Zagazig University Medical Journal
www.zumj.journals.ekb.eg

July.2021 Volume 27 Issue 4

Manuscript ID ZUMJ-1907-1309 (R1)

DOI 10.21608/zumj.2019.14444.1309

ORIGINAL ARTICLE

Computed Tomography Versus Magnetic Resonance Imaging in Assessment of Recto-Sigmoid Cancer Local Recurrence in Patients with Elevated Carcinoembryonic Antigen

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Submit Date	2019-07-11
Revise Date	2019-09-25
Accept Date	2019-10-08

ABSTRACT

Background: Colorectal cancer is widely distributed. It is considered the third most common cancer worldwide. Despite performing potentially curative operations 25% to 40% develop tumor recurrence. The optimal strategy to detect recurrences at the earliest stage remains controverse. The aim of this study was to assess recto-sigmoid cancer local recurrence in patients with elevated CEA by contrast enhanced CT and contrast enhanced MRI and compare between both modalities.

Methods: This study was carried out on 24 patients who underwent surgical excision of primary recto-sigmoid cancer and under post-operative follow up with elevated CEA level. CT and MRI were done, and the results were compared.

Results: Our study included 24 their age's ranged from 23-76 years with the mean age 53 years. Twenty cases (83%) were confirmed to have recurrence while 4 cases elevated CEA levels were considered false positive. CT accuracy (79%), sensitivity (100%) and specificity (55%). These results were not as high as those of MR imaging where MRI accuracy, sensitivity and specificity were 96%, 100% and 91% respectively. There was no significant difference between CT and MRI in detection and assessment of locally recurrent recto sigmoid cancer patients with P value 0.3843.

Conclusion: MRI has higher specificity than CT in determining pelvic recurrence of recto-sigmoid cancer in patients with elevated CEA level. It can differentiate recurrent masses from post-operative scar tissue and determine preciously the site and type of local recurrence. However, CT is mandatory in these patients as a screening modality and follow up.

Key words: recto-sigmoid; CEA; CT; MRI.

INTRODUCTION

Colorectal cancer is the fourth most common cancer and the second most common cause of cancer deaths in the world [1]. At least, one third (25–49% reported) of patients treated with stage II or stage III cancer colon will experience a recurrence [2, 3]. The diagnosis of asymptomatic recurrence is more likely to result in curative reoperation. Even with an intensive investigative program, up to 50% of asymptomatic recurrences may not be detected [4].

Follow up typically consists of periodic consultations with laboratory and radiological examinations. The most optimal follow up schedule has not been defined and follow up is generally outlined by national guidelines with some inter-hospital variability. Serum carcino-embryogenic antigen (CEA) measurement and contrast-enhanced CT are the most frequently used monitoring methods. However, increasing tumor markers cannot indicate the true extent of the disease [5].

The imaging strategy for identifying pelvic local recurrence currently involves CT, MRI

and PET-CT. Although current recommendations for postoperative surveillance neither include PET-CT or MRI, these modalities are still needed in selective patients with clinical or biochemical suspicion of recurrence with normal findings on previous imaging modalities [6].

Magnetic resonance imaging (MRI) performs better in differentiating local recurrence from scar tissue when compared to CT [7]. This work was carried out to compare the role of CT and MRI in detection of local recurrence of recto sigmoid cancer in patients with elevated CEA.

PATIENTS & METHODOLOGY

This prospective study was conducted at Radiodiagnosis department, Zagazig university hospitals and Radiodiagnosis department, Mit-Ghamr Oncology Center. The study was approved by the Institutional Review Board (IRB), Faculty of Medicine, Zagazig University (ZU-IRB#4682/11-6-2018). Informed consent was obtained from patients. The privacy rights of human subjects had been observed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans..

All recto-sigmoid cancer patients who treated surgically and on routine follow up with elevated CEA during the period from July 2018 to February 2019 were included. We excluded; non-operated patients, operated rectosigmoid or rectal cancer patient with no elevation in the CEA level, known metastatic patient, contraindicated for CT or contrast administration and hemodynamic or respiratory instability.

Detailed history was obtained from all patients or taken from the patient profile. Routine laboratory investigation including renal function test. Estimation of CEA level (> 5 ng/ml considered high).

