Inversion Recovery (STIR), DWI on B0, B500, and B1000 mm^2/s, and DTI on B400 and 32 diffusion-weighted directions. Our acquisitions are detailed in Table 1.

Imaging analysis

The original data were transported to the workstation and processed using the FA and ADC mapping software. A senior radiologist with 10 year-experience (MM) assessed the picture quality and determined the ADC and FA values of the scanned regions of interest (ROIs). Circular-shaped ROIs (constant diameter with a minimum area of 0.1 cm^2) were manually delineated on ADC and FA maps. On the greatest suspected area, ROIs were manually delineated on DTI images and overlaid on ADC and FA maps. It was measured three times, and the average value was calculated and recorded.

Furthermore, the lesions were split into two ROIs (the fistulous area and the normal- area). In our study, the puborectalis was chosen as the normal area. Each lesion had two ROIs: The fistula area was designated with the first ROI, which was positioned in the center of the lesion. The second ROI was identified as a distant normal-appearing area and was put on the normally appearing puborectalis muscle.

Surgical analysis

The surgical procedure was performed under spinal anesthesia. According to the intraoperative findings (presence of pus during dissection), patients were allocated into two groups: the inactive group included patients without

Table 1 Our detailed MRI acquisitions in the study

	Parameters	TR/TE (ms)	Bandwidth (kHz)	Section thickness (mm)	FOV (mm)	Matrix size	Scan time
Conventional MRI	T1 Non & Post contrast FAT SAT	520/8	22	6	400 × 400	320 × 16	2 min
	T2	4000/100	20	4	250 × 250	320 × 240	2 min & 52 s
	STIR	4900/60	20	4	250 × 250	320 × 240	2 min & 53 s
Diffusion MRI	DWI	6400/101	173	5	340 × 270	76 × 85	3 min
	DTI	3250/48	173	2	200 × 200	80 × 80	5 min & 47 s

pus on surgical assessment, and the active group included the remaining cases who had pus during the operation. Furthermore, patients of the two groups were assessed intraoperatively for intraoperative bleeding, operative time, and choice of surgical procedure whether in one or two stages. Postoperatively patients of the two groups were assessed for the hospital stay, postoperative wound infection, postoperative bleeding, postoperative incontinence, time for optimal wound healing, and the period the patients need to restore their normal activities. The intraoperative and postoperative data were compared between the two groups and correlated with the preoperative MRI findings.

Statisctial analysis

The data were coded and analyzed using SPSS software. The comparison between the two groups was made using the Chi-square test (Fischer's exact test/Monte Carlo test), and our data were expressed as mean ± standard deviation (SD). The optimal cutoff value of ADC and FA to differentiate between the two groups was determined using the receiver operator characteristic (ROC) curve. P-values less than 0.05 were considered significant for all the applied tests.

Results

In brief, our included patients had mean ages of 36.15 and 40.1 years in the inactive and active groups, respectively. Most patients in the two groups were men, and the trans sphincteric type was the most encountered fistula type among our cases. Sociodemographics of our included sample with regard to age, gender, clinical presentation, duration of symptoms, and fistula type were presented in detail with no statistically significant difference between both the active and inactive fistula groups in Table 2.

All diffusion parameters, including ADC and FA, showed a significant decline in the active group compared to the inactive one ($p < 0.05$) when measured at the fistulous tract area (Fig. 2). ADC had mean values of 1.414 and 0.760×10^{-3} mm^2/s, whereas FA had mean values of 0.657 and 0.507 in the inactive and active groups, respectively. There was no statistically significant difference in the FA and ADC measurements of the normal puborectalis muscle area in both groups (Table 3).

ADC had a higher area undercurve when compared to the FA values. ADC had sensitivity and specificity of 100% and 90%, respectively, for differentiating active from inactive cases, using a cutoff value of 1×10^{-3} mm^2/s, whereas the same values were 100% and 55%,

Table 2 Demographics of the study participants

Study data	Inactive group (n = 20)	Active group (n = 10)	*p* value
Age (years) mean ± SD	36.15 ± 7.92	40.10 ± 8.05	0.211
Gender			0.542
Male	16 (80%)	7 (70%)	
Female	4 (20%)	3 (30%)	
Presentation			
Perianal pain	18 (90%)	8 (80%)	0.448
Perianal discharge	20 (100%)	10 (100%)	1
Duration of symptoms (months)	4 (2–8)	3 (1–8)	0.263
Type of fistula			0.206
Intersphincteric	6 (30%)	4 (40%)	
Transsphincteric	8 (80%)	6 (60%)	
Extrasphincteric	6 (30%)	0 (0%)	

