INTRODUCTION

Colorectal cancer is the third most common cancer worldwide. In United States it is the second leading cause of death. The incidences of colorectal cancers has been increasing in South East Asia specially Pakistan for the last decade. In Pakistan, colorectal cancers constitute 25.4% of gastrointestinal malignancies in males and 20.1% of gastrointestinal malignancies in females. According to cancer registry of Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, colorectal cancer is among top four malignancies. About 40 - 50% of large bowel cancers occur in rectum. Adenocarcinomas are most frequent comprising approximately 98% of rectal cancers.

Patients with rectal cancer can present with bleeding per rectum, weight loss, abdominal pain and obstructive symptoms. As a first step of clinical management, colonoscopy is carried out. In case of visible tumour or suspicious area, biopsy is performed and biopsy material is sent for histopathological examination. If malignancy is confirmed by histopathology, pre-operative radiological investigations are performed to determine the stage and extent of disease. Various radiological modalities are available for this purpose; these include Magnetic Resonance Imaging (MRI), Computed Tomography (CT) and Endorectal Ultrasound (ERUS). MRI is considered more sensitive and specific to determine tumour relation to mesorectal fascia. Radiological investigation provides information regarding tumour size, lymph node status, any metastatic deposit and distance of tumour from mesorectal fascia.

The most important factor influencing prognosis is complete mesorectum removal (circumferential margin status). Complete mesorectal removal is also known as Total Mesorectal Excision (TME). Another very important factor which determines clinical outcome of rectal cancers is the distance of tumour from mesorectal fascia; incidences of local recurrence increases as tumour reaches closer to the circumferential margin. When comparison between radiological and pathological finding is done, radiological findings show discordant results to histopathological findings. Accuracy of MRI of predicting mesorectal fascia status is 76% with sensitivity and specificity of 96.9% and 73.8% respectively.

ABSTRACT

Objective: To compare mesorectal fascia status on histopathological findings with MRI based radiological mesorectal fascia status in patients with rectal carcinoma taking histopathology finding as gold standard.

Study Design: Analytical study.

Place and Duration of Study: Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, from January 2011 to April 2012.

Methodology: Biopsy proven cases of rectal adenocarcinoma undergoing abdominoperineal resection were included in this study. Microscopic examination of slides was done to determine mesorectal fascia status as involved or otherwise without knowing the results of mesorectal fascia status on MRI. Mesorectal fascia status of MRI was determined by a radiologist who was not aware of the histopathological assessment of mesorectal fascia. Mean and standard deviation was calculated for age. Frequency and percentage were calculated for gender and mesorectal fascia status. 2 x 2 table was generated to calculate sensitivity, specificity, positive predictive value and negative predictive values and diagnostic accuracy of MRI for mesorectal fascia involvement taking histopathology as gold standard.

Results: The sensitivity of MRI to detect mesorectal fascia involvement was 23.07% and specificity was 70.5%. Positive predictive value of MRI was 10% and negative predictive value was 54.54%. Diagnostic accuracy of MRI for mesorectal fascia involvement was calculated as 50%.

Conclusion: MRI findings regarding mesorectal fascia status as involved or otherwise are not helpful when compared with histopathological findings which is the gold standard.

Radiology has limitations; it cannot differentiate between stage-1 and stage-2 cancers and it is sometimes very difficult to differentiate tumour from desmoplastic reaction (tissue reaction against the tumour in the form of fibrosis and inflammation).

The aim of this study was to determine the diagnostic accuracy of MRI to determine mesorectal fascia status, keeping histopathological results of assessment of mesorectal fascia as gold standard. This may help to avoid undue neoadjuvant chemotherapy, surgery or palliative treatment and vice versa.

**METHODOLOGY**

The study was conducted in Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, from January 2011 to April 2012. It was a cross-sectional review. Approval of study was taken from Institutional Review Board (IRB) of SKMCH and RC. Thirty cases of rectal adenocarcinoma were included in this study. Sampling technique was non-probability purpose. All male and female patients diagnosed as rectal adenocarcinoma on biopsy and later undergoing abdominoperineal resections were included in this study. Poorly preserved specimens were excluded.

Abdominoperineal resection specimens were collected in pathology department. Each case was given a case number and a medical record number and demographic details of patients were recorded. The specimens were fixed overnight in 10% buffered formalin. After complete fixation, specimens were examined and grossed next day according to approved guidelines. It started with the categorization of mesorectum into complete, near complete and incomplete. Indian ink was applied to mesorectal fascia, proximal resection margin and distal resection margin. Specimen was thinly and serially sliced in such a way that each slice was less than 3 millimeters in thickness. Each slice was carefully examined to note the relationship of tumour to Indian ink. Tumour size, its distance from inked mesorectal fascia, proximal and distal resection margins were also calculated. Sections were taken from the site where tumour was closest to the inked mesorectal fascia. Lymph nodes were sampled. These sections were placed in the cassettes and processed in automated processor. In this processor, tissue is passed through different steps including dehydration, clearing, and impregnation of wax. After processing, tissue sections were made with the help of microtome and sections were stained with hematoxylin and eosin.

