



LONG COURSE RADIOTHERAPY VERSUS PATHOLOGICAL COMPLETE RESPONSE IN CARCINOMA RECTUM

Pathology

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ABSTRACT

Neoadjuvant therapy has become the standard of care for locally advanced mid-low rectal cancer. Pathological complete response (pCR) can be achieved in 12%-38% of patients. Patients with pCR have the most favorable long-term outcomes. Intensifying neoadjuvant therapy and extending the interval between termination of neoadjuvant treatment and surgery may increase the pCR rate. Growing evidence has raised the issue of whether local excision or observation rather than radical surgery is an alternative for patients who achieve a clinical complete response after neoadjuvant therapy. Herein, we highlight many of the advances and resultant controversies that are likely to dominate the research agenda for pCR of rectal cancer in the modern era.

KEYWORDS

Rectal cancer; Neoadjuvant therapy; Pathological complete response; Local excision

INTRODUCTION

Multidisciplinary therapy is the basic principle of rectal cancer treatment, and radical surgery remains the main treatment. For early tumors, radical total mesorectal excision (TME) is curative. However, for locally advanced low rectal cancer (T3/T4 or N+) with a relatively high risk of locoregional recurrence, neoadjuvant therapy followed by TME has become the standard of care in order to downstage the tumor, thereby facilitating dissection and improving surgical outcomes.¹ Tumor regression after chemoradiotherapy (CRT) is observed in most patients, with 12%-38% cases showing a pathological complete response (pCR) in postoperative specimens.¹ The predictive factors of pCR include the primary tumor size, histological type, pretreatment clinical stage, neoadjuvant therapy regimens, and interval between neoadjuvant therapy and surgery.² Achievement of pCR after neoadjuvant CRT is associated with greatly improved cancer outcomes and significantly decreased local recurrence (LR) in locally advanced rectal cancer (LARC).^{3,4} Recently, it has been suggested that radical surgery should be avoided in patients who achieve a clinical complete response (cCR). Selected patients may benefit from the management of local excision (LE) or simple observation ("wait and see" or "wait and watch" strategy), improving the possibility of organ preservation with comparable survival.⁵ Here, the latest advancements in clinical research on pCR after neoadjuvant therapy are reviewed, focusing on current imaging, predictive factors, prognosis and management.

METHODS:

20 patients are selected from GSL cancer hospital, Rajahmundry, who are biopsy proven carcinoma rectum over a period of 1 year. MRI pelvis was done to decide the stage and for Neoadjuvant therapy.

Neoadjuvant therapy include Short-course radiotherapy does not include administration of sensitizing chemotherapy. Long-course radiotherapy includes administration of sensitizing therapy, most commonly 5-fluorouracil (5-FU).

Patients who achieved clinically complete response was identified by no visible or palpable lesion clinically and on colonoscopy.

All the patients in this study underwent surgery either low anterior resection or abdominoperineal resection accordingly.

Post operative histopathology report was noted and patients who achieved clinically complete response was compared with pathological complete response on HPE.

RESULTS:

The study was undertaken from January 2020 to January 2021 in the department of general surgery, GSL medical college, Rajanagaram.

The observations of the study are as follows:

10 patients treated with short course radiotherapy
10 patients treated with long course radiotherapy with 5-FU.
15 patients underwent low anterior resection.
5 patients underwent abdominoperineal resection.

6 patients in long course group achieved clinically complete response, out of which 4 patients have got clinically complete response (64%).

4 patients in short course group achieved clinically complete response, out of which 1 patient has got pathologically complete response (16%).

Table 1: % of cCR and pCR among the treatment groups.

TOTAL 20 CASES	Long course		Short course	
	10		10	
	4 male	6 female	5 male	5 female
cCR(64%)	2	4	2	2
pCR(16%)	1	1	1	-

DISCUSSION:

Restaging after neoadjuvant therapy for rectal

Cancer

Neoadjuvant therapy course induces deep modifications of cancer tissue and surrounding structures such as fibrosis with mucin pools, deep stroma alteration, bowel wall thickening, muscle disarrangement, tumor necrosis, calcification, and inflammatory infiltration. As a result, Sensitivity, specificity, and accuracy of computed tomography (CT), endorectal ultrasonography (EUS), and magnetic resonance imaging (MRI) to preoperatively determine locoregional neoplastic extension are suboptimal for restaging.

CECT-CT scanning is commonly considered an unreliable restaging technique to assess pCR. In terms of nodal involvement, CT has an accuracy of 82% by using a cutoff of 10 mm.⁶ On the contrary, in a 5-mm cutoff setting, the accuracy has been reported to be 62%.

EUS-The accuracy of EUS ranged from 27% to 72% in T restaging but only 0%-60% in correctly diagnosing ypT0. Its accuracy in restaging lymph nodal involvement ranged between 39% and 83%.

Diffusion-weighted MRI, especially at high b values, would be effective for the prediction of treatment outcome and early detection of tumor response. The addition of diffusion-weighted imaging to standard rectal MRI improves the selection of complete responders after chemoradiation.⁷ Dynamic contrast-enhanced magnetic resonance imaging is reported to have a sensitivity of 100% for distinguishing complete and incomplete responses.⁸ Nodal staging by

using MRI usually relies on size criteria but was a poor predictor of nodal status.

Management of cCR It has been suggested that radical surgery be omitted in patients with cCR, especially in patients with distal tumors, avoiding a permanent stoma.

LE may offer the possibility of organ preservation for the management of selected patients after neoadjuvant CRT. Callender et al⁹ reported that full-thickness LE offers a comparable local control, disease-free survival (DFS), and overall survival (OS) to that achieved with proctectomy and TME. LE also enables primary tumor staging with 100% accuracy after neoadjuvant therapy. In case of poor response or non-pCR, a salvage TME surgery could be performed timely.¹⁰

The non-surgical, observation-only replacement therapy ("wait and see") was first introduced by Habr-Gama et al. In a prospectively observed cohort of patients with a cCR, no initial surgical intervention was performed. During almost 5