N, Number

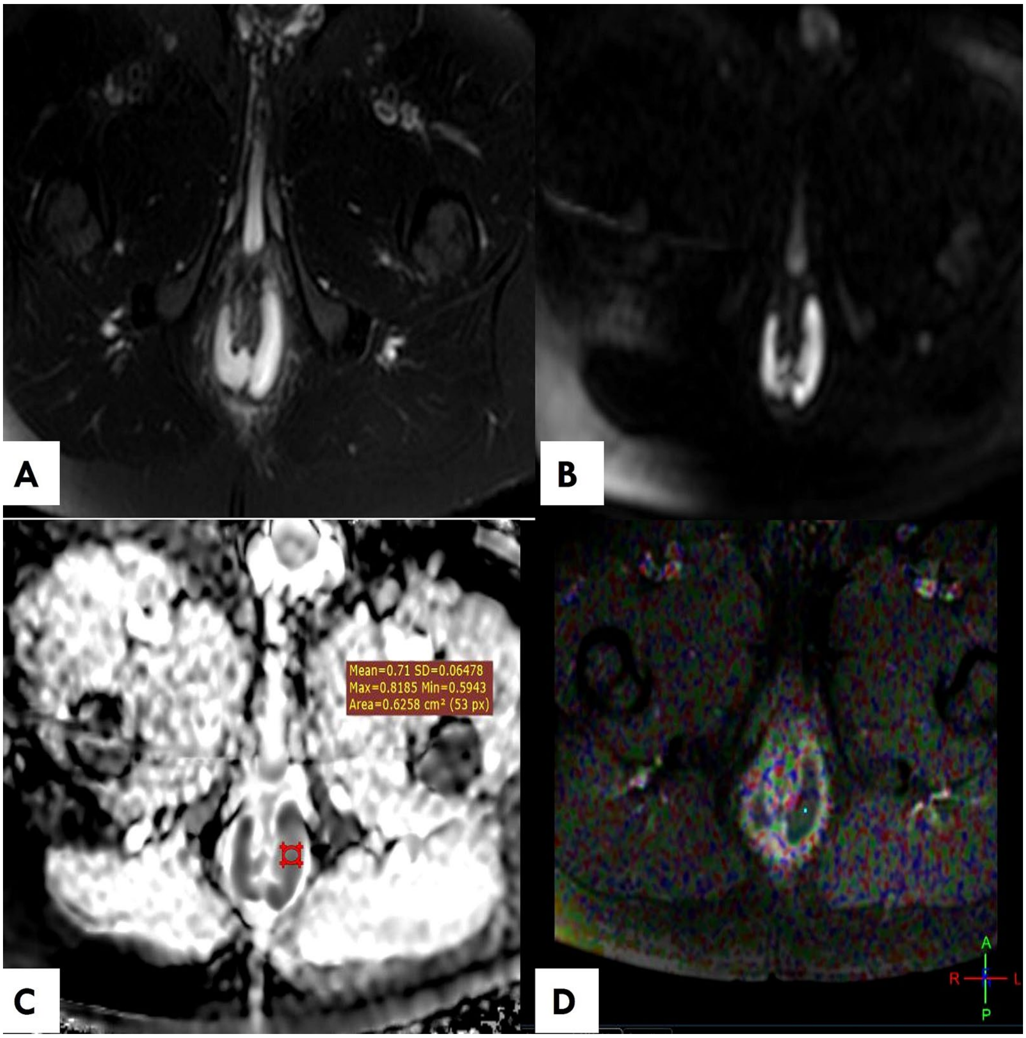

Fig. 2 Horseshoe-shaped intersphincteric fistula with positive inflammation activity. **A** Axial STIR image revealed intersphincteric fistula of abnormal high SI. **B**, **C** DWI & ADC map revealed high SI of fistula on b1000 images and low SI on ADC map with ADC value ~ 0.71×10^{-3} mm^2/s. **D** axial fractional anisotropy (FA) map showed a value of 0.539