Radiological examination included:

- Contrast enhanced chest, abdomen and pelvis: 64MDCT (Siemens Medical Systems) was used for 11 patients and 128MDCT (Philips ingenuity 128) was used for 13 patients. The axial cuts were taken from the base of the neck till the symphysis pubis in slice thickness of 5 mm and 5 mm interval. Oral contrast medium (15 ml of water soluble contrast 300mg I/ml (teleprix – omnibaque) was added to 1000 ml of water) and IV contrast medium (100 to 120 ml of the same contrast) was used.
- Pre and post contrast pelvic MRI was done (2-4 weeks) before or after CT examination. Eleven cases underwent pelvic MRI on 0.3T (Siemens Medical Systems) and 13 cases on 1.5T (Philips Achiva II Medical Systems). Phased array surface coil was used. Gadopentetate dimeglumine (Magnevist), IV contrast medium was used in a dose of 0.1mmol/Kg.
- Examination protocol:

Sagittal and coronal localizer T1-weighted images (TR 300-600ms/TE 10-20ms). Axial fast spin echo T1WI (TR 300-600ms/TE 20-30ms). Axial fast spin echo T2WI(TR/ TE 3000/100ms). Sagittal T1 weighted turbo spin echo(TR/ TE 440/15ms). Sagittal T2 weighted turbo spin echo (TR/TE 3301/85ms). Post-contrast series: axial, sagittal and coronal fast spin echo T1WI. - Diffusion weighted image was done for 13 cases with b-values 0, 500, 1000 s/mm2, TR 3900, TE 70ms, EPI factor 128, flip angle 90.

Reference standard:

The standard reference was histopathologic examination in 18 cases or correlation with tumor markers, clinical and imaging follow-up evaluation in 6 cases. A suspected tumor site was considered true-positive if the histologic findings were positive or if the lesion exhibited either resolution after successful treatment or progression at follow-up imaging after unsuccessful therapy.

Statistical analysis:

All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 17 for Microsoft Windows. Chi-square test was used to compare qualitative variables between groups, P values less than 0.05 was considered statistically significant. Sensitivity, Specificity, Positive predictive value, Negative predictive value and accuracy were calculated.

RESULTS

Our study included 24 patients who underwent surgical excision of primary recto-sigmoid or rectal cancer and under post-operative follow up, table (1).

From the 12 cases who underwent abdomino-perineal resection (APR) operation, 11cases (92%) were confirmed to have recurrent lesions (local or metastatic) 6 of them were local recurrences. While from the 10 cases who underwent low anterior resection (LAR) operation, 7 cases (70%) were confirmed to have recurrent lesions 6 of them were local recurrences. The two cases who underwent sigmoidectomy were confirmed to have recurrent lesions, one of them was local recurrence. From the 19 cases who received post-operative adjuvant therapy, 15 cases (79%) were confirmed to have recurrent lesions, table (2).

The interval between the operative procedure and elevated serum CEA level observations in our study ranged from 6 months up to 3 years during follow up after the operation. 8 patients had elevated CEA level within the 1st year, 10 cases during the 2nd year and 6 cases during the 3rd year after surgical resection. CEA level using cut off value (5ng/ml) ranged from 7ng/ml to 372 ng/ml with the mean level 45.125 ng/ml.

In our 24 patients with post-operative elevated serum CEA level, 20 cases (83%) were confirmed to have recurrence (local or metastatic recurrence) while in 4 cases elevated CEA level were considered false positive elevation.

Interpretation of the post-operative contrast enhanced CT findings:

Out of 24 patients, the CT finding was free in 2 patients (8%). 18 patients (75%) showed local recurrence (local recurrence in 8 cases and combined local and distant metastatic lesions in 10 cases). 4 patients (17%) had metastatic lesions only with normal pelvic CT findings. All metastatic lesions were confirmed by clinical and imaging follow-up evaluation after 3 months

Different patterns of local recurrence were defined: wall thickening with fat stranding (11%) wall thickening with loco-regional LNs (28%), mass lesion with fat stranding (22%) and mass lesions with loco-regional LNs (17%). Also wall thickening with mass lesion and fat stranding was detected in (17%) and combined wall thickening, mass lesion with fat stranding and loco-regional LNs was detected in only (5%).

