The role of magnetic resonance imaging and magnetic resonance diffusion weighted image in preoperative staging of rectal cancer in comparison to postoperative histopathology

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Abstract

Background: With outstanding soft tissue contrast, functional imaging capabilities, and multiplanar capacity, high-resolution phased-array magnetic resonance imaging MRI is considered as a basic imaging modality for preoperative local staging of rectal cancer. And so MRI fills a void in clinical practice by allowing for precise local staging of rectal cancer prior to treatment decisions. The diffusion-weighted image used as enhancing utility for MRI in patients with rectal cancer.

Objectives: The aim of work was to assess the role of MRI imaging including the (diffusion weighted imaging DWI and Apparent diffusion coefficient ADC map) in preoperative rectal cancer staging, in comparison to post-operative histopathology.

Patients and methods: A total of 50 patients were included in the study, presented to South Valley University hospital and underwent MRI examination in MRI unit at South Valley University hospital.

Results: Regarding the circumferential resection margin (CRM) infiltration, MRI diagnosed CRM involvement in 15 cases while rest 35 cases showing free CRM. From these positive cases only 13 were truly positive with histopathology, other two cases proved to be positive with histopathology not diagnosed by MRI. MRI showed MRF infiltration in only 18 cases. Histopathological assessment showed that MRF infiltration in only 15 cases and the rest 35 cases showing free MRF (agreement 83.3%).

Conclusion: The results of this study demonstrate that preoperative MRI has a great value in achieving the best treatment strategy through accurate staging of rectal cancer, prediction of negative CRMs and involvement of the perirectal and pelvic LNs.

Keywords: Diffusion-Weighted Image, Magnetic Resonance Imaging, Rectal Cancer , Histopathology.

Introduction

The third most frequent cancer on the world is colorectal cancer with 30-40 % of its cases represented in rectum , making it , cancer rectum alone , accounting for 5 % of over all malignant tumors and ranking it as the fifth most prevalent cancer **(Siegel et al., 2020).**

Rectal cancer is known as a tumor with an aboral margin evaluated with a rigid rectoscope that is 16 cm or less from the anal verge and is classified as such. This distance is used to divide rectal cancer into three categories: tumors in the upper third (12–16 cm), tumors in the middle third (6–12 cm), and tumors in the lower third (less than 6 cm).

cancer has many risk factors including polyposis syndromes, inflammatory bowel disease, and a nutritional imbalance between fat, protein, and fiber are all risk factors **(Haggar and Boushey, 2009).**

In recent years, the current trends in the treatment of rectal cancer have pointed toward a more general recognition of neo adjuvant pre-operative therapies as a viable option for patients. As a result, there is an increasing demand for noninvasive preoperative imaging tools to identify high-risk patients who may benefit from more aggressive multimodality therapy regimens **(Yu et al., 2019).**

As a result of its excellent high-contrast soft-tissue resolution and the possibility to depict in great detail the anatomy of the rectal wall, peri rectal tissues, and pelvic organs, MRI has proven to be a fundamental strength, which has been most evident since the introduction of thin section high resolution imaging patterns **(Taylor et al., 2014).**

In addition to giving precise anatomical information, MRI has recently demonstrated the potential for diffusion weighted imaging (DWI) to be used as an additional tool in the staging of primary rectal cancer as well as post operative local cancer recurrence in patients with primary pelvic malignancy **(Figueiras et al., 2010)**.

The technique called DWI evaluates the random Brownian motion of water molecules, which is reliant on the features of the tissue, such as cell density, cell membrane integrity, blood vessel density, and the viscosity of extracellular fluid. There is no need for contrast media or ionizing radiation to measure or express these qualities, which are quantified and reported as an apparent diffusion coefficient (ADC) **(Thoeny and Keyzer, 2007).**

For all that, MRI imaging is supposed to be the modality of choice for accurate staging of rectal cancer. It has high soft tissue contrast resolution providing excellent information regarding the site and size of tumor, the depth of mural and extramural tumor spread, involvement of the circumferential resection margin, the extent of any sphincteric involvement, extramural vascular invasion (EMVI), lymph nodes spread and overall tumor staging **(Arya et al., 2020).**The aim of this work was to assess the role of MRI imaging including the (DWI and ADC map) in preoperative rectal cancer staging, in comparison to post-operative histopathology.

