DOI: 10.7860/JCDR/2017/30848.10842

Original Article

Surgery Section

Complete Response after Neoadjuvant Therapy in Rectal Cancer- Does T0 Mean N0?

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ABSTRACT

Introduction: Rectal resection after neoadjuvant chemoradiotherapy is the standard of care for rectal cancer. Non-operative management of rectal cancer is the new frontier. Selection of these patients is based on the absence of mucosal disease after neoadjuvant therapy. The question that is quintessential is whether absence of mucosal disease means absence of nodal disease.

Aim: To see the correlation between absence of mucosal disease and mesorectal disease in rectal resections after neoadjuvant therapy for rectal cancer.

Materials and Methods: A retrospective study was done on 479 patients of locally advanced carcinoma rectum from 2008 to 2015. All patients received neoadjuvant therapy which was mainly long course radiation therapy with 5040cGy over duration of 28 days with concurrent chemotherapy. Some patients underwent neoadjuvant chemotherapy. After an interval of approximately 6 weeks they underwent curative surgery. The patients who had complete pathological response were analysed in this study.

Results: Out of the 479 patients, 76 patients were found to have no disease in the rectal wall. Only 1 patient (1.3%) had node positive disease without having any rectal disease (T0N1). The rest had no tumour either in the rectum or the mesorectal nodes. Thus, 75 patients had a pathological complete response (15.6%).

Conclusion: In patients with rectal cancer undergoing neoadjuvant chemoradiotherapy followed by radical resection, absence of tumour in the rectum correlates well with absence of disease in the mesorectum and absence of nodal disease. Thus, absence of mucosal disease can be taken as marker of complete response to neoadjuvant therapy.

Keywords: Chemoradiotherapy, Mucosal disease, Nodal disease

INTRODUCTION

Rectal cancer treatment has changed over the last two decades. Multimodality treatment is the standard of care and the role of neoadjuvant therapy has been firmly established [1,2]. In locally advanced carcinoma rectum such as T3 and T4 with or without node positivity in the mesorectum the benefit of radiation has been well documented [3,4]. Radiation decreases local recurrence and may improve survival. The mechanism of this is through downstaging of the tumour and increasing the chance of a negative margin at surgery.

Another benefit of neoadjuvant therapy is increased chance of sphincter saving surgery thus converting the abdominoperineal excisions to low anterior resections [5]. Thus, the rate of permanent stomas decreases and patient acceptability increases.

Neoadjuvant radiation therapy more so the long course chemoradiation therapy can cause complete regression of the tumour which is known as complete pathological response. Pathological complete response is known to be associated with higher disease free and overall survival and thus has become a benchmark for assessing the effect of neoadjuvant therapy [6]. Complete response rates vary anywhere from 12-34% in different series and the thrust of research is in trying to modify neoadjuvant therapies so as to get the highest complete response [7-9].

The pathological complete response questions the need for radical rectal resection. The group from Sao Paulo has proven that a select group of patients who respond extremely well to neoadjuvant chemoradiotherapy and have no appreciable disease in the rectum both clinically and radiologically, can be managed on a "Watch and Wait" protocol [10]. This entitles a close follow up of the patient, multiple clinical examinations and regular imaging. These patients may not need the radical rectal resection which is the standard of care for such cases the world over. Multiple studies have shown that these patients have comparable, disease free and overall survival rates as compared to the patients getting the standard care [11-13].

Though this "Watch and Wait" protocol is gaining acceptance slowly it is still not standard of care. This is mainly because of the unreliability of the clinical complete response [14]. Clinical complete response can only assess the mucosa and cannot assess the mesorectum. T3 and T4 tumours have a high nodal positive rate and the question remains whether the tumour is present in the mesorectal nodes even though it has regressed in the rectal wall. Therefore, the study was done with an aim to correlate the absence of tumour in the rectal wall with disease in the mesorectum in the resected rectal resection specimen.