Histo-pathological examination matched CT finding in 13 cases confirming the presence of locally recurrent malignant disease and was negative in 5 cases which diagnosed by pathology as: scar tissue in 4 cases and infected granulation tissue in one case. All CT negative pelvic findings (6 cases) were confirmed by clinical and imaging follow-up evaluation after 3 months.

Interpretation of the post-operative contrast enhanced pelvic MRI findings:

Out of 24 patients, the pelvic MRI was free in 6 patients (25%) excluding local recurrence. Four patients (17%) showed scar tissue at the operative bed and 14 patients (58%) showed local recurrence.

local recurrence appeared as wall thickening with fat stranding (7%), wall thickening with loco-regional LNs (36%). mass lesions with fat stranding(22%) while in (14%) mass lesions were associated with loco-regional LNs. Both wall thickening and mass lesions with fat stranding was detected in (14%), and combined wall thickening and mass lesion with fat stranding and loco-regional LNs in (7%).

In the 14 patients diagnosed by MRI as locally recurrent malignant lesions, all cases showed iso signal intensity on T1WIs. The signal intensity on T2WIs ranged from low, mixed to high (7%, 29% and 64% respectively). In post contrast images 50% of cases with local pelvic recurrence displayed diffuse homogenous enhancement, table (3).

DWIs were done for 8 cases, all of them locally recurrent lesions displayed high signal intensity in DWI and low signal intensity in their corresponding ADC map with ADC value ranging from $0.9x10^{-3}$ mm^2/s to $0.7x10^{-3}$ mm^2/s denoting restricted diffusion and suggesting malignant nature.

The Pelvic MRI finding showed post-operative scar tissue at the operative bed in 4 cases, eliciting iso to low signal intensity in T1WIs and low signal intensity in T2WIs in 2

cases, the other two cases displayed iso and high signal intensity in T2WIs. Post contrast images, scar tissue showed faint enhancement in one case and the other 3 cases showed no evidence of enhancement. DWIs were done for 2 cases with no evidence of restriction and displayed high signal intensity in DWI and iso to high signal intensity in ADC map with ADC value 1.8 $x10^{-3}$ mm^2/s.

In our study, local recurrences were axial anastomotic recurrence in 10 cases. Six cases were axial intra-mural anastomotic recurrences, appeared as irregular wall thickening at the anastomotic site. Three cases were axial extra-mural anastomotic recurrences, appeared as mass lesions at the anastomotic site while one case was combined intra and extra mural anastomotic recurrence.

Local recurrences were axial perineal recurrence in 2 cases, appeared as mass lesions at the primary site after APR. Anterior recurrence was found in two cases, appeared as mass lesion or irregular wall thickening involving the genitourinary tract. Posterior recurrence was found in 6 cases, appeared as mass lesion with adhesion to the presacral fascia without bone involvement.

From our 24 patients, histo-pathological examination was done in 18 cases that had pelvic findings. Histo-pathological examination matched MRI finding in 17 cases confirming the presence of locally recurrent malignant disease in 13 cases and presence of post-operative scar tissue in 4 cases.

Histo-pathological examination didn't match MRI finding and was negative in only one case which diagnosed by pathology as infected granulation tissue. The other 6 cases with negative MRI findings were confirmed by clinical and imaging follow-up evaluation after 3 months.

To compare the previous results accuracy, sensitivity, specificity, positive predictive value (PVP) and negative predictive value (PVN) for CT and MRI were calculated and shown in table (4), however, there was no significant difference between CT and MRI in detection and diagnosis of locally recurrent recto-sigmoid cancer patients with P value 0.3843.

Case presentation:

Case (1) CEA level was 22ng/ml, (A) axial post contrast CT cuts showing operative bed pre-coccygeal soft tissue lesion with fat stranding, It is inseparable from the posterior bladder wall. (B) axial CT cuts pulmonary window shows multiple well-defined metastatic nodules. (C&D) axial T1WI pre and post-contrast show pre-coccygeal soft tissue non-enhanced lesion. On axial T2WI (E) it measures about 7x4cm. On DWI (F) the lesion displays low signal intensity denoting facilitated diffusion and benign nature, figure (1).

