

Role of Diffusion-Weighted MRI in Colorectal Cancer

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Abstract

Background: To reveal the adding value of diffusion-weighted Magnetic Resonance Imaging (MRI) in the detection and differential diagnosis of the colorectal cancer, comparing the results of Apparent Diffusion Coefficient (ADC) value with histopathological studies.

Aim of Study: The aim of the study was to determine the effectiveness of MRI in the diagnosis of colorectal cancers and to reveal the adding value of DWI in the detection and differential diagnosis of the colorectal cancer, comparing the results of ADC value with histopathological studies.

Material and Methods: Fifteen patients with suspected colorectal cancers clinically, endoscopically or by CT and US images were included in this study. All cases have been evaluated with 1.5 MR scanner. In addition to the conventional sequences (T2-axial, sagittal and coronal weighted images (WI), axial T2 STIR, T1 WI and a Diffusion-Weighted Images (DWI) with 4 different b-values (0, 400, 600 and 1000s/mm² and ADC maps were obtained then the results have been compared to histopathological diagnosis.

Results: All cases of malignant colorectal cancer showed high signal (restricted diffusion) on DWI. Receiver Operating Curve (ROC) analysis of ADC values yielded an Area Under Curve₅(AUC₅) of 0.912, setting a threshold ADC value of $<1.1 \times 10^{-3}$ mm²/sec yielded a sensitivity of 82.8% and specificity of 100% in detecting the malignant colorectal masses.

Conclusion: DWI with high b-values and ADC value is a feasible method and has the potential to be effective in detection of colorectal cancer.

Key Words: Colonic cancer – MRI – DWI – Apparent diffusion coefficient (ADC).

Introduction

COLORECTAL Cancer (CRC) is the third most common cancer in the United States in both men and women and it is very common in Egypt. About 65% of CRC are distal to the splenic flexure and potentially detectable by the sigmoidoscopy. Con-

trariwise, 35% of CRC are proximal to the sigmoid and not detectable by the sigmoidoscopy. About 20% to 25% are presented with Dukes D colon cancer with identifiable distant metastases [1]. MRI is considered one of the most accurate and sensitive diagnostic tools for the detection of CRC and its loco-regional spread.

Diffusion-Weighted MRI (DWMRI) is becoming increasingly important in the assessment of malignant tumors [2,3]. It is generally accepted that DW-MRI enables noninvasive characterization of biologic tissues on the basis of their water diffusion properties [4].

By performing DWI using different b-values, quantitative analysis is possible with the calculation of the ADC, measured in mm²/sec. Areas of restricted diffusion show low ADC values. ADC values are inversely correlated with tumor cellularity and reductions in ADC correlate with response to cytotoxic therapy.

Moreover, DWI has been shown to be feasible as an early marker of treatment response because cell death and vascular alterations typically occur before size changes. Increases in ADC values with treatment reflect decreases in cellularity and thus provide indirect assessment of chemotherapy induced cell death [5].

Patients and Methods

Study population:

During a period of 16 months between May 2014 and September 2015, a prospective observational study was applied on a total of 15 patients with suspected colorectal cancers either clinically, endoscopically or by CT and US images were found in our institution and were included in this study. The selected sample was obtained from the

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Department of Surgery, Unit of Endoscopy and the MRI Unit at Assiut University Hospitals.

Inclusion criteria:

Patients in different ages with suspected colorectal cancers clinically, endoscopically or by CT and US images were included in this study.

Exclusion criteria:

- 1- Prior biopsy.
- 2- Any general contraindication of MRI as presence of any paramagnetic substance as pacemakers or those with claustrophobia; and
- 3- Severely ill patients or inability of patients to cooperate when performed MR imaging.