Table 3 Diffusion tensor imaging parameters of both fistula and normal areas (puborectalis muscle) in the study participants

DT-MRI parameter	Inactive group, Fistulous area (*n* = 20)	Active group, Fistulous area (*n* = 10)	*p* value	Inactive group, Normal puborectalis muscle (*n* = 20)	Active group, Normal puborectalis muscle (*n* = 10)	*p* value
ADC ($\times 10^{-3}$ mm^2/s)	1.414 ± 0.316	0.760 ± 0.138	< 0.001	1.819 ± 0.450	1.786 ± 0.253	0.832
FA	0.657 ± 0.169	0.507 ± 0.119	0.019	0.743 ± 0.191	0.714 ± 0.090	0.653

DT-MRI: Diffusion tensor magnetic resonance imaging, FA: Fractional anisotropy, ADC: Apparent diffusion coefficient

respectively, for the FA when a cutoff value of 0.621 was applied. The combination between the FA and ADC increased the specificity to 95% in the determination of the active fistula (Fig. 3).

Comparing the intraoperative findings among the two study groups; it was found that intraoperative bleeding was significantly higher and occurred in 50% of cases of group 1 (active fistula) in comparison to only 15% of cases of group 2 (inactive fistula); these results were statistically significant. Additionally, the operative time was longer in group 1 active fistula cases and the post-operative wound infection incidence was higher in the

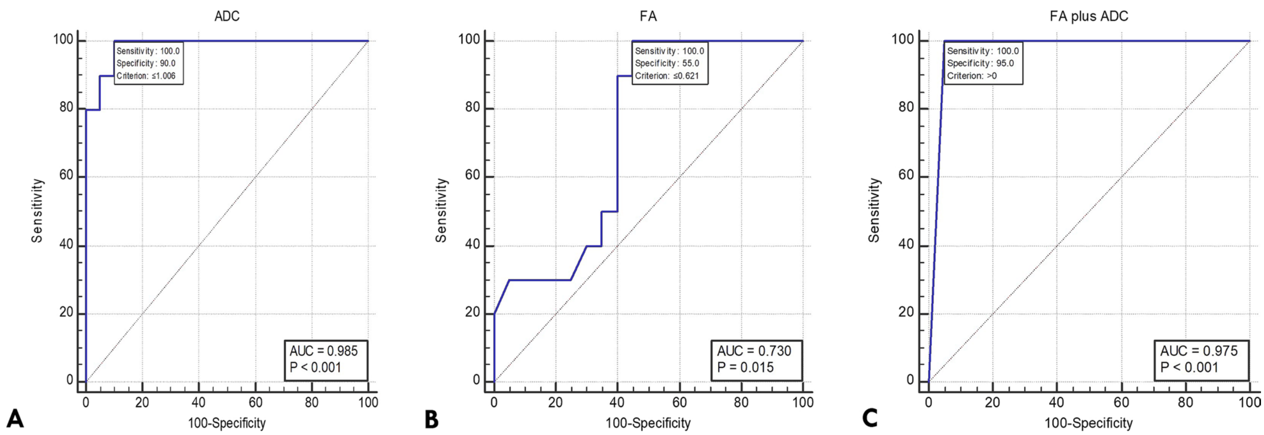

Fig. 3 **A** Reciever operating curve (ROC) for apparent diffusion coefficient (ADC). **B** ROC curve for fractional anisotropy (FA) to differentiate between active and inactive disease. **C** FA combined with ADC accuracy for determination of the fistula activity

active fistula group. Operative details are explained in Table 4.

In correlating the preoperative MRI radiological findings (FA & ADC) in our study with the incidence of postoperative complications (wound infection, bleeding & fecal incontinence), the AUC was fair with FA values (0.615) and a cutoff point (0.6725), (73.7%) sensitivity, and (45.5%) specificity. With regard to the ADC

Table 4 Comparison of intraoperative and postoperative data among the studied groups