Case (2) CEA level was 19ng/ml, (A) axial post contrast CT cuts show soft tissue density lesion at the rectosigmoid junction in the operative bed with cystic changes. Locoregional LNs is seen in (B). Few well defined soft tissue densities nodules are seen in the anterior abdominal wall muscle the largest in (C) (arrow). (D&E) Axial and sagittal T2WI show lobulated outline abnormal heterogeneous high signal intensity lesion indenting and inseparable from the uterus. (F&G) axial and sagittal T2WI shows few anterior abdominal wall muscle well defined deposits (arrow). (H) axial post-contrast T1WI showing intense heterogeneous enhancement. (I) DWI shows restricted diffusion displaying high signal intensity denoting recurrence (asterisk), figure (2).

Table 1. Clinical characteristics of 24 patients included in the study.

Characteristics	No. (%)
Age in years	
Range	23-76
Mean	53
Gender	
Male	12 (50%)
Female	12 (50%)
Histopathology	
Adenocarcinoma	24(100%)
GI	1(4%)
GII	21(88%)
GIII	2(8%)
Type of operation	
Sigmoidectomy	2(8%)
LAR	10(42%)
APR	12(50%)
Post-operative adjuvant therapy	
Received	19(79%)
Not received	5(21%)

Table 2. Correlation between occurrence of recurrence and type of surgery & post-operative adjuvant therapy.

		Recurrence (local or metastatic)		Local recurrence	
		No. of cases	percentage	No. of cases	percentage
Type of operation:	APR	11/12	92%	6/12	50%
	LAR	7/10	70%	6/10	60%
	Sigmoidectomy	2/2	100%	1/2	50%
Adjuvant therapy:	received	15/19	79%	10/19	53%
	not received	5/5	100%	3/5	60%

Table 3. appearance of the locally recurrent lesions by MRI.

	T1WI	T2WI			Post contrast enhancement		
	iso	low	mixed	high	faint	moderate	intense
No. of cases	14	1	4	9	2	7	5
Total	14	14			14		
Percentage	100%	7%	29%	64%	14%	50%	36%

Table 4. Validity of CT and MRI among the studied patients.

Modality	Accuracy	Sensitivity	Specificity	PVP	PVN
CT	79%	100%	55%	72%	100%
MRI	96%	100%	91%	93%	100%

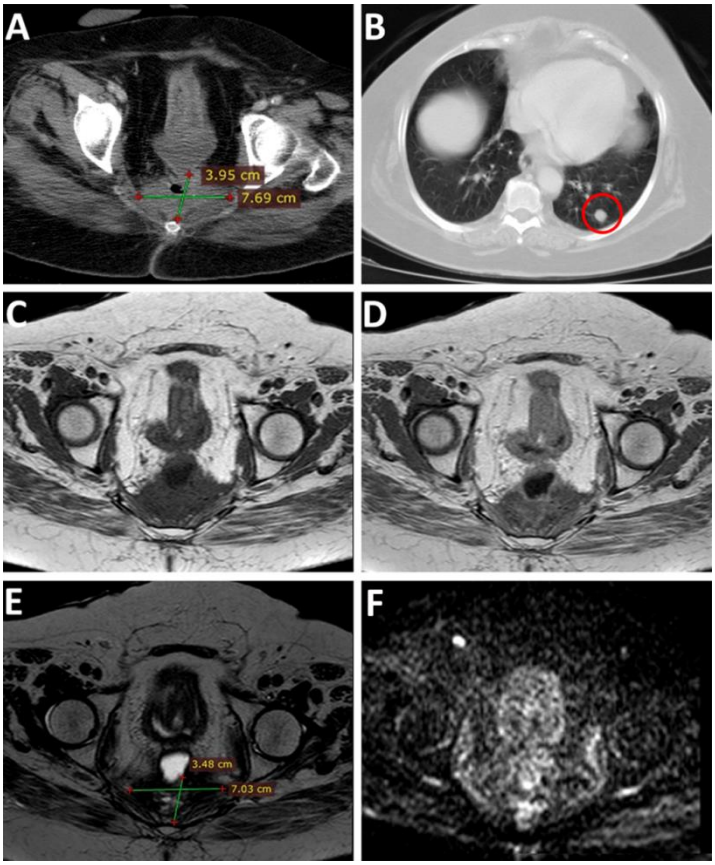

Figure 1. Case (1), (A) axial post contrast CT, (B) axial CT cuts pulmonary window, (C&D) axial T1WI pre and post-contrast MRI, (E) T2WI and (F) DWI.