Each patient was subjected to the following:

A- Radiological assessment: MRI abdomen and pelvis:

The standard MRI protocol performed for all patients was as follows: MRI examination was performed using a 1.5 Tesla MR Imager scanner (Achieva; Philips Medical Systems) using abdominal phased array Torso coil in the supine position. The following sequences were obtained:

- 1- Coronal turbo spin-echo T2-weighted image: Repetition time (TR) 526ms, Echo time (TE) 80ms, slice thickness 5mm, Field of View (FOV) 425mm, matrix 304 X 264, Flip Angle (FA) (900) and Acquisition time 1:06min.
- 2- Axial turbo spin-echo T2-HR weighted image: TR 1670ms, TE 100ms, slice thickness 5mm, FOV 375mm, matrix 400 X 224, FA (900) and Acquisition time 4:03min.
- 3- Sagittal turbo spin-echo T2-weighted image: TR 526ms, TE 80ms, slice thickness 5mm, FOV 425mm, matrix 304 X 264, FA (900) and Acquisition time 1:06min.
- 4- Axial T1 FFE-weighted image: TR 260ms, TE 46ms, slice thickness 5mm, FOV 375mm, Matrix 240 X 118, FA (800) and Acquisition time 15sec.
- 5- Axial T2-STIR weighted sequence: TR 768ms, TE 80ms, slice thickness 7mm, FOV 273mm, Matrix 304 X 209, FA (900) and Acquisition time 2:36min.
- 6- DWI, an axial single shot echo-planar pulse sequence with 4 different b-values (0, 400, 600 and 1000s/mm²) was acquired with a single breath-hold without requiring the injection of paramagnetic contrast. ADC map performed and ADC value measured. TR 1348ms, TE 65ms, slice thickness 7mm, FOV 375mm, matrix 124 X 100, FA (900) and Acquisition time 2:36min.

B- Biopsy: The results have been compared to histopathological diagnosis:

Data analysis and image interpretation:

MR imaging analysis:

MR images were analyzed for the following:

- 1- Site, size and signal intensity of the mass.
- 2- Infiltration of the perilesional fat planes.
- 3- Infiltration to the surrounding structures.
- 4- Presence of enlarged regional lymph nodes.
- 5- Presence or absence of distant metastasis and their sites.
- 6- Associated other MRI findings as ascites.

Interpretation of DWI:

Qualitative analysis:

Evaluation of the signal intensity: The mass may show one of the following appearances:

- Low signal intensity on diffusion images with low signal in the corresponding ADC maps (facilitated).
- High signal intensity on diffusion images with lowering of the signal in the corresponding ADC maps (restricted).

Quantitative analysis:

Regarding the quantitative analysis of DWI, we generated the ADC map data on the work station. ADC values from the mass were measured using the largest possible Region of Interest (ROI) for each patient (about 37cm²). The ADC measurements were repeated three times with different ROI's placed in a different part of the mass. The average of these measurements was calculated.

Statistical analysis:

Data were checked, entered and analyzed using computer programs Microsoft Excel 2010 and statistical program for social science, Version 15 (SPSS Inc., Chicago, Illinois, USA) as follows: Description of quantitative variables as range, mean, Standard Deviation (SD), median, frequencies (number of cases) and percentages when appropriate; description of qualitative variables as number and percentage, Sensitivity, specificity, accuracy, predictive values of positivity and negativity of MRI study and DWI were recorded. *p*-values < 0.05 was considered statistically significant.

Results

Fifteen patients (6 males and 9 females patients with ages ranging from 25 to 66 years and average age of 47.6 years) were included in our study.

In our study, the most common risk factor for CRC among the patients is family history of CRC by percent of (20%).

According to (Table 1), the most common location of colorectal mass among our patients is (the recto-sigmoid region) with the liver presenting the most common site of CRC metastasis.

According to (Table 2), the most common histopathological subtype of colorectal mass among our patients is (the moderately differentiated adenocarcinoma) with percent of (53.3%).

Distribution of patients as regards histopathological diagnosis was as follows 12 patients were positively diagnosed (80%) and 3 patients was negatively diagnosed (20%).

Diffusion weighted image and ADV values:

According to exhibit of MRI-DWI of colorectal masses in our study, we found significant change in signal intensity of colorectal masses-either benign or malignant-on DWI which is statistically significant as shown in (Table 3).

The mean ADC values of the benign and malignant colorectal mass in ADC maps were compared by independent *t*-test and showing statistically significant in ADC as illustrated in (Table 4) and Fig. (1).