Patients and methods

There were 50 participants in the study presented to South Valley University hospital and underwent MRI examination in MRI unit at South Valley University hospital.

Prior diagnosis of cancer rectum in these patients was already established based on their symptomatology, clinical examination, proctoscopy and biopsy. no criteria for age predication. no criteria for sex predication

Inclusion criteria

Already diagnosed cancer rectum by proctoscopy and biopsy.

All patients have been histological proved rectal cancer and were not treated with neoadjuvant chemo/radiotherapy. Histopathological findings used as gold slandered (specimens obtained at surgery, laparoscopy, laparotomy, LN biopsy). Sufficient data were presented to construct agreement with absolute numbers of positive and negative findings compared with the reference standard for invasion of the submucosa, muscularis propria, perirectal tissue, adjacent organs or lymph node involvement (perirectal or distant LNs).

Exclusion criteria: Non-neoplastic rectal masses, cases with neoadjuvant chemo/radiotherapy and cases with previous rectal cancer surgery.

Methods:

Each patient subjected to: Detailed past history, with particular emphasis on the history of the current disease, which may be indicative of rectal cancer, such as constipation and the existence of fresh blood in the stool.

Laboratory evaluation of renal function test to allow safe intravenous contrast medium injection.

All patients with proved rectal cancer were subjected to pelvic MRI examination performed on 1.5T magnet with pelvic phased array coil. All the cases interpreted with the reader being blinded by the results of the histopathology in order to find accuracy of the MRI in staging.

Statistical Analysis: all the Data statistically described in the term of mean ± standard deviation (± SD), as well as median and range, or in frequencies (number of cases) and the percentages when appropriate. All statistical calculations were done using the SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) software, release 25 for Microsoft Windows 7. For all the results significant P value considered with $P < 0.05$.

Results:

All the patients were histopathological proven to be rectal carcinoma by lower endoscopy and biopsy , with presentation of 35 case as adenocarcinoma , 8

cases as mucinous adenocarcinoma , 5 as signet ring adenocarcinoma, and 2 cases of undifferentiated carcinoma. Table (1)

By MRI, none of the 50 patients where staged as T1 stage, 34 patients were diagnosed as T2 stage, 10 patients as T3 and 6 patients as T4 stage. Histopathological examination showing none of patients as T1 stage, 31 patients as T2 stage, 15 patients as T3 and only 4 patients as T4 stage. From the 34 patients staged with MRI T2 , 31 patient proved to be T2 by histopathology while 3 patients proved to be T3 by histopathology (agreement 91.1%). All the 10 patients staged as T3 by MRI proved to be T3 by histopathology (agreement 100%). The 6 patients staged as T4 by MRI, only 4 was proved to be T4 by histopathology , while 2 patient proved to be T3 by histopathology (agreement 66.6%). The histopathological agreement in different T stages equal 90%, P value for T stage is <.0001 which is considered statistically significant. Table (2)

By MRI 21 cases where found to be N0, 23 cases where N1 and only 6 cases where N2. Histopathological examination confirmed the diagnosis of N0 in 19 cases, N1 in 24 cases and N2 in 7 cases. From the MRI diagnosed 21 N0 cases only 19 proved N0 by histopathology while the rest 2 cases proved to be N1 (agreement 90.5%). From the MRI diagnosed 23 N1 cases, 22 case was proved to be N1 by histopathology, while one case proved to be N2 by histopathology (agreement 95.6%). From the 6 cases diagnosed by MRI as N2, all of them proved to be N2 by histopathology (agreement 100%). Table (3)

MRI under estimated the number of involved nodes in three patients (6.6%). Table (4)

This representing 93.6% sensitivity and 96% accuracy in nodal involvement criteria. Table (5)

MRI showed MRF infiltration in only 18 cases while the rest 32 has no MRF infiltration. Histopathological assessment showing MRF infiltration in only 15 cases and the rest 35 cases showing free MRF (agreement 83.3%) Table (6)

Regarding the (CRM) infiltration, MRI diagnosed CRM involvement in 15 cases while rest 35 cases showing free CRM. From the these positive cases only 13 were truly positive with histopathology , while there are other two case proved to be positive with histopathology not diagnosed by MRI. Table (7)

Table 1: Percentage of Pathological Types of Cancer Rectum

Pathological type	No.	%
Adenocarcinoma	35	70
Mucinous adenocarcinoma	8	16
Signet ring adenocarcinoma	5	10
Undifferentiated type	2	4
Total	50	100.0

Table 2: T Staging for Patients By MRI in Comparison to Post-Operative Histopathological Staging.