Microscopic examination of slides was performed to confirm the mesorectal fascia status as involved or uninvolved. This was done by measuring microscopic distance of tumour from inked margin of mesorectal fascia. Following the international guidelines, mesorectal fascia was called involved when tumour was involving or was less than 1 millimeter from the inked mesorectal fascia and was recorded as uninvolved when tumour was more than 1 millimeter from inked mesorectal fascia. Findings of MRI regarding the status of mesorectal fascia involvement were noted with the help of radiologist and compared with the results of microscopic evaluation of mesorectal fascia.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 17. Mean and standard deviation were calculated for quantitative variable like patient's age. Frequencies and percentages were calculated for qualitative variables like sex and mesorectal fascia status. A 2 x 2 table was generated to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI for mesorectal fascia involvement, taking histopathology as gold standard.

**RESULTS**

A total of 30 cases of rectal adenocarcinomas fulfilling inclusion criteria were studied. Mean age was 44.17 ± 15.75 years. Age range was from 24 years to 81 years. Distribution of age in various decades was following; 8 patients in 5th decade (26.67%), 7 patients in 2nd decade (23.33%), 6 patients in 4th decade (20%), 5 patients in 3rd decade (16.67%), 2 patients in 7th decade (6.67%), 1 patient in 6th (3.33%) and 1 patient in 8th decade (3.33%). In these patients, 21 patients (70%) were males and 9 patients (30%) were females.

Distance of tumour was measured on MRI from mesorectal fascia. Mesorectal fascia was considered involved when tumour was involving the mesorectal fascia or when it was within one millimeter from mesorectal fascia (Figure 1b). Mesorectal fascia was considered uninvolved when tumour was more than one millimeter from the mesorectal fascia (Figure 2b). On MRI, 10 patients (33.33%) had involved mesorectal fascia. Rest of the 20 patients (66.67%) had no involvement mesorectal fascia (Table I). Distance of adenocarcinoma from mesorectal fascia was also measured on histopathological examination of slides taken from submitted specimen without knowing the results of MRI about mesorectal fascia status. Micro-

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<th>Table I: Status of mesorectal resection margin on MRI and histopathology.</th>
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Comparing histopathological and magnetic resonance imaging based mesorectal fascia status in patients with rectal carcinoma
scopically mesorectal fascia was identified by the presence of Indian ink which was applied on mesorectal fascia and fixed during surgical grossing of submitted specimen (Figure 1a). Histopathologically, mesorectal fascia was considered involved when adenocarcinoma was involving the mesorectal fascia or was within one millimeter from mesorectal fascia (Figure 2a). Mesorectal fascia was considered uninvolved when adenocarcinoma was more than one millimeter from mesorectal fascia (Figure 1a). On histopathology, 6 patients (20%) had involved mesorectal fascia and 24 patients (80%) had uninvolved mesorectal fascia (Table I).

Keeping histopathology as gold standard, findings of histopathology regarding mesorectal fascia as involved or uninvolved were compared with findings of MRI regarding mesorectal fascia as involved or uninvolved. True positive, true negative, false positive and false negative cases were identified. A 2 x 2 table was generated to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI to detect mesorectal fascia as involved or uninvolved by tumour. Sensitivity of MRI to detect mesorectal fascia was 23.07% and specificity of MRI mesorectal fascia was 70.5%. Positive predictive value of MRI was 10% and negative predictive value was 54.54%. Diagnostic accuracy of MRI was 50%.

DISCUSSION

Rectal cancer is one of the leading malignancies worldwide. It is the third most common cancer across the world and also among the leading causes of mortality. To reduce the morbidity and mortality caused by rectal cancers many studies have been done. The aim and objective of these studies were focused on diagnosis of this cancer as early as possible, to identify the factors influencing the prognosis and to predict outcome and disease-free survival. Nowadays, it is believed that distance of tumour from mesorectal fascia is the strongest predictor of outcome. The more is the distance of tumour from the mesorectal fascia, better will be the outcome and prolonged disease-free survival rate, and lesser the distance of tumour from mesorectal fascia, the poorer will be the prognosis and there will be chance of early recurrence. For this purpose, pre-operative radiological investigations are routinely performed.