Receiver Operating Characteristic (ROC) analysis was used to calculate the Area Under the Curve (AUC) for determining a threshold ADC value that best separated the benign and malignant masses while maximizing average specificity and sensitivity.

The ADC value could significantly differentiate the malignant colorectal masses with cut off value <1.1 at a sensitivity of 82.8% and specificity of 100% (Table 5) and Fig. (2).

Table (1): Show location of the colorectal mass, distant metastasis and site of these metastases.

	No.	%
<i>Mass location:</i>		
Colon	2	13.3
Rectum	1	6.7
Ano-rectum	3	20.0
Sigmoid	3	20.0
Recto-sigmoid	6	40.0
<i>Metastatic:</i>		
Yes	4	26.7
No	11	73.3
<i>Site of metastasis:</i>		
Liver	3	20.0
Lung	0	0.0
Peritoneal deposit	1	6.7
Vertebral body	1	6.7

Table (2): Show the histopathological results of colorectal masses in our study.

Histopathology	No.	%
Chronic inflammation	3	20.0
Mod. diff. adenocarcinoma	8	53.3
Poorly diff. adenocarcinoma	3	20.0
Mucinous	1	6.7

Table (3): Comparison between MRI-DWI in benign and malignant colorectal masses.

	Benign (n=3)		Malignant (n=12)		<i>p</i> -value
	No	%	No	%	
<i>DWI b 150:</i>					
Facilitated	2	66.7	0	0	0.002**
Restricted	1	33.3	12	100	
<i>DWI b 500:</i>					
Facilitated	2	66.7	0	0	0.002**
Restricted	1	33.3	12	100	
<i>DWI b 1000:</i>					
Facilitated	2	66.7	0	0	0.002**
Restricted	1	33.3	12	100	

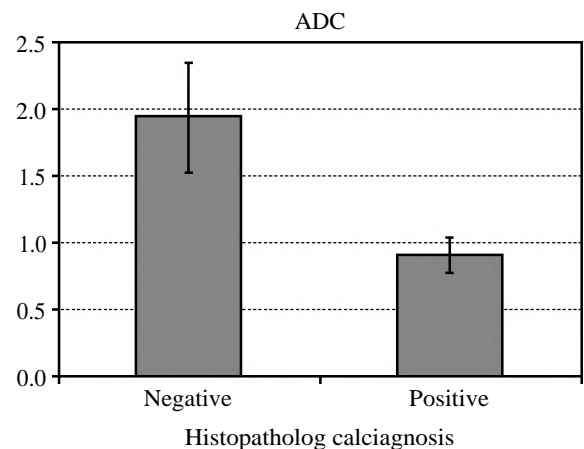


Fig. (1): Graph show relation between histopatho logical diagnosis and ADC.

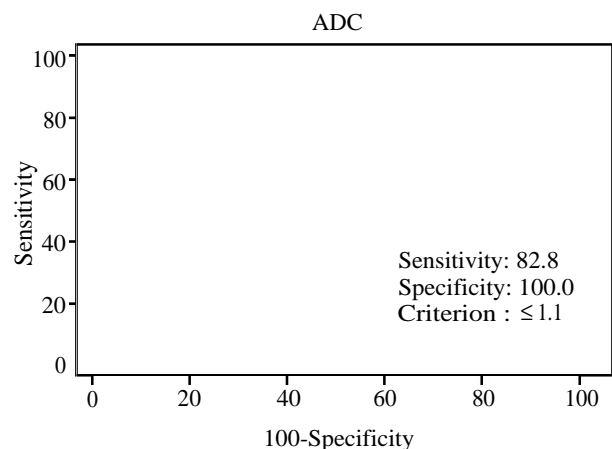


Fig. (2): Diagram show ROC curve of ADC value for cut off to histopathological diagnosis.