MRI Staging	Total	Histopathology Staging			
		T1	T2	T3	T4
T1	0	-	-	-	-
T2	34	-	31	3	-
T3	10	-	-	10	-
T4	6	-	-	2	4
Total	50	-	31	15	4

Table 3: N Staging for Patients by MRI in Comparison to Post-Operative Histopathological Staging

MRI Staging	Total	Histopathology Staging		
		N0	N1	N2
N0	21	19	2	-
N1	23	0	22	1
N2	6	-	-	6
Total	50	19	24	7

Table 4: Correctly diagnosed N stage, over staged and under staged cases by MRI

Correctly diagnosed cases	Over staged	Under staged
93.4%	0%	6.6%

Table 5: Sensitivity, specificity, PPV, NPV and accuracy of MRI in evaluation of lymph nodes involvement in correlation to the histopathological examination

Sensitivity	Specificity	PPV	NPV	Accuracy
93.6%	100%	100 %	90.5 %	96%

Table 6: MRF infiltration for Patients by MRI in Comparison to Post-Operative Histopathological assessment

MRF with MRI	Total	HISTOPATHOLOGY	
		MRF INF 0	MRF INF 1
MRF 0	32	31	1
MRF 1	18	3	15
Total	50	34	16

Table 7: CRM infiltration for Patients by MRI in Comparison to Post-Operative Histopathological Assessment

CRM infiltration with MRI	Total	Histopathology	
		CRM infiltration MRI 0	CRM infiltration MRI 1
CRM 0	35	33	2
CRM 1	15	2	13
Total	50	35	15

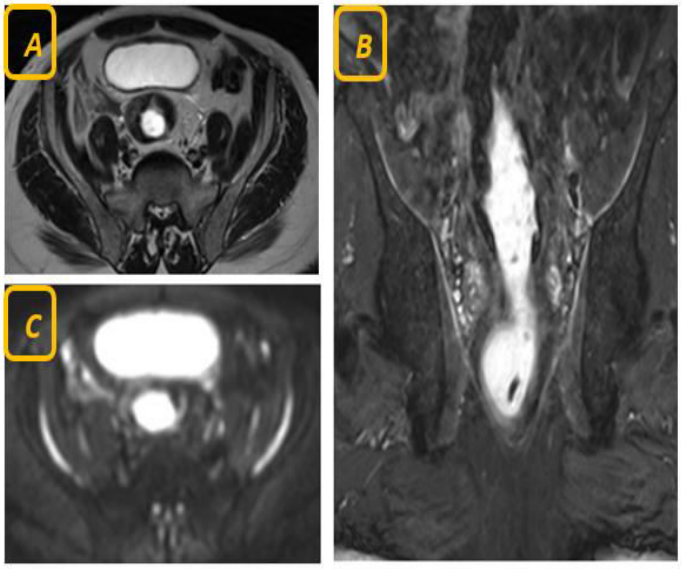

Figure 1 : A 68 year-old male patient presented with bleeding per rectum. Endoscopy and biopsy revealed adenocarcinoma. A, B and C axial T2WI , coronal STIR and axial DWI respectively, showing whole wall circumferential thickness of the upper third rectum , more at the anterolateral walls. No detected atypical enlarged LNs. MRI staging: T2N0 Post-operative histopathological assessment T2N0