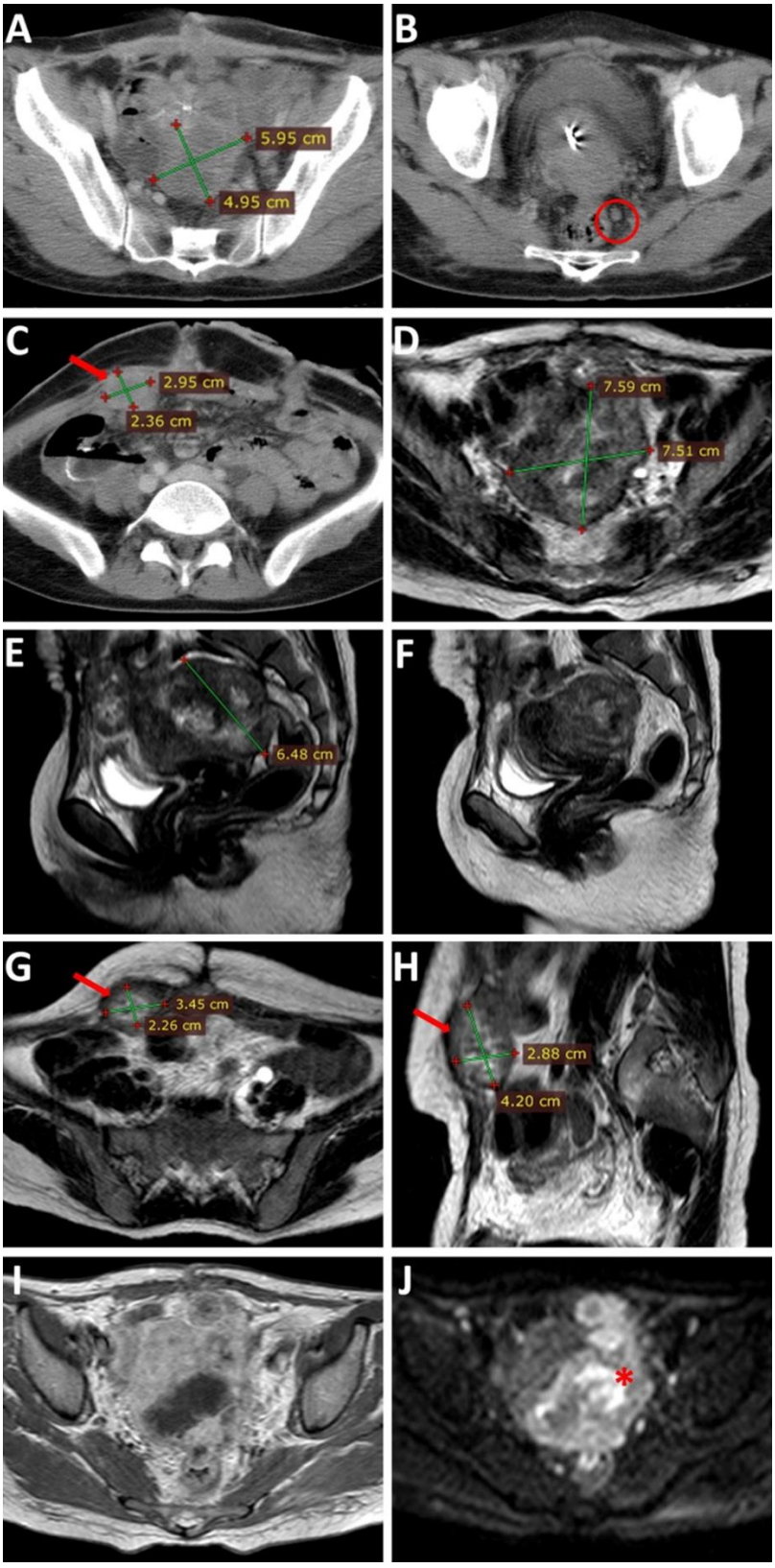

Figure 2. Case (2), (A, B & C) axial post contrast CT, (D,E& F) Axial & Sagittal T2WI, (G& H) T2WI at higher level, (I) axial T1WI post-contrast, (J) DWI.