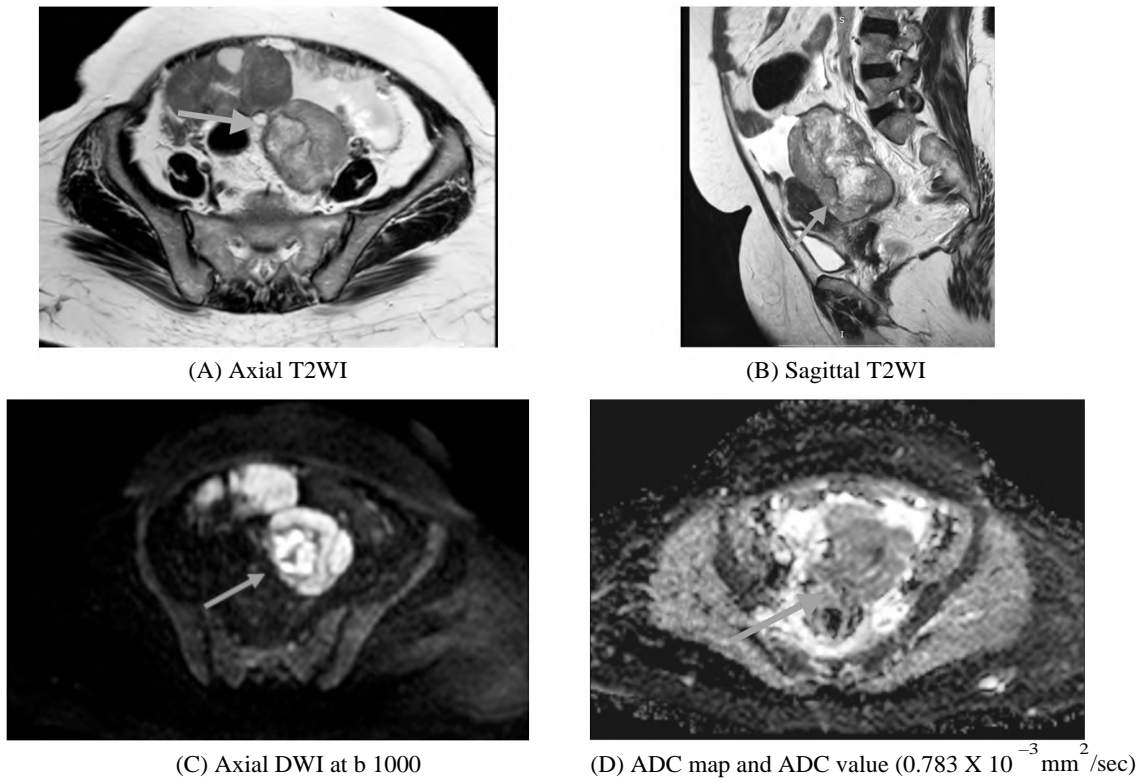


Fig. (3): Female patient, 55 years old, presented by bleeding per rectum. (A,B) Images show heterogenous intensity soft tissue mass involving the rectosigmoid region in term of diffuse circumferential annular thickening with multiple peritoneal deposits and mild ascites, (C,D) Images show restricted diffusion at the above-mentioned rectosigmoid mass with ADC value= $0.783 \times 10^{-3} \text{ mm}^2/\text{sec}$. The histopathological diagnosis was Adenocarcinoma Grade II.