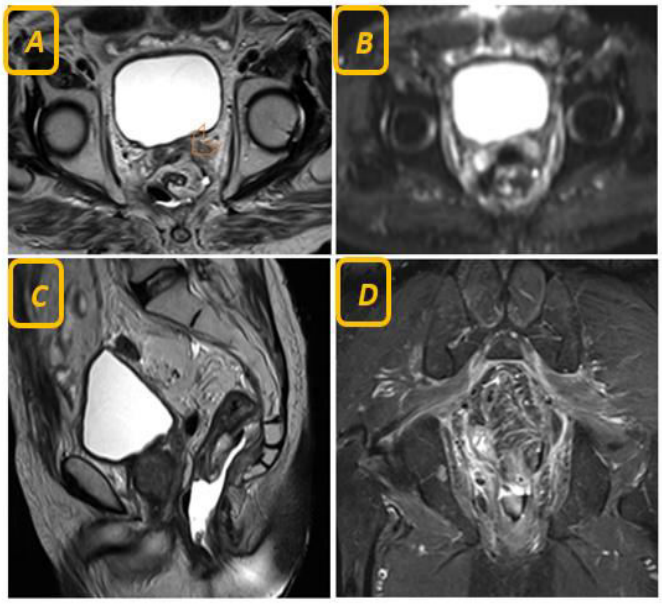

Figure 2: A 67 year old male patient presented with bleeding per rectum. Endoscopy and biopsy revealed adenocarcinoma. A,B and C Axial T2WI, Axial DWI, coronal and sagittal T2WI respectively showing anterolateral rectal wall

thickening with fungating intra luminal growth , the lesion involving the full thickness of the muscularis propria being more impressive at the anterior wall with that seen infiltration the MRF, Bilateral enlargement of internal iliac lymph nodes group with irregular out line denoting metastasis. MRI staging T4N2, Post-operative histopathology T3N2.

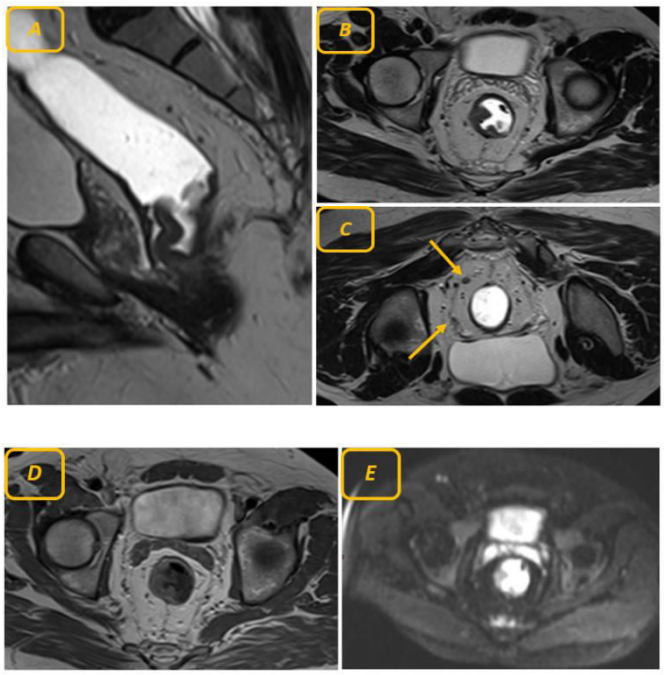

Figure 3 : Male patient 50 years old complaining of bleeding per rectum. Endoscopy and biopsy revealed infiltrating adenocarcinoma. A, B and C: sagittal T2WI, Axial T2WI and Axial T2WI respectively, showing a lower rectal circumferential mass lesion involving the whole thickness of the muscularis propria with multiple enlarged LNs some of them showing irregular outlines, the right lateral wall showing small extension like from the rectal mass invading the MRF. D and E : axial post contrast T1WI and axial DWI respectively Post contrast showing faint contrast enhancement for this extension , however MRI diffusion showing no restriction outside the muscular propria outlines, making tumor staging as T2N2 instead of T3N2 Post-operative histopathological assessment T3N2

Discussion

According to GLOBOCAN 2018 data, colorectal cancer (CRC) is the third most deadly and fourth most commonly diagnosed cancer in the world. Nearly 2 million new cases and every year, it is projected that approximately 1 million people would die. Colorectal cancer is the seventh most prevalent cancer in Egypt, accounting for 3.47% of male cancers and 3 % of female cancers in the country. In 2015, the estimated number of rectal cancer patients (excluding those with other types of colon cancer) was approximately one thousand cases **(Ibrahim et al., 2014).**

The survival rate is closely related to the extra mural extension and involvement of the mesorectum with subsequent ability of achieving clean surgical circumferential resection margins **(Jemal et al., 2011)**.

This study included 50 patients, all presented with primary rectal cancer that confirmed by colonscopy and histopathological biopsy. The study focused on evaluating role of MRI with diffusion on staging of the rectal malignancy in comparison to post-operative histopathological staging as gold stander.

Patient age ranging from 30 to 82 years with mean age of 56.7 years, that is almost agree with **(Akasu et al., 2005)** study who stated that the main age was 57 years.