Different radiological modalities are available to determine distance of mesorectal fascia from tumour. Among different radiological investigations, MRI more accurately determines the distance of tumour from mesorectal fascia.13 Pre-operative MRI is routinely done in patients of rectal cancer. It is intended for staging of cancer, and in addition, it also provides information regarding mesorectal fascia and its distance from tumour.14 However, the statistical data available regarding the results of MRI to predict mesorectal fascia as involved and uninvolved is controversial. This study was performed to compare MRI based radiological findings regarding mesorectal fascia as involved or uninvolved with histopathological findings regarding mesorectal fascia as involved or uninvolved keeping histopathology as gold standard. Wieder performed a study to predict tumour-free circumferential resection margin using MRI and confirmed his findings by comparing it with histopathological evaluation of circumferential margin. According to his analysis, MRI accurately predicts the circumferential resection margin with sensitivity of 100% and specificity of 88%.15 This study suggested that MRI can play a vital role for early diagnosis of disease and to determine the distance of tumour from mesorectal fascia. When results of this study were compared with other studies, results were not the same. These differences in the results of studies may be due to different protocols followed by radiologists at different institutes for imaging. The imaging can be compliant or non-compliant. One of the study shows that compliant imaging predicts the tumour more accurately.16 In compliant imaging comparatively
less sequences of images are taken which are more accurate than the other imaging techniques especially when the tumour is invading the mesorectum anteriorly. Suzuki showed that sensitivity and specificity of compliant rectal imaging was 86% and 94% respectively when compared with histopathology.16 These values were high as compared to this study. Hancock showed that accuracy of MRI to predict mesorectal fascia status is 76% with sensitivity and specificity of 96.9% and 73.8% respectively.12 Rao in his study claimed that MRI had 88% accuracy to predict mesorectal fascia involvement by tumour whereas sensitivity, specificity, positive predictive value and negative predictive values in his study were 80%, 90.4% 70.6% and 94% respectively.17

If results from different studies regarding mesorectal fascia status are compared, results show variation with broad range. One reason can be the skills, knowledge and experience of the radiologist. Better results of MRI are associated with training of radiologist, workshops and seminars attended. Videhult in his study found that accuracy of MRI for mesorectal fascia was 86% with interobserver variability of 80% and 100%. He also admits that it is very difficult to distinguish the tumour invading into mesorectal fat from the tumour which is not. MRI has poor performance to differentiate between the tumour and desmoplastic response. Desmoplastic response is tissue reaction surrounding the tumour. Many times tumour is limited to mesorectal fat with desmoplastic response which extends to the mesorectal fascia and MRI occasionally misinterprets it as positive margin. This is very clear from the above mentioned studies, as sensitivity of MRI in all studies is lower as compared to specificity. In this study also the sensitivity was 23.07% and specificity for mesorectal fascia was 70.5%.

From the knowledge of anatomy it is known that the amount of mesorectal fat is not same in males and females. In males the amount of mesorectal fat both anteroposteriorly and in lateral dimension is more as compared to females especially toward the anterior surface. This variation of fat in both genders can have complications in females especially on anterior surface can lead to false situation cautiously. Thus, a low bulk of mesorectum in females which comprise 57.1% of false positive patients. Another important factor could be the bias of the radiologist to prove radiological investigation have better outcome. Majority of the studies have been done by radiologists. In this study, this bias was minimized by performing this study in pathology department and radiologists were blinded from the results of histopathological findings. Comparing the age of patients of rectal adenocarcinoma in this study which represent the Pakistani population, majority of the patients were in 5th and 2nd decade. i.e. 8 patients in 5th decade (26.67%), 7 patients in 2nd decade (23.33%). In developed countries, the peak incidences of rectal adenocarcinoma are 5th and 6th decade. Younger age group is commonly not affected by this disease. Only younger people with this disease in developed countries are affected by Adenomatous polyposis coli genes (APC)/beta-catenin pathway. However, in developing countries like in Pakistan there is bimodal presentation of rectal adenocarcinoma. One peak is in 2nd to 3rd decade and second peak is in 5th to 6th decade. The only limitation of this study was a small number of cases. This is because of low socioeconomic status of our population which cannot bear the expensive management of rectal adenocarcinoma.

CONCLUSION
Assessment of mesorectal fascia status with MRI did not prove helpful and comparable to histopathological based mesorectal fascia status as involved or uninvolved. Histopathological mesorectal fascia status was taken as gold standard. Histopathology should be done in each and every case of rectal carcinoma with involved or uninvolved mesorectal fascia status on MRI to avoid undue neoadjuvant chemotherapy, surgery or palliative treatment and vice versa.

REFERENCES
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