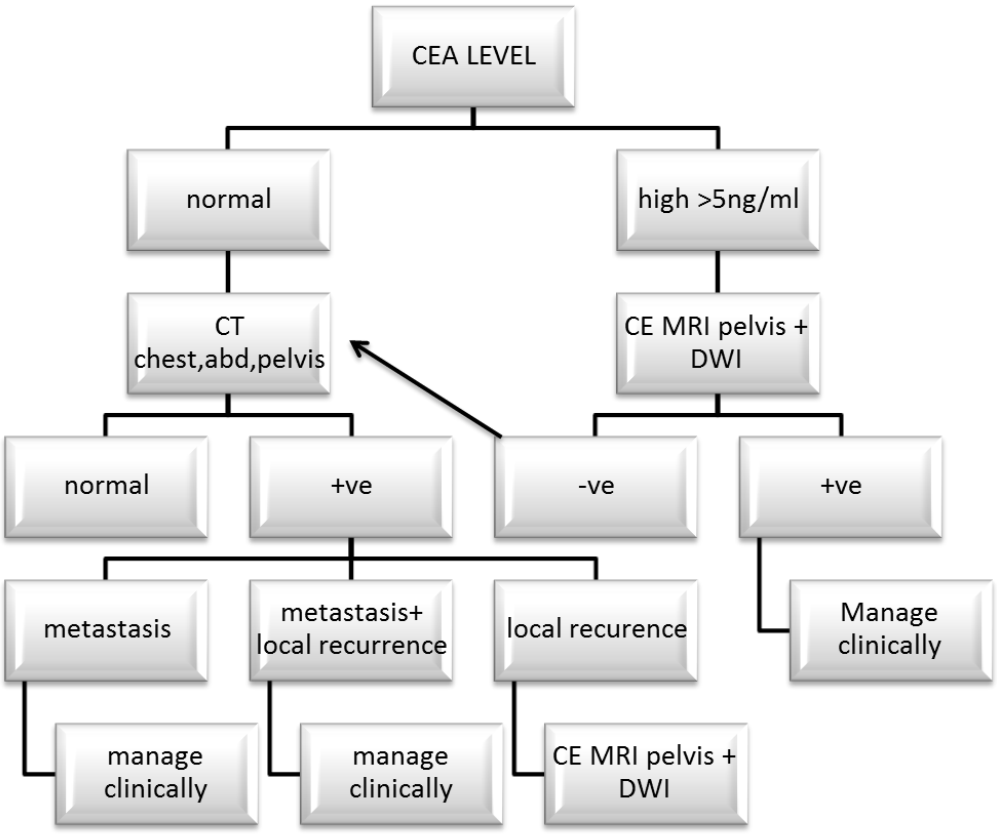

Figure 3. algorithm for diagnosis of local recurrence during follow up of a known patient with operated recto-sigmoid cancer.

DISCUSSION

Colorectal cancer is considered the third most common cancer worldwide with an estimated 1.2 million new cases per year, nearly one third of these cases are rectal cancers. Ultimately, colorectal cancer is responsible for 8% of all cancer deaths. [8]

Follow up is generally outlined by the national guidelines with some inter-hospital variability according to available resources. Typically, follow up consists of periodic consultations and assessment with laboratory and radiological examinations. [9]

One of the most commonly used parameters for biochemical follow up is serum carcino-embryonic antigen (CEA). Contrast-enhanced CT is the most frequently used monitoring radiological method [5]. while MRI are not listed in the recent recommendations. It is only performed in selective patients with clinical or biochemical recurrence suspicion and normal findings in previous imaging modalities. [6]

In the current study we estimated the role of CT and MRI in detection and assessment of recto sigmoid cancer locoregional recurrence in patients with elevated CEA level. we compared the two modalities to evaluate the effectiveness of using MRI in routine follow up.

