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RESEARCH ARTICLE

Evaluation of Activity of Perianal Fistulas by Diffusion-Weighted Imaging

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ABSTRACT

Aim: The aim of this study was to evaluate the role of diffusion-weighted magnetic resonance imaging (MRI) in assessing the activity of perianal fistulae.

Method: This retrospective, cross-sectional study included 30 patients with perianal fistula. MRI with diffusion-weighted imaging (DWI) was performed with 1.5 T-scanner. The MRI findings were correlated with local clinical examination and or postoperative findings as reference.

Results: A total of 42 perianal fistulae in 30 patients were identified. The detection rate of perianal fistula by DWI was less than by T2-weighted (T2W) and combined DWI-T2W imaging. Thirty-three perianal fistulae (76.2%) were clearly diagnosed in 42 fistulae on DWI, 40 (88.1%) on T2W, and 41 fistulae (95.2%) on DWI-T2W images. The mean of apparent diffusion coefficient (ADC) values was significantly different between active fistulae at 0.919±0.165 $x10^{-3}$ mm^2/s and inactive fistulae at 1.235±0.220 $x10^{-3}$ mm^2/s ($p<0.0035$). A cut-off mean ADC value of 1.005 $x10^{-3}$ mm^2/s was used to differentiate active from inactive fistula with a sensitivity of 84% and a specificity of 71.5%.

Conclusion: These results showed that the ADCs measured from active and inactive perianal fistulae differ significantly in patients who were on an antibiotic treatment. Therefore, DWI may be used to evaluate the activity of a perianal fistula and identify patients with a higher likelihood of recurrence.

Keywords: Perianal fistulae, activity, diffusion-weighted MRI

Introduction

Perianal fistulae and abscesses have a prevalence of 1 per 10,000 of the population, with an underlying cause of anal glandular infection, Crohn's disease, radiotherapy, or secondary malignancy.[1,2] Perianal fistulae usually result from anal gland obstruction with subsequent infection, associated secondary abscess formation, and its complications. Once a fistula has formed healing may take considerable time and recurrences occur, often after apparent healing.[1,2] The therapeutic approach to the fistula largely depends on the presence of the activity of the fistula, so an accurate assessment of fistula activity is clinically important in deciding whether a medical or a surgical treatment will be more appropriate. Recurrence of fistula occurs in up to 25-30% of patients after surgery, usually due to an infection that went unnoticed during surgery and/or due to a poorly treated fistula.[3]

The presence, extent and activity of perianal fistulae are evaluated by various methods, including anal ultrasound, examination under anesthesia, computed tomography fistulography and magnetic resonance imaging (MRI). Evaluation of a fistula by anal ultrasound and (preoperative) examination under anesthesia can be done easily, however these methods can miss an abscess and the relationship of the fistula with the adjacent perianal muscle layers may not be established by these methods.[4] MRI, on the other hand, not only demonstrates the fistula tract and its course, but can also show an abscess in the vicinity of the fistula tract that lies beyond the reach of the digital exam.[5-8] Accurate preoperative evaluation of a fistula by MRI can therefore determine optimal surgical planning, may decrease the rate of recurrence and can have an impact on the surgical outcome.[5]
The activity of a perianal fistula can also be evaluated by MRI. Active fistulae that are filled with pus and granulation tissue

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and have mural edema are detected by high signal on T2-weighted images (T2W).[5-8] On post-contrast T1-weighted imaging (T1W) mural granulation tissue of an active fistula will enhance against the hypointense fluid in the fistula lumen and any inflammation that extends to adjacent soft tissues will also enhance.[7,8]

Diffusion-weighted MRI (DWI) has also been suggested to aid in the evaluation of the activity of perianal fistulae, as hypercellularity seen in inflammatory processes and abscesses cause diffusion restriction.[9] Studies using DWI with higher b-value provided better contrast, more tissue diffusibility, and less T2 shine-through effect.[10] Some studies also suggested that the mean apparent diffusion coefficient (ADC) values compared between active and inactive fistulae differed significantly and thus could be used to differentiate between these entities.[11-14]

The purpose of this study was to assess the usefulness of DWI and ADC values to evaluate perianal fistula activity.