	Group 1 (Active fistula) N = 10	Group 2 (Inactive fistula) N = 20	Test of significance
Intraoperative detection of pus			
No	0	20 (100)	$\chi^2 = 30$
Yes	10 (100)	0	$p < 0.001$*
Intraoperative difficulty (bleeding)			
No	5 (50)	17 (85)	$\chi^2 = 4.18$
Yes	5 (50)	3 (15)	$p = 0.041$*
Operative time (minutes) mean ± Standard deviation (SD)	44 ± 9.66	26 ± 5.03	$t = 6.77$ $p < 0.001$*
One or two-stage procedure			
One stage	2 (20)	12 (60)	$\chi^2 = 4.29$
Two stage	8 (80)	8 (40)	$p = 0.038$*
Postoperative wound infection			
− ve	4 (40)	16 (80)	$\chi^{2FET} = 4.8$
+ ve	6 (60)	4 (20)	$p = 0.028$*
Postoperative bleeding			
− ve	5 (50)	16 (80)	$\chi^2 = 2.86$
+ ve	5 (50)	4 (20)	$p = 0.091$
Postoperative fecal incontinence			
− ve	7 (70)	18 (90)	$\chi^{2FET} = 1.92$
+ ve	3 (30)	2 (10)	$p = 0.166$
Time to wound healing mean ± SD	8.2 ± 1.75	4.95 ± 1.05	$t = 6.37$ $p < 0.001$*
Time of return to normal activity mean ± SD	3.10 ± 0.568	1.65 ± 0.489	$t = 7.26$ $p < 0.001$*

χ^2, Chi-Square test; FET, Fischer exact test

*Asterisk refers to statistically significant data values, the AUC also was good (0.775); the cutoff point was (1.3645), the sensitivity was (78.9%), and the specificity was (63.6%). The combination of both the FA and ADC values increased the AUC to (0.785) with sensitivity (73.7%) and specificity (63.6%) in the detection of postoperative complications (Table 5).

Discussion

DTI is a special kind of DWI that was initially applied in the nervous system for better delineation of the white matter tracts [16]. Nevertheless, it has been introduced for the assessment of other organs, including the kidney [17], skeletal muscles [18], and pelvic floor structures [19, 20]. We conducted this study to elucidate the role of DT-MRI in evaluating the activity state of the perianal fistula. In our study, we noted a significant decrease in ADC in patients with active fistula with very good efficacy in the determination of perianal fistula activity. Although the FA measurements showed lesser efficacy than ADC in differentiating active fistula from inactive disease, adding the FA to ADC measurements increased the overall accuracy in the determination of the fistula activity.

Wang et al. reported a significant decline in ADC values of the fistula area in the active group compared to the inactive one (0.979 ± 0.441 vs. $1.393 \pm 0.256 \times 10^{-3}$ mm^2/s, respectively—$p = 0.004$). Using a cutoff value of $1.069 \times 10^{-3} mm^2/s$, ADC had sensitivity and specificity of 100% and 57.14% in differentiating active from inactive lesions [5]. Yoshizako and his coworkers also reported that ADC had mean values of 0.908 ± 0.171 and $1.124 \pm 0.244 \times 10^{-3}$ mm^2/s in the active and inactive groups, respectively, with a cutoff value of 1.019×10^{-3} mm^2/s, ADC had sensitivity and specificity of 95.7% and 50%, respectively, to differentiate between active and inactive groups [10]. Furthermore, Baik et al. reported that the mean ADC values of patients with active fistulas were significantly lower than that of the inactive lesions with sensitivity and specificity of 64% and 92%, respectively, when differentiating active from inactive lesions when a cutoff value of 1.09×10^{-3} mm^2/s was applied [21]. Similarly, Boruah and his colleagues also confirmed the previous findings [22]. Therefore, our study further confirmed the previous studies' findings with similar results.

A previous Egyptian study conducted at Minia University contradicted the previous findings. The authors did not find any significant association between ADC and fistula activity. ADC had mean values of 1.3×10^{-3} mm^2/s and 1.43×10^{-3} mm^2/s in the active and inactive groups, respectively, with no significant difference between the two groups ($p = 0.45$) [23]. This could be attributed to the application of different methods of ADC measurement between different studies. Some radiologists prefer to use a free ROI encompassing the whole lesion and calculate the mean ADC value in the whole lesion. On the other hand, some prefer to use a small ROI within the center of the active to calculate the ADC value. Another point to be considered is the presence of abscesses within the fistulous tract, as it could induce some overlap in the final ADC values. Guo et al. reported that small abscesses might yield ADC values higher than larger ones. This could be explained by the difficult identification of the ROI in patients with small abscesses [24].