In our study recurrence (local or metastatic) was more frequent among patients who had APR operation than patients who had LAR (92% Vs. 70%). This may be attributed to more advanced tumors in patients needing APR not due to the surgical approach itself.

While local recurrence was nearly equal between the two types of surgery among our cases (50% and 60%). This didn't coincide with Minna et al. [10]. This can be explained by selection bias between the two studies. More over local recurrence is multifactorial disease not only depending on the surgical approach.

In our study, although most of cases (19/24) received post-operative adjuvant therapy,

recurrence was founded in (79%) of these cases. 53% (10/19) had local recurrence. Recurrence was more frequent among cases that didn't receive post-operative adjuvant therapy (100%) and local recurrence was confirmed in 3 cases (3/5, 60%). So, we agree with Räsänen et al. [11] who stated that there was no patient-related factor that associated with local recurrence, including neoadjuvant therapy or type of the operation.

During this study, the time between the operative procedure and the elevated serum CEA level ranged from 6 months up to 3 years. Nearly half of the patients 42% showed the elevated CEA level during the 2nd year after surgical resection. While 33% of patients were within the 1st year and 25% were during the 3rd year. This nearly agree with a study by Bhatti et al. [12]

In the current study, 20 out of 24 cases (83%) of the patients with elevated CEA level had recurrence (local or metastatic). On the other hand, the 4 other cases (17%) were considered false positive elevation. We nearly agree with Metser et al. [13] who stated that (65.5%) of elevated CEA level showed the presence of tumor recurrence or metastatic disease. This slightly higher ratio in our study may be due to smaller number of patients in our study.

In this study, CT suspected the local recurrence in18 patients (75%) in addition, 4 patients (17%) had metastatic lesions only with normal pelvic CT. In our study metastatic lesions were more frequent in the liver (9/14, 64%) and lungs (7/14, 50%). This nearly agreed with Ferlay et al. [9].

Histopathological examination matched CT finding in 13 cases confirming the presence of locally recurrent malignant disease. However, contradicted CT finding in 5 cases. All CT negative pelvic findings (6 cases) were confirmed by clinical and imaging follow-up evaluation after 3 months to be free from local recurrence. There were 5 false positive results by CT, they were presacral scar tissue in 4 cases and infected granulation tissue in one case.

Accuracy, sensitivity, specificity, positive predictive value (PVP) and negative predictive value (PVN) for CT in detection of pelvic recurrence in this study were as follows: accuracy= 79%, Sensitivity= 100%, Specificity= 55%, PVP= 72%, PVN= 100.

CT demonstrated recurrent tumor in 82% (9 of 11) with two false negatives. Overall, CT demonstrated accuracy of 68% with sensitivity of 82% and specificity of 50%, a positive predictive value (PPV) of 69%, and a negative predictive value (NPV) of 67%. [14]

In a study by Dresen et al. [7], among the 101 patients who had chest and abdomen CT and were confirmed to have recurrence/metastases in the follow-up period with sensitivity and specificity of 79.2% and 45%, respectively. As we notice, in our study CT had higher sensitivity up to 100% as all our cases had elevated CEA this raises the suspicious for recurrence.

In the current study, the pelvic MRI in 4 patients (17%) showed scar tissue at the operative bed. 14 patients (58%) showed local recurrence. axial anastomotic recurrence and posterior recurrence were the most common forms (founded in 10 and 6 cases respectively) this agree with Colosio et al. [16].

In the 14 patients diagnosed by MRI as locally recurrent malignant lesions in the present study, all cases show iso signal intensity on T1WIs. Hyperintensity on T2WIs was the most common signal detected in (64%) of cases. This agreed with Pema et al. [14] who reported that, in 8 of 10 (80%) cases, tumor recurrence demonstrated high signal on T2 weighted images relative to Tl -weighted images.

Histo-pathological examination matched MRI finding in 17 cases confirming the presence of locally recurrent malignant disease in 13 cases and presence of post-operative scar tissue in 4 cases. Histo-pathological examination didn't match MRI finding in only one case. From 13 cases with truly positive local recurrence, MRI was able to detect all of them and correctly ruled out 10 cases from 11 cases. There was only one false positive result. The case was reported by MRI as positive for recurrence although there was no disease by histopathological examination and diagnosed as infected granulation tissue.