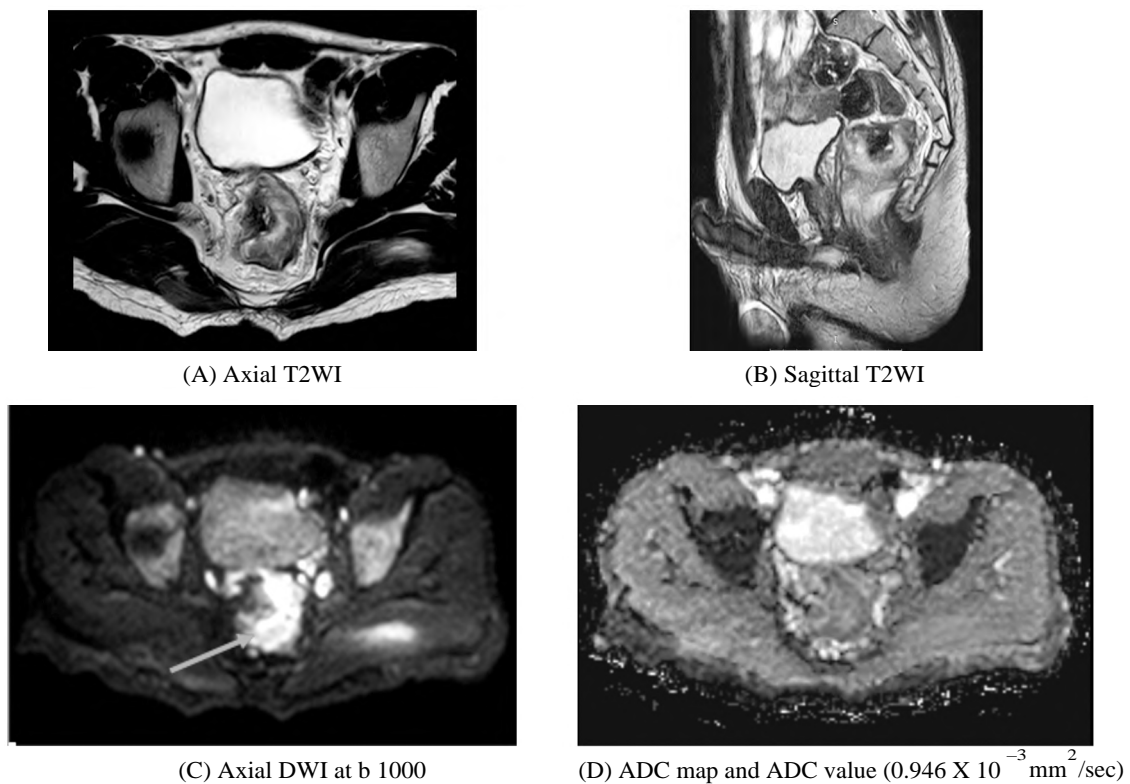


Fig. (4): Male patient, 30 years old, presented by intestinal obstruction and constipation. (A,B) Images show anorectal mass with infiltration of perirectal fascia and deep pelvic, iliac, obturator and inguinal lymph nodes. (C,D) Images show restricted diffusion at the above-mentioned anorectal mass with ADC value= $0.946 \times 10^{-3} \text{ mm}^2/\text{sec}$. The histopathological diagnosis was moderately differentiated mucinous carcinoma.