Materials and Methods

All procedures performed in studies involving human participants were in carried out in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Haydarpaşa Numune Training and Research Hospital Ethics Committee (approval number: E-62977267-771, date: 25.01.2022). Informed consent was obtained from all individual participants included in the study. We reviewed the MRI images of 37 patients who were referred to the radiology department for an MRI exam because of suspected clinical symptoms of a perianal fistula. Claustrophobic patients and patients with an implanted pacemaker (n=4) and patients with recurrent symptoms of a previously healed fistula (n=3) were excluded from the study, leaving 30 patients (18 men and 12 women, mean age, 39 years) to be included. Of these, 15 had anal glandular infection with no obvious underlying disease, 10 had Crohn's disease and 5 had ulcerative colitis. All 30 patients were put on antibiotic treatment for an average of 1 week before the MRI examination (range: 4-11 days).

MRI Examination

All patients were examined in a supine position with a 1.5-T MRI-unit (Optima 760w, GE Medical Systems, Milwaukee, WI, USA) using a pelvic phased-array coil. No anti-peristaltic agent or oral/rectal contrast agent was given before the exam. Non-contrast, T1W [repetition time/time to echo (TR/TE), 600/14 ms] and fat-suppressed T2W images (TR/TE 2863/90 ms) were obtained in the axial plane.

The MRI parameters were: 3 mm slice thickness, 1 mm inter-slice gap, Matrix size 330x265, and a field of view (FOV) of 35x35 cm.

DWI, which is a single-shot, spin-echo, echo-planar imaging, was acquired in the axial plane with the application of three gradients in three orthogonal planes. DWI parameters were: TR/TE of 4000/84 ms, Flip angle of 90°, slice thickness 5 mm, inter-slice gap 0.5 mm, Matrix size 256x256, FOV 40 cm and b-values of 0 and 800 s/mm^2.

0.2 mL/kg Gadoterate Meglumine was administered as intravenous contrast agent at a rate of 2 mL/s. Total scan time was approximately 25 minutes. The MR protocol is summarized in Table 1.

Analysis of MRI Images

The perianal fistula was evaluated using T1W, T2W, DWI and fat-suppressed post-contrast T1W sequences.

Table 1. MR protocol

Parameter	Oblique axial T1W TSE	Oblique coronal T2W TSE	Oblique axial T2W TSE	Axial DWI	Oblique axial 3D T1W GRE
TR/TE (ms)	600/14	2863/90	2863/90	4000/84	550/10
Bandwidth (Hz/pixel)	50	125	62.5	1628	520
Rectangular FOV (cm)	35	35	35	40	32
Slice thickness (mm)	3.5	3.5	3.5	5	2.6
Inter-slice Gap (mm)	1	1	1	0.5	1
ETL	3	28	30		4
NEX	1	1.5	1.5	4	2
Matrix	288x192	330x265	212x186	256x256	320x256
Phase encoding	AP	Transverse (RL)	Transverse (RL)	AP	S/I

MR: Magnetic resonance, T1W: T1-weighted imaging, DWI: Diffusion-weighted Imaging, GRE: Gradient-echo Imaging, TR/TE: Repetition time/time to echo, FOV: Field of view, ETL: Echo train length, NEX: Number of excitations

The images were reviewed by one radiologist with more than 17 years of experience in abdominal radiology and the following features were recorded: identification of the primary fistula tract with its internal opening; any secondary ramification(s); and any finding of inflammation or abscess. The appearance of a perianal fistula was defined as a linear or oval structure surrounded by an irregular area, hypointense to isointense on T1W and isointense to hyperintense on T2W images. An inflammation was defined as an area of increased signal intensity on T2W image and showing an ill-defined, diffuse post-contrast enhancement, whereas an abscess was identified as an area of diffusion restriction with irregular peripheral contrast enhancement (Figure 1A-E). Then the fistulas were classified according to the St. James's University Hospital.[15] The definition of fistulae according to St. James's University Hospital classification is: A grade 1 fistula is a simple linear intersphincteric fistula; a grade 2 fistula is a grade 1 fistula with a concomitant abscess or an additional fistulous tract; a grade 3 fistula traverses the external sphincter; a grade 4 fistula is a trans-sphincteric fistula with an abscess or an additional tract in the ischiorectal fossa; and a grade 5 fistula is a supralevator or translevator fistula.