Sensitivity, specificity, positive predictive value (PVP) and negative predictive value

(PVN) for MRI in detection of local recurrence were calculated. The results were as follows: accuracy= 96%, Sensitivity= 100%, Specificity= 91% PVP=93%, PVN= 100.

We nearly agree with other study carried by Titu et al. [17] who examined 226 patients. The sensitivity, specificity, the positive (PPV) and negative (NPV) predictive values for MRI were 87%, 86%, 48% and 98%, respectively. MRI was the only positive diagnostic test in four (13%) patients with pelvic recurrence located in the perirectal tissue [17]. This higher sensitivity in our study may be due to different inclusion criteria between the two studies

Magnetic resonance revealed that 4 of the presacral masses seen on CT were post-operative scar tissue at the operative bed in our study. According to Pema et al. [14], Magnetic resonance findings clarified the CT findings in 40% (8 of 19) of the cases. Also, Lambregts et al. [18] published in their study that 11 patients had undergone CT imaging prior to MRI. In eight (73%) cases CT showed equivocal findings and patients had to be referred for further imaging. In this study setting, all 8 patients were correctly diagnosed by standard MRI, suggesting that MRI has superior sensitivity and specificity compared to CT.

MRI was the most effective imaging modality with an accuracy of 87.5% compared with CT, which correctly diagnosed recurrent cancer in 76% [19]. This agree with our study as MRI was more accurate (96% Vs. 79%) and more specific (91% Vs. 55%) than CT in detecting the recurrence. However, the higher cost of MRI and its limited value in detecting lung metastases precludes its routine use over CT for post-operative surveillance.

MRI provides superior soft tissue contrast compared to CT, thus facilitating the distinction of presacral scarring from recurrent tumor [15]. MRI examinations detected only four (<2%) cases with local recurrence missed by other tests [17]. Consequently, they suggested that pelvic MRI has little to offer when used as a routine surveillance tool following curative surgery for colorectal tumors.

This emphasized the results in our study, as by comparing the CT and MRI results using chi square test, there was no significant difference between CT and MRI in detection and diagnosis of locally recurrent recto sigmoid cancer patients with P value 0.3843.

ASCO and ESMO do not recommend MRI imaging for routine use inside surveillance programs for recurrent CRC [20]. Despite the advantages over other imaging tests, the use of MRI as part of routine pelvic surveillance after curative resection of CRC is not justified. Instead, MRI should be reserved for selectively imaging patients with clinical, colonoscopy, and/or biochemical suspicion of recurrent disease.

We concluded an algorithm in follow up patients with operated cancer recto-sigmoid during follow up (fig 3), so, MRI pelvis is recommended in any case with high CEA level and any case with positive CT for recurrence while CEA was normal), MRI has higher specificity than CT in determining pelvic recurrence and can differentiate recurrent masses from post-operative scar tissue. It also can determine preciously the site and type of local recurrence. However, CT is also mandatory in these patients with elevated CEA as a screening imaging modality for detecting metastasis.

Conflict of interest: All the authors confirm that they have no any Conflict of interest with other persons or organizations that could influence the work inappropriately.

Financial disclosure: All the authors announce that this research was not supported by any grants from funding organizations in the public, commercial, or not-for-profit sectors.

Author contribution: We acknowledge that all authors have contributed to the concept and design, analysis and interpretation of data, drafting or revising of the manuscript, and that they have approved the manuscript as submitted.

Abbreviations:

APR: abdomino-perineal resection
LAR: low anterior resection
ASCO: American Society of Clinical Oncology
ESMO: European Society of Medical Oncology

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How to Cite

Mohsenah, H., Zidan, E., Al Smmak, A., Almola, R. Computed Tomography Versus Magnetic Resonance Imaging in Assessment of Recto-Sigmoid Cancer Local Recurrence in Patients with Elevated Carcinoembryonic Antigen. *Zagazig University Medical Journal*, 2021; (724-734): -. doi: 10.21608/zumj.2019.14444.1309