MATERIALS AND METHODS

A retrospective study was conducted in a tertiary care centre in Southern India. Patients with a primary diagnosis of rectal cancer from April 2008 to March 2015 who were treated with preoperative combined modality therapy were identified from the rectal cancer database. All data was collected and recorded in a prospectively maintained database and the pathologic features for each patient were reviewed retrospectively. All patients underwent resection after preoperative therapy. The indications for preoperative therapy in most patients included T3, T4, or node-positive disease as determined by MR imaging of the pelvis. In general, preoperative combined modality therapy consisted of two cycles of 5-fluorouracil–based therapy plus concurrent 50.4Gy of pelvic radiation, followed 6 to 8 weeks later by surgery.

Patients with metastatic disease and synchronous lesions were excluded from the study.

A total of 479 patients with carcinoma rectum were included in the study from April 2008 - March 2015. The pathological specimens were used for the study and pathological complete response was defined as no tumour in the rectal wall or the mesorectum.

RESULTS

A total of 479 patients were included in this study. A 61% (293) of patients were male and 39% (186) were female. The mean age of the

patients was 48.2 years (SD 14.9) ranging from 18 to 89 years.

Out of the 479 patients, 76 had no disease in the rectal wall ypT0. Out of the 76 patients, 75 patients had no disease in the mesorectum also. Thus, the number of patients with pathological complete response was 75 with a pathological complete response rate of 15.6%. One patient out of the 76 patients had a positive lymph node (pT0N1). Thus, only one patient had no tumour in the rectal wall but had tumour in the mesorectum.

DISCUSSION

Rectal cancer response to chemoradiotherapy can be variable. It is assessed with a clinical examination and a MRI of the pelvis about 8 to 10 weeks after completion of chemo radiotherapy. This provides an idea as to the response of the tumour and the patient is usually planned for surgery. Complete clinical response is described as absence of tumour on digital rectal examination. This however cannot assess the nodal response to neoadjuvant therapy. MRI of the pelvis also cannot ascertain nodal response rate accurately [15]. Thus, only the pathological specimen after radical rectal resection can accurately assess nodal positivity. In this study in the pathological specimens of the rectal resections it was seen that when there was no tumour in the rectal wall there was a very small chance that there would be tumour in the mesorectal nodes.

Watch and wait protocol is the new method of managing complete clinical response. This protocol has been described in low rectal cancers and is applicable when there is a complete response on digital rectal examination after neoadjuvant chemoradiotherapy. The major burden of diagnosing the complete clinical response is on the clinician's finger. Corroborative evidence is by the MRI imaging of the pelvis.

The major criticism of the watch and wait protocol is the fact that there is no consensus of complete clinical response [16]. The question remains that if the clinicians feels that there is no tumour in the rectal wall does that mean there is no microscopic disease in the mesorectum. This could give rise to disease progression and metastases which could be prevented by rectal resection [17].

Neoadjuvant chemoradiotherapy is standard of care for T3 and T4 disease with or without nodal disease. The rate of nodal metastases can be as high as 50% in these tumours. Thus, it is important to be sure that there is no nodal disease before enrolling the patient in the watch and wait protocol.

In this study, it has been shown that in the pathological specimens the absence of disease in the rectal wall correlates well with no disease in the mesorectum. Most of the patients with no tumour in the rectal wall did not have disease in the mesorectum. Only one patient had no disease in the rectal wall but had disease in the mesorectum as a positive lymph node.

Though this should not be interpreted as complete clinical response is equal to no disease in the rectum it can be taken that if there is no disease in the rectal wall the chance of disease being in the mesorectum is less. This further corroborates the body of evidence for the watch and wait protocol. Further evidence is required to correlate complete clinical response and complete absence of disease in the rectal wall but once that is established a certain group of patients could be managed non-operatively successfully.

LIMITATION

The limitations of the study were the small number of patients and the lack of correlation between complete clinical response and pathological complete response.

CONCLUSION

In patients of rectal cancer undergoing neoadjuvant chemoradiotherapy followed by radical rectal resection absence of disease in the rectal wall correlates well with absence of disease in the mesorectum. It is very rare to see disease in the mesorectum without disease in the rectal wall.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jun 12, 2017**
Date of Peer Review: **Jul 17, 2017**
Date of Acceptance: **Oct 06, 2017**
Date of Publishing: **Nov 01, 2017**