An ADC map was generated automatically following the acquisition of DWI. The radiologist who was unaware of the clinical and post-surgical findings selected a slice which showed the most of the lesion compared to the other views and drew a circular region of interest (ROI) with a minimum area of 6 mm^2 on the ADC map (Figure 1B). Measured ADC values from the ADC map were recorded for each lesion. The positions of the ROIs were determined by reviewing both DW and fat-suppressed T2W images. If a patient had multiple lesions, all lesions were analyzed and the lowest ADC was recorded.

Reference Standards

Surgical findings were used as the gold standard for the assessment of active and inactive fistulae in 28 patients who underwent surgery. Fistulae were confirmed as active if pus was identified during surgery. Two patients who did not undergo surgery were evaluated based on findings of local clinical examination. When pus and or signs of inflammation (redness, pain, and swelling around the perianal fistula) were seen on local examination, the fistula was defined as active. Fistulae that did not reveal any of these signs or pus were defined as inactive.

At our institution a patient with signs and symptoms of a perianal fistula is routinely put on antibiotic treatment as a first-line therapeutic approach. If antibiotic therapy fails to be effective for healing, fistula surgery is contemplated. The decision for surgery (either open surgery or the use of setons) depends on the presence of several findings, including the presence of pus, clinical signs of active inflammation, elevated serum C-reactive protein levels (>2 mg/L), and no improvement of symptoms during medical treatment.

Definition of Active and Inactive Perianal Fistulae

Fistulae which needed surgical intervention within one week after the MRI examination, and which were confirmed to have inflammation during surgery, were defined as active. The time between surgery and MRI exam was constrained by a one-week interval to avoid inclusion of newly developed fistulae. Fistulae that did not need surgery within one week of the MRI examination, and lesions which were confirmed with an absence of inflammation during surgery, were defined as inactive.

The surgeon had access to MRI images and used MRI for the purpose of lesion localization only, rather than for the evaluation of disease activity.

Detection of Fistulae

The detection of a perianal fistula was evaluated on a 3-point scale from 0 to 2. Score 0: no visible fistula, 1: probable fistula, and 2: clearly visible fistula. To assess the diagnostic performance of DWI in the evaluation of a perianal fistula, the appearance of a fistula was scored on DWI, T2W, combined T2W-DWI images, and post-contrast T1W where the combined T2W-contrast enhanced MRI images were taken as reference for grading.[14,16]

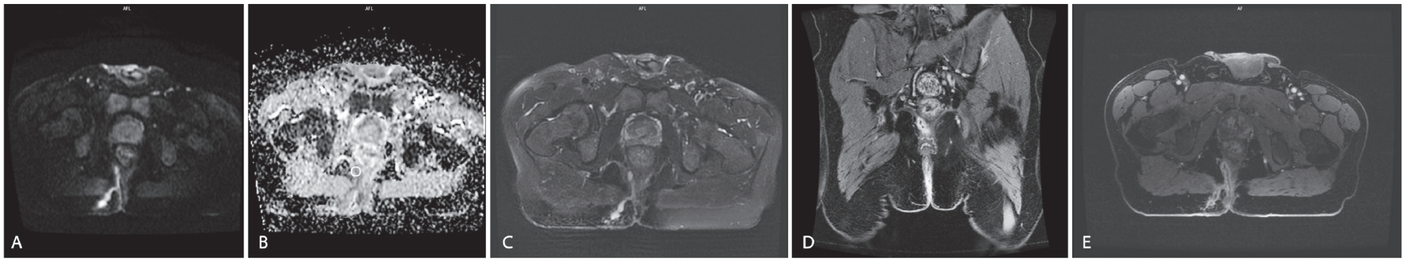

Figure 1. A) DWI of a grade 1 perianal fistula with increased signal along the fistula tract. B) ADC image of DWI showing decreased signal intensity within the fistula lumen, consistent with diffusion restriction and thus inflammatory pus. The circle denotes the position of the ROI, which measured a mean ADC of 0.910x10-3 mm2/s. The fistula was classified active. C) Fat-suppressed T2W of the same fistula with high signal of the fistula lumen against a background of low signal. D, E) Post-contrast coronal and axial T1W images showing intense mural contrast enhancement of the fistula tract
DWI: Diffusion-weighted imaging, ADC: Apparent diffusion coefficient, ROI: Region of interest, T2W: T2-weighted, T1W: T1-weighted