In our study, FA had mean values of 0.507 and 0.657 in the active and inactive groups, respectively, with sensitivity and specificity of 100% and 55%, for identifying patients with the active disease when a cutoff value of 0.621 was used, and this was relatively similar to a previous study, where fistulae with positive activity expressed significantly lower FA values compared to the negative-activity group (0.134 ± 0.046 vs. 0.183 ± 0.057, respectively—$p = 0.009$) with a 69.23% sensitivity and a 76.19% specificity in differentiating active from inactive fistulae when a cutoff value of 0.15 was applied [5]. Moreover, our study was the first to calculate the overall accuracy of combined DT-MRI parameters of FA and ADC in the determination of the fistula activity and revealed higher overall accuracy of 96.7% and specificity of 95% rather than depending on each parameter solely, recommending calculating both parameters in our clinical routine MRI practice for better evaluation of the fistula activity.

In our study, intraoperative bleeding and postoperative wound infection occurred at a higher rate in active fistula than inactive disease, and this was similar to Garg et al. in whom intraoperative bleeding was higher in active disease [25] and was similar to another study where patients with the active disease showed higher postoperative wound infection [26]. The combination of both the FA

Table 5 Diagnostic accuracy of diffusion tensor parameters in the detection of complications

Parameters	AUC (95%CI)	*p* value	Cut off point	Sensitivity%	Specificity%
FA	0.615 (0.402–0.828)	= 0.302	0.6725	73.7	45.5
ADC	0.775 (0.610–0.940)	< 0.01*	1.3645	78.9	63.6
FA + ADC	0.785 (0.622–0.948)	< 0.01*	0.498	73.7	63.6

AUC: Area under the curve

*Asterisk refers to statistically significant data and ADC values increased the AUC to (0.785) with sensitivity (73.7%) and specificity (63.6%) in the detection of postoperative complications, and these findings were not investigated in detail in the previous studies [25, 26] as in our study.

Our study had a few limitations. First, a relatively small number of patients were included in our study; further, study with a larger sample of patients is recommended for better establishment of our measurements. Second, this study used only two-dimensional ROI for the estimation of the FA and the ADC values. The use of advanced post-processing such as machine learning might improve the assessment of the fistula. And last, we only focused on FA and ADC parameters and did not study further DTI parameters such as mean diffusivity (MD) and radial diffusivity (RD), which we aim to include in future studies on a larger sample to investigate further the whole DTI parameters.

Conclusions

DT-MRI could be used as a valid option to differentiate patients with active perianal fistula disease from inactive ones. ADC and FA expressed lower values in association with disease activity. The ADC values were promising in predicting postoperative outcomes in patients with perianal fistula. Although ADC value seemed to be a more reliable indicator in the evaluation of the fistula activity than FA, adding FA to the ADC increased the overall accuracy of the diagnosis of the active fistula and it is recommended to calculate both parameters for better assessment of the fistula activity in our routine clinical setting.

Abbreviations

ADC	Apparent diffusion coefficient
AUC	Area under curve
DTI	Diffusion tensor imaging
DT-MRI	Diffusion tensor magnetic resonance imaging
DWI	Diffusion weighted images
FA	Fractional anisotropy
FAT-SAT	Fat suppression
FOV	Field of view
MD	Mean diffusivity.
MRI	Magnetic resonance imaging
RD	Radial diffusivity
ROC	Receiver operating curve
ROI	Region of interest
SD	Standard deviation
STIR	Short tau inversion recovery

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Author contributions

The study concept and design were proposed by MM, ME, &MAE. Statistical analysis of data were contributed by ME, MAG &MMM. Writing the original manuscript was contributed by MM. Revision of the manuscript for important intellectual content were contributed by ME, MMM & MAE. All authors read and approved the final manuscript.

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Availability of data and materials

All the scientific data are available and presented in the manuscript. The source data are available on request.

Declarations

Ethics approval and consent to participate

Written informed consent was waived by the institutional review board (IRB); institutional review board (IRB) was obtained, IRB approval: R.21.01.1179.R1.

Consent for publication

Al the patients were consented and informed of possible research publication. All authors hereby confirm all the copyrights if such work will be accepted in the Egyptian Journal of Radiology and Nuclear Medicine (EJRNM).

Competing interests

The authors declare that they have no competing interests.

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