In this study we found in 20 cases the lesion represented at the upper rectum with 40 % from all lesions, that disagree with **(Rao et al., 2007)** study which shows upper rectal cancer representing 67% from their patients.

Adenocarcinoma was the main pathological type in this study with 35 patients from the 50 patients representing 70% from the patients , this agrees with **(Akasu et al., 2005)** study which also showing adenocarcinoma as the most histopathological type followed by the mucinous adenocarcinoma.

The idea of MRI DWI is simple , using radio frequency pulse labelling water molecules present in a volume of tissue and then resampling same volume to estimate the proportion of labelled water molecules, so in most densely packed cell membranes, as in most of tumors including rectal cancer, the motion of water molecules is hindered , restricted diffusion , than in normal tissue , facilitated diffusion, **(Soyer et al., 2010).**

MRI with DWI has shown greater value in diagnosis of colorectal cancer specially in cases of coexisting inflammatory lesions , differentiating true tumor extension from desmoplastic reaction as the first with show restricted diffusion while the later one will showing facilitated diffusion **(Hoeffel et al., 2009).**

In this study the included MRI DWI in examination protocol facilitated in the differentiation of T2/T3 and T3/T4 staging also is used as one of the differentiating parameters for nodal involvement as in cases No 3.

As the circumferential resection margin (CRM) defined as the distance from the tumor to resection plane used by the surgeon at intra operative. total mesorectal excision (TME) operation, it representing the full circumference of the mesorectal fascia. The CRM considered involved if the tumor extend to less than or equal to 1mm from it **(Brown, 2006).**

Although in previous study MRI proven to be very reliable in predicting the clear margin with 91% accuracy rate, but in other larger meta-analysis study , the MRI sensitivity and specificity for detection of the CRM with 1 mm cut off , it showed only 67% and 88% sensitivity and specificity respectively , this leads to change the MRI cut off margin to be less than 5mm to be considered as CRM involvement **(Hunter and Brown, 2016).**

The RCM involvement showing strong association with post-operative local recurrence with 20% versus only 7.1% in negative CRM involvement cases **(Taylor et al., 2014).**

CRM infiltration considered as indication for neoadjuvant thereby in both NCCN and ESMO guidelines **(Glynne-Jones et al., 2017).**

In our study, we found regarding the detection of mesorectal fat infiltration, MRF, sensitivity 93.75% and specificity 91.18% with accuracy rate 92%. This agrees with previous study that stated accuracy rate 91%. **(Akasu et al., 2005)**

Regarding the detection of the CRM infiltration, our study showed 87.50% sensitivity, 100% specificity, PPV 100 % and 94.44% NPV with 96% accuracy. This agrees with previous larger study which shows sensitivity, specificity 89.5% and 96.3% respectively with overall 94.5% accuracy **(Iannicelli et al., 2014).**

The more recent studies showing the malignant nodal infiltration can be detected by combining data from the nodal size, irregular outlines, speculated margins and heterogenous signal intensity in addition to the restricted MRI diffusion pattern.

In a recent study, it was discovered that nodal margins and internal nodal characteristics are the most dependable predictors of malignancy. In addition to the confined diffusion pattern of the affected node, irregular or speculated nodal margins, heterogeneous signal intensity, and irregular or speculated nodal margins are also characteristics of malignancy. It is necessary to get high-resolution pictures that include all relevant LNs, including the superior rectal and pelvic sidewall LNs, in order to evaluate these characteristics**. (Figueiras et al., 2010)**.

Recent studies focused upon lymph nodes specific contrast agents , like Ultra small super paramagnetic iron oxide (USPIO), it is a specific agent that actively uptake by healthy lymph nodes, and so on the malignant infiltrated nodes will be hyper intense compared to normal ones **(Tonolini & Bianco, 2013) .**

This was not applicable in this study due to the unavailability of this contrast agent in our region.

In this study, sensitivity, specificity and accuracy of MRI in detection lymph nodes involvement were 93.6%, 100% and 96%, respectively. This differ with **(Zhang et al., 2008)** who stated that sensitivity, specificity and accuracy were 64.7%, 90.5%, 79%, respectively. This difference my be due to the larger sample in the later study

Conclusion:

The results of this study demonstrate that a preoperative HRMRI is extremely useful in determining the most effective treatment strategy for rectal cancer, including correct staging, prediction of negative CRMs, and presence of the perirectal and pelvic lymph nodes (LNs)

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