Statistical Analysis

Kolmogorov-Smirnov tests were used to test if the distribution of ADC values of two different groups (i.e. active and inactive) conformed to a normal pattern. ADCs of both groups were compared using an unpaired t-test. If a significant difference in ADCs between both groups was found, additional receiver operating characteristic (ROC) curve analysis was conducted to calculate the area under the curve and the optimal cut-off ADC with corresponding sensitivity, specificity, positive predictive value, and negative predictive value. A p values smaller than 0.05 were considered statistically significant. Statistical analyses were done using SPSS, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

This retrospective, cross-sectional study included 30 patients, (18 men and 12 women). The mean ± standard deviation (SD) age was 35±1.4 years. Twelve (40%) out of 30 patients had more than one fistula with a total of 42 perianal fistulae in all patients. Twenty-one patients (70%) had 31 active fistulae and nine patients (30%) had 11 inactive fistulae. In 17 patients (56.7%) secondary branch-offs from the primary fistula tract were present. Horseshoe-appearing fistula was found in three patients (10%). Abscess formation adjacent to the perianal fistula was seen in 11 patients (36.7%). According to SJUH classification, there were 22 grade 1, 12 grade 2, and eight grade 3 fistulae. The patient characteristics of the study population are shown in Table 2.

Table 2. Patient characteristics of the study group

Mean ± SD age, (years)	35±1.4
Gender n (%)	
Female	12 (40)
Male	18 (60)
Fistulae	
Total	42
Inactive	11 (26.2%)
Active	31 (73.8%)
Secondary tracts	17 patients
Horse-shoe	3 patients (10%)
Abscess formation	11 patients (36.7%)
Fistula classification	
Grade 1	22 (52.4%)
Grade 2	12 (28.6%)
Grade 3	8 (19.0)

SD: Standard deviation

ADC Values of Perianal Fistulae

ROI placement within the perianal fistula is shown in Figure 1B for active and inactive fistulae. Mean size of ROIs used for ADC measurements was 10.3 mm^2 (range: 6-18.2 mm^2). The mean ± SD ADC value of active perianal fistulae was 0.919±0.165x10^{-3} mm^2/s and that of inactive fistulae was 1.235±0.220 x10^{-3} mm^2/s. Although the boxplot of mean ADC values of active and inactive fistulae shows some overlap between the two groups there was a statistically significant difference between them with a p-value of 0.0035 (Figure 2).

The area under the ROC curve (AUC) was 0.725. A cut-off mean ADC value of 1.005x10^{-3} mm/s to differentiate an active fistula from an inactive one yielded a sensitivity of 84%, a specificity of 71.5%, a positive predictive value of 84.5%, a negative predictive value of 71.2%, and a diagnostic accuracy of 79.93% (Table 3, Figure 3).

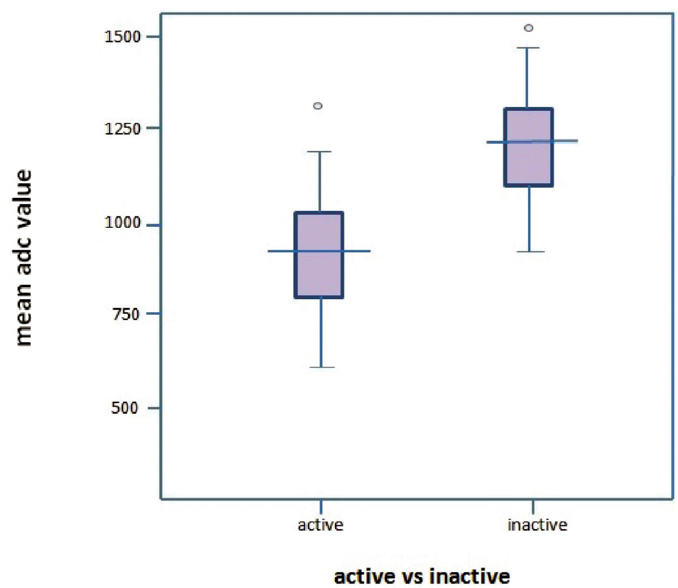

Figure 2. Boxplot showing the range of distribution of the mean ADC values of active and inactive perianal fistulae
ADC: Apparent diffusion coefficient

