



## PATHOLOGICAL RESPONSE AFTER NEOADJUVANT CHEMORADIATION IN LOCALLY ADVANCED RECTAL CANCER

### Oncology

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### ABSTRACT

**Background:** Locally advanced rectal cancer can be downstaged by neoadjuvant therapy and the resultant tumour response can be quantified histologically.

**Aim:** To assess pathological response in patient with locally advanced rectal cancer treated by neoadjuvant chemoradiation.

**Methods And Materials:** A total of 30 consecutive patient with locally advanced rectal cancer treated in father muller medical college were reviewed. Pre-operative neo-adjuvant chemo radiation was delivered with a total dose of 50.4 Gy in 28 fraction concurrent with Tab.capecitabine 825mg/m<sup>2</sup>. Surgery was planned at 6-8 weeks from completion of neo-adjuvant chemo radiation. The pathological response to therapy was assessed by histopathological report of surgical specimen.

**Results:** A total of 30 patient with 17 male and 13 female patient. Initial clinical staging of patient revealed 90% were staged T3/T4 N1-2M0 and 10% were staged T3N0. Patient received neo-adjuvant chemo radiation followed by surgery as per protocol. In which 50% underwent Abdominoperineal resection, 23.3% underwent Anterior resection, 20% underwent low Anterior resection, 6.6% underwent Pelvic exenteration. Complete pathological response was observed in 23.3% and partial response in 76.7% of patient. Positive lymph node metastasis was confirmed in 35% of cases.

**Conclusion:** Neoadjuvant chemoradiation is a reasonable option for cases of locally advanced rectal cancer to achieve pathological response and sphincter preserving surgery.

### KEYWORDS

Neo-adjuvant Chemo Radiation, Abdominoperineal Resection, Anterior Resection, Low Anterior Resection, Pelvic Exenteration, Pathological Response.

### INTRODUCTION

Colorectal cancer remains a major worldwide health problem. Colorectal cancer is the third most commonly diagnosed malignancy and the fourth leading cause of cancer death in world, accounting for about 1.4 million new cases and almost 700000 death in 2012<sup>1</sup>.

Rectal cancer accounts for nearly 30% of all colorectal cancer<sup>2</sup>. Surgery is the cornerstone in treatment of rectal cancer. Following resection, 5 year varies according to disease extent<sup>3,4</sup>.

After establishing the diagnosis and completing the staging work-up, a decision is made whether to pursue immediate resection/administer pre-op chemo radiation<sup>5</sup>.

Strategy of performing pre-op instead of post-op treatment has the proven advantage of lower acute toxicity<sup>6</sup>, lower total dose of radiation needed<sup>7</sup> and eventually tumor regression and down staging to enable curative resection and even sphincter preservation<sup>7-12</sup>.

Objective of this study to assess the pathological response in patient with locally advanced rectal cancer treated by neo-adjuvant chemo radiation in father Muller medical college, Mangalore between 2018-2019.

### MATERIALS AND METHODS

A total of 30 consecutive patients with locally advanced rectal cancer treated in father Muller medical college were reviewed.

Pre-operative Neo-adjuvant chemo radiation was delivered with a total dose of 50.4Gy in 28 fraction, 2Gy per fraction, 5 fraction per week by conformal technique concurrent with Tab.capecitabine 825mg/m<sup>2</sup>. Total mesorectal excision of the rectal tumor either by Anterior/ APR was planned at 6-8 weeks from completion of pre-operative Neo-adjuvant chemo radiation. The pathological response to therapy was assessed by histopathological report of surgical specimen. Report included presence of lymph nodes and if they were involved or not. Data was introduced and analyzed by computer program (SPSS version 17).

### RESULTS

A total of 30 patient with 17 male and 13 female patients. Initial

clinical staging of patient revealed 90% were staged T3/T4 N1-2 and 10% were staged T3N0M0. More than 53% of cases have tumor between 4-8cm from anal verge (Fig:1).

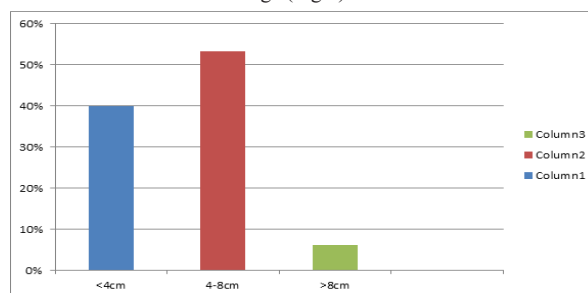


Figure 1: Tumor Site From Anal Verge

Patient received neo-adjuvant chemo radiation and followed by surgery after 6-8 weeks as per protocol. In this study about 50% of cases underwent APR, 23.3% underwent AR, 20% underwent LAR and 6.6% underwent pelvic exenteration (in Fig :2).