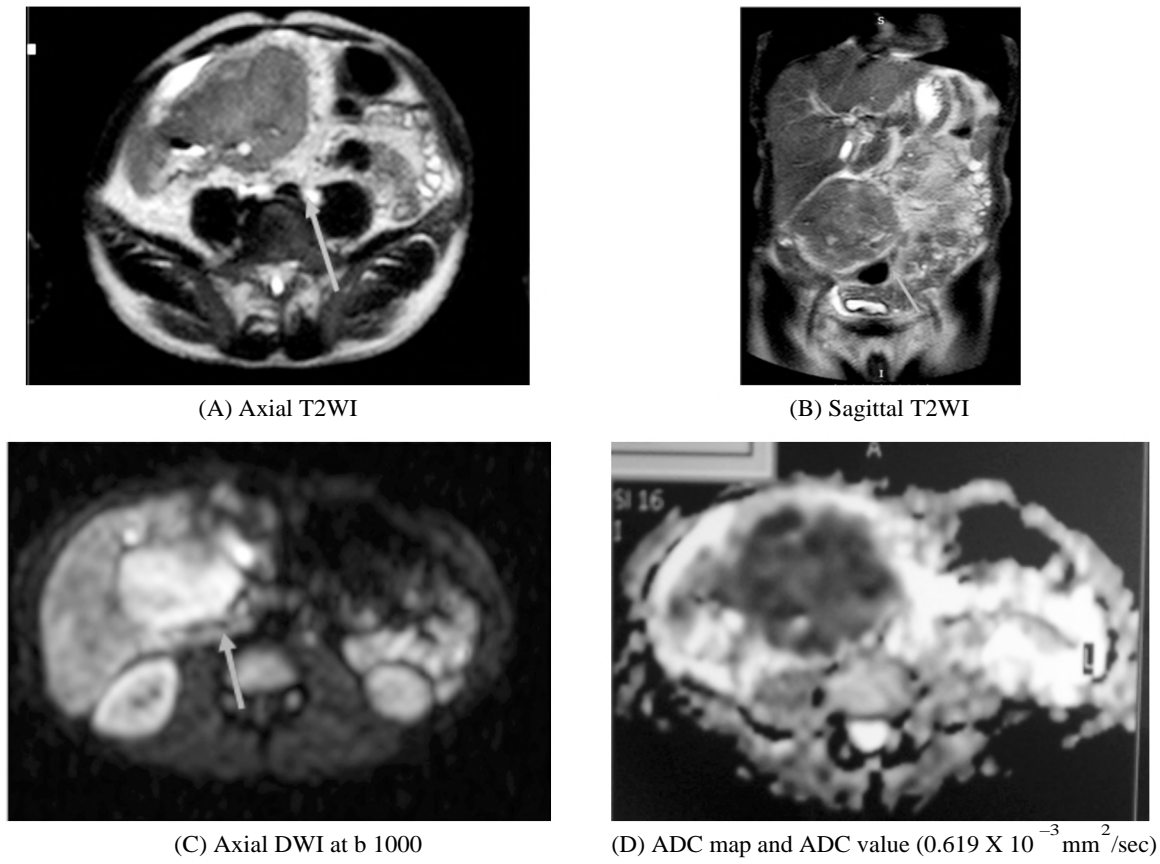


Fig. (5): Male patient, 50 years old, presented by Anaemia and right hypochondrial mass. (A,B) Images show hypoechoic mass measures 11 X 13cm affecting hepatic flexure and proximal transverse colon with infiltration of surrounding fat planes. (C,D) Images show restricted diffusion at the above-mentioned hepatic flexure mass with ADC value=0.619 X 10⁻³ mm²/sec. The histopathological diagnosis was poorly differentiated adenocarcinoma.

Table (4): Comparison between positive and negative histopathological diagnosis as regards ADC.

	Histopathological diagnosis		t-test	
	Negative	Positive	t-test	p-value
ADC, mean ± SD	1.93±0.41	0.91±0.13	7.23	<0.001**

** : Statistically significant difference (p-value <0.05).

Table (5): Cut off value, sensitivity, specificity, PPV, NPV and accuracy of ADC to predict histopathological diagnosis.

	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
ADC	0.912	≤1.1	82.8	100.0%	100.0%	60.0	86.7

PPV: Positive Predictive Value.
NPV: Negative Predictive Value.

Discussion

Rectal cancer is considered as one of the most common malignant tumors of the gastrointestinal tract. It is considered the third most common cancer in both men and women [6]. In addition it is considered to be one of the most common tumors in developed countries [7].

DW-MRI is a functional imaging technique that yields qualitative and quantitative information and provides unique insights regarding tumor cellularity, integrity of cell membranes, and microcirculation. The motion of water molecules is more restricted in tissues with a high cellular density that are associated with numerous intact cell membranes (e.g., tumor tissue). ADC, which are quantitative expressions of diffusion characteristics of tissues, tend to decrease in diffusion restricted areas, whereas diffusion Signal Intensity (SI), which is the qualitative parameter of diffusion, increases in those areas [8].

Our study included a total of 15 patients with suspected colorectal cancers either clinically, endoscopically or by CT and US images. In our study, all patients were subjected to clinical and laboratory assessment. For full evaluation of the pelvis we used axial and sagittal T2WI, Axial T2-STIR, Axial T1WI and DWI. Coronal T2WI was also done for evaluation of the whole abdomen. These sequences were also used by Sun YS & colleagues [9].

In our study, we correlated the DWI findings and the ADC values with the histopathological

results in predicting the malignant colorectal masses. A study done by Kaur et al., studied the correlation between established DWI with the histopathological findings [7].

In our study, the most common risk factor for CRC among the patients is family history of CRC by percent of (20%); this is in agreement with the study done by Thoeny HC et al., [3].