Detection of a an Active vs Inactive Perianal Fistula on DWI, T2W, and Post-Contrast MRI

Of 42 perianal fistulae in 30 patients, 33 perianal fistulae (76.2%) were clearly identified (score 2) on DWI, compared to 40 fistulae (88.1%) on T2W, 41 fistulae (95.2%) on combined DWI-T2W, and 41 fistulae (90.5%) on post-contrast MRI. In nine patients, a fistula was probably present (score 1) on DWI compared to two patients on T2W, one inactive fistula on post-contrast MR and one inactive fistula on combined DWI-T2W. The detection scores on DWI did not differ significantly from that of T2W (p=0.347) and both were less than the detection score of combined DWI-T2W. However, the detection scores of active perianal fistulae on DWI were significantly different from that of inactive fistulas (p=0.0035) whereas the detection scores on T2W, contrast-enhanced MRI, and combined DWI-T2W did not show any statistically significant difference between the active and inactive fistulae (Table 4).

Discussion

Following antibiotic treatment, a perianal fistula may not heal completely and remain active exhibiting ongoing inflammation. In these cases surgical excision of fistulous tracts and drainage of any associated abscess with preservation of the anal sphincteric complex becomes the primary treatment.[16] Postoperative recurrence of a fistula is usually caused by failure to treat or detect an active (inflamed) fistula and/or abscess at the time of surgery.[17] Preoperative detection of an active fistula is therefore important to prevent this recurrence. Our study results showed that MRI using DWI can differentiate an active perianal fistula from an inactive one. In particular, ADC values measured from the fistula helped to identify an active fistula.

The detection rate of fistula by preoperative MRI has been reported to be around 86-88% when surgical findings are taken as reference.[7,18] T2W sequence, with and without fat-suppression, and contrast-enhanced T1W sequence are usually used for the initial evaluation of a perianal fistula. The added value of DWI in diagnosing perianal fistula was studied by Hori et al.[19] who found that the confidence scores of the combinations of DWI and TW sequence and of contrast-enhanced and T2W were statistically significantly greater than those with T2W images alone (p=0.0047 and p=0.014, respectively). Similarly, Mohsen and Osman[13] and Boruah et al.[14] reported higher detection rates of fistulae with the combined use of DWI-T2W images compared to T2W, DWI and post-contrast T1W images alone. However, Baik et al. [20] suggested that the performances between combined DWI-T2W images and contrast-enhanced MRI to detect a perianal fistula were comparable.

DWI depicts increased signal in areas with high cellular density, such as in abscess formation and inflammatory processes.[21] So the role of MRI has not only been investigated for the detection of fistulae, but also to evaluate the activity of the fistula owing to its ability to depict signal in areas.[22-24] Liu et al.[25], studied the role of preoperative DWI to predict the activity of perianal fistulae. They found that the ADC value of a perianal fistula was inversely proportional to the activity of the anal fistula. They concluded that the lower the ADC value of a preoperative fistula, the more likely the fistula will recur after surgery.[25] Similarly, the results of a study conducted by Boruah et al.[14] suggested preoperative

Table 3. Diagnostic performance of ADC cut-off values

Criteria (cut-off ADC value)	Sensitivity (%)	Specificity (%)
≤0.912	68	98
≤1.105	84	71.5
≤1.190	89	62