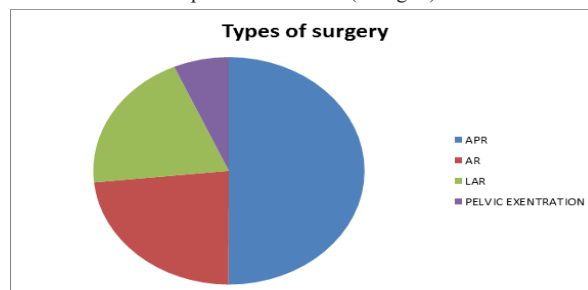


Fig 2:Surgery

Following surgery post-operative histopathological report was reviewed and found that complete pathological response was observed in 23.3% of cases and partial response was observed in

76.7% of cases (in Fig:3). Positive lymph node metastasis was confirmed in 35% of cases.

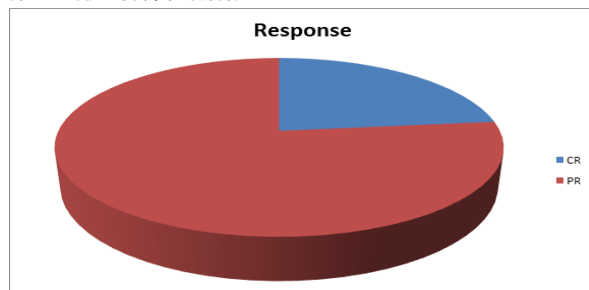


Fig 3:Response

## DISCUSSION

Advances in colorectal cancer treatment create a development of a neo-adjuvant chemo radiation which became widely accepted now<sup>13</sup>. Neo-adjuvant chemo radiation is very effective in reducing the tumor mass as 7 out 30 patient showed no palpable mass, per digital rectal examination (DRE), after Neo-adjuvant chemo radiation. All cases were amenable for surgery after neo-adjuvant chemo radiation including those who presented with fixed tumor. This reflected the effectiveness of NACRT in the study.

## Patient Characteristics

|                           |                     |
|---------------------------|---------------------|
| Total no.of patient       | 30                  |
| Medianage                 | 51years(21-68years) |
| Male                      | 17                  |
| Female                    | 13                  |
| Grade:                    |                     |
| Welldifferentiated        | 16                  |
| Moderatelydifferentiated  | 9                   |
| Poorlydifferentiated      | 5                   |
| Tumor site fromanalverge: |                     |
| <4cm                      | 12(40%)             |
| 4-8cm                     | 16(53%)             |
| >8cm                      | 2(6%)               |
| Stage:                    |                     |
| T3/T4N1-2                 | 27(90%)             |
| T3N0M0                    | 3(10%)              |
| Radiationdose             | 50.4Gy/28fraction   |
| Concurrentchemotherapy    | Tab.capecitabine    |
| Surgery                   |                     |
| APR                       | 15(50%)             |
| AR                        | 7(23.3%)            |
| LAR                       | 6(20%)              |
| Pelvicexentration         | 2(6.6%)             |
| Patho logical staging     |                     |
| YpT0N0                    | 7(23.3%)            |
| ypT1-2N0-1                | 7(23.3%)            |
| YpT3-4N0-2                | 16(53.3%)           |

In this study 90% of our patient had T3/T4 N1-2 staged disease and post chemo radiation almost 45% of patient had down staging of disease. 10% of patient who had T3N0 staged disease had complete response with down staging of disease of 100%.Radiological complete resolution was observed in 40% of cases. Overall down-staging in this study was observed in 70%. In comparison with a study done by Rashid A et.al they showed down-staging was found in 56.7% of cases<sup>14</sup>. Duke's university study showed down-staging in 82% of cases, and this was compatible with our findings<sup>15</sup>.

In a study conducted in shanghai (2001-2005), 105 patients were studied, of these 13 patient showed complete tumor response after chemoradiation and they spared the operation<sup>16</sup>. In our study 7/30 patients (23.3%) had complete pathological response which was comparable to findings of Dunst et.al<sup>17</sup>, they have pathological complete response was achieved in six patients (7%, 95% confidence interval: 3-14%). In another study conducted in Karachi, Rashid A et.al found that pathological complete response of tumor was achieved in 3.3%<sup>14</sup>.

In our study, Positive lymph node metastasis was confirmed in 35% of cases, this correlates well with the series reported by De laFuente

SG et.al<sup>18</sup>, who found that fewer total lymph nodes were retrieved in the neo-adjuvant therapy patients compared to those who did not receive pre-operative chemo radiation.