In the present study, the most common location of colorectal mass among our patients is (the rectosigmoid region) with the liver presenting the most common site of CRC metastasis. This is reported by Mayer RJ [6].

Statistical significant difference was found between the mean ADC values of the benign and malignant colorectal masses in ADC maps which were compared by independent *t*-test. Same results were mentioned by Kim DJ & colleagues [10].

In our study, significant change was found in signal intensity on DWI of colorectal masses-either benign or malignant-which is statistically significant. This is similar to the results reported by Song & Colleagues [11].

The results of current study showed that using histopathology for diagnosis of Colorectal Cancer regarding to comparison between positive and negative histopathological diagnosis versus ADC revealed a statistical significant difference at *p*-value <0.01. This result revealed the accuracy of ADC in diagnosis of colorectal cancer which is in agreement with study done by Marouf et al., as their study reported that correlation of ADC with histopathological results revealed an accurate diagnosis of the tumor. So this finding reflected that ADC values may indeed be a powerful prognostic indicator during the assessment and treatment of colorectal cancer [12].

ROC analysis of ADC values yielded an AUC of 0.912, setting a threshold ADC value of $<1.1 \times 10^{-3} \text{ mm}^2/\text{sec}$ yielded a sensitivity of 82.8% and specificity of 100% in detecting the malignant colorectal masses.

Similar results reported by Kilickesmez O et al., with cut-off value for carcinomas of $1.14 \times 10^{-3} \text{ mm}^2/\text{s}$ yielded a sensitivity and specificity of 93.3% and 93.3%, respectively [13].

A study reported by Afifi & colleagues showed that addition of DWI to the conventional MR images lead to increased sensitivity and specificity compared to the use of conventional MRI (T2WI only) 96.1% and 100% respectively. PPV was

100%, NPV was 80% and accuracy for detection was 96.6% [14]. In addition to similarity results were reported by Haider et al., and Kumar et al., as both of studies revealed the improvement of imaging when combined with DWI due to improving of sensitivity level from 54% to 81% [15,16].

Conclusion:

DWI with high b-values and ADC value is a feasible method and has the potential to be effective in detection of colorectal cancer.

Conflicts of interest:

There are no conflicts of interest.

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دور الرنين المغناطيسي في خاصية الانتشار في سرطان القولون والمستقيم

إن استخدام تقنية الرنين المغناطيسي بخاصية الانتشار قد بات أداة هامة في تشخيص الأورام المختلفة، ولا سيما في تشخيص أورام القولون والمستقيم الخبيثة. وقد أصبح الإعتماد على هذه التقنية متزايد في الآونة الأخيرة نظرا لأنها أداة تعتمد على الرنين المغناطيسي والتي لا تخترق الأنسجة مقارنة بأخذ عينات من الأنسجة لتحليلها باثولوجيا.

وتعتمد هذه التقنية على قياس خصائص الأنسجة البيولوجية نتيجة إنتشار الماء من نسيج إلى آخر. كما أنها تستطيع التمييز بين الأنسجة الحميدة والأخرى الخبيثة نتيجة لإختلاف خصائص إنتشار الماء طبقا لإختلاف تركيب النسيج الناتج عن الورم.

الهدف من الدراسة: في هذه الدراسة نحاول تقييم دور الرنين المغناطيسي باستخدام خاصية الانتشار في تشخيص أورام القولون والمستقيم الخبيثة، وإمكانية التفرقة بينها وبين الأورام الحميدة.

وقد إشمطت هذه الدراسة على ١٥ مريض وقد تم عمل رنين مغناطيسي وتصوير باستخدام خاصية الانتشار ولقد تم تحليل البيانات وقد قورنت النتائج بالتحليل الباثولوجي للأنسجة.

وقد وجد إرتباط قوى بين معامل الانتشار الظاهر لخاصية الانتشار ونتائج تحليل الأنسجة باثولوجيا في قياس شدة إلتهاب البنكرياس.

من دراستنا نستنتج أن التصوير بالرنين المغناطيسي وخاصية الانتشار بإمكانه تشخيص حالات أورام القولون والمستقيم الخبيثة وتفرقتها من الأورام الحميدة.