ADC: Apparent diffusion coefficient

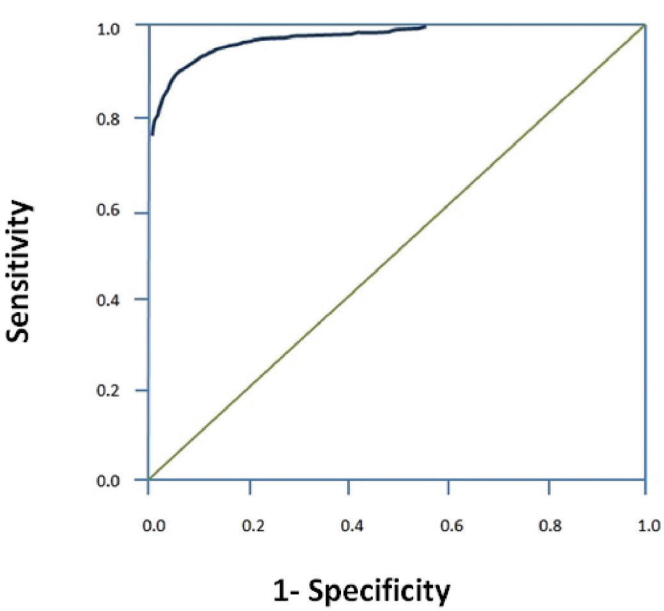

Figure 3. Receiver operating characteristic curve of the mean apparent diffusion coefficient values for perianal fistulae

Table 4. Distribution of detection scores according to MRI sequences

Sequence	Detection score	Total number (n=42)	Active fistula (n=30)	Inactive fistula (n=12)	p
Contrast-enhanced MR	Score 2	41	31	10	0.060
	Score 1	1	0	1	
	Score 0	0	0	0	
T2W	Score 2	40	28	13	0.390
	Score 1	2	1	1	
	Score 0	0	0	0	
T2W-DWI	Score 2	41	30	11	0.450
	Score 1	1	0	1	
	Score 0	0	0	0	
DWI	Score 2	33	27	6	0.0035
	Score 1	9	4	5	
	Score 0	0	0	0	

DWI: Diffusion-weighted imaging, T1W, T2W: T1-weighted, T2-weighted, MR: Magnetic resonance

DWI may predict the activity of a fistula as the ADC values obtained from patients with active fistulae in their study were significantly lower than the ADC values obtained from inactive fistulas. They also found an ADC cutoff of 1.105 $x10^{-3}$ mm^2/s which differentiated active from an inactive fistula with a sensitivity of 87.5% and specificity of 73.3%.[14] Yoshizako et al.[26] also showed that ADCs of active fistulae were significantly lower than those of the inactive group; however, they also reported that a significant overlap between the two groups existed. It has been suggested that the overlap between active and inactive fistulae may be caused by various factors, such as variable viscosities of the pus found within the inflammatory area of a fistula, which, in turn, affected the measured ADC value.[14] Furthermore, the viscosity of the fistula pus may change over time, as seen in abscesses elsewhere outside the perianal area.[27] Finally, fibrosis that develops over time at and around the fistula tract may also lower the measured ADC value, resulting in overlapping of ADC values of active and inactive fistulae. Nevertheless, our study results showed that a cutoff of 1.005 $x10^{-3}$ mm/s ADC can be used to differentiate between active and inactive fistulas, which is comparable to other studies.[14,26]

Baik et al. [20] suggested that the performance of combined DWI-T2W images and contrast-enhanced MRI to detect a perianal fistula were comparable. Moreover, considering the added ability of DWI to assess the activity of a fistula, it appears reasonable to use DWI in evaluating a perianal fistula, especially in patients with contraindication to contrast agents, as DWI obviates the use of contrast agents. DWI is also a widely available sequence in most MRI scanners with a short scan time (approx. 2 min 30 sec in our MR unit).

Study Limitations

Our study has some limitations. The retrospective nature of the study with its small number of subjects prevents generalization of the conclusion, so studies with larger number of subjects are needed. Second, the use of antibiotics before the MR examination may have affected the fistula activity in the intervening duration. So the results of this study may only be applicable to this particular patient population and may not be generalized. However, as all patients received antibiotics any patient selection bias was avoided. Third, only two b-values (0 and 800 s/mm^2) were used for ADC calculation. To increase the accuracy of the measured ADCs and the calculated ADC cut-off, studies implementing more b-values can be conducted in the future. Finally, the ADC measurements were performed by one radiologist. A study with more observers where a kappa value assessing inter-observer agreement can be calculated may increase the accuracy and reliability of the results.

Conclusion

The present study showed that the ADCs measured from active and inactive perianal fistulae differ significantly in patients who were all on antibiotic treatment. Therefore, DWI may be used to evaluate the activity of a perianal fistula and identify patients with a higher likelihood of recurrence.

Ethics

Ethics Committee Approval: This study was approved by the Haydarpaşa Numune Training and Research Hospital Ethics Committee (approval number: E-62977267-771, date: 25.01.2022).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

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