## CONCLUSION

Neoadjuvant chemoradiation is a reasonable option for cases of locally advanced rectal cancer to achieve pathological response and sphincter preserving surgery.

## REFERENCES:

1. International Agency for Research on Cancer WHO. GLOBOCAN 2012: Estimated Cancer Incident, Mortality and Prevalence Worldwide in 2012. [http://globocan.iarc.fr/Pages/fact\\_sheets\\_population.aspx](http://globocan.iarc.fr/Pages/fact_sheets_population.aspx)
2. American cancer society, author. Cancer facts & figures. Vol. 1951. New York: American Cancer Society; 2007.
3. Jessup JM, Stewart AK, Menck HR. The national cancer data base report on patterns of care for adenocarcinoma of the rectum, 1985–1995. *Cancer*. 1998;83:2408. [Pub Med]
4. Willett CG, Lewandrowski K, Donnelly S, et al. Are there patients with stage I rectal carcinoma at risk for failure after abdominoperinealresection? *Cancer*. 1992;69:1651–1655. [Pub Med]
5. Zinner Michael J, Ashley Stanley W. maingot's abdominal operations. 11th edition. New York: McGraw-Hill; Chapter 25. Cancer of the rectum; p. 2000.
6. Minsky BD, Cohen AM, Enker WE. Combined modality therapy of rectal cancer: decreased acute toxicity with the preoperative approach. *JClin Oncol*. 1992;10:1218–1224. [Pub Med]
7. Frykholm GJ, Isacson U, Nygard K, et al. Preoperative radiotherapy in rectal carcinoma. Aspects of acute adverse effects and radiation technique. *Int J Radiat Oncol BiolPhys*. 1996;35:1039–1048. [Pub Med]
8. Holm T, Singnomklao T, Rutqvist LE, Cedermark B. Adjuvant preoperative radiotherapy in patients with rectal carcinoma. Adverse effects during long-term follow-up of two randomized trials. *Cancer*. 1996;78:968–976. [Pub Med]
9. Letschert JGJ, Lebesque JV, Aleman BMP, et al. The volume effect in radiation-related late small bowel complications: results of a clinical study of the EORTC Radiotherapy Cooperative Group in patients treated for rectal carcinoma. *Radio ther Oncol*. 1994;32:116–123. [Pub Med]
10. Swedish rectal cancer trial. Improved survival with preoperative radiotherapy in resectable rectal cancer. *N Engl J Med*. 1997;336:980–987. [Pub Med]
11. Martling A, Holm T, Johansson H. The Stockholm II trial on preoperative radiotherapy inrectal carcinoma: long-term follow-up of a population-based study. *Cancer*. 2001;92:896–902. [Pub Med]
12. Ceelen WP, Van Nieuwenhore Y, Fierens K. Preoperative chemoradiation versusradiation only for stage II and III resectable rectal cancer (review) *Cochrane data base for systemic reviews*. 2009 [Pub Med]
13. Abdalla Ahmed A, Alshaihk Ahmad A, Abuldris Daffalla O, MohamedElfatih M. Neoadjuvant chemoradiation for rectal cancer: analysis of clinical outcomes for patients treated in Wad Medani TeachingHospitaland National Cancer Institute (Sudan) in the period 2006–2011. *Sudan Med J*. 2012 Aug;48(2):129–134.
14. Rashid A, Ahmed S, Ali M, Fareed M, Bilal M. Role of neo-adjuvant chemoradiation in locally advanced rectal cancer. *J Coll Physicians SurgPak*. 2010 Mar;20(3):175–180. [Pub Med]
15. Onaitis Mark W, Noone Robert B, Hartwig Matthew, et al. Neoadjuvantchemoradiation for rectal cancer: analysis of clinical outcomes from a 13-year institutional experience. *Ann Surg*. 2001 Jun;233(6):778–785. [PMC free article] [Pub Med]
16. Yu BM, Zhang M, Wu WQ, et al. Efficacy of neoadjuvantradiochemotherapy in treatment of locally advanced low rectal cancer. *ZhonghuaWaiKeZaZhi*. 2007 Apr;45(7):445–448. [Pub Med]
17. Dunst J, Debus J, Rudat V, et al. Neoadjuvant capecitabine combined with standard radiotherapy in patients with locally advanced rectal cancer: mature results of a phase II trial. *Strahlenther Onkol*. 2008 Sep;184(9):450–456. Epub 2008 Sep 19. [Pub Med]
18. De la Fuente SG, Manson RJ, Ludwig KA, Mantyh CR. Neoadjuvantchemoradiation for rectal cancer reduces lymph-node harvest inproctectomy specimens. *J Gastrointest Surg*. 2008 Oct;45(7):445–448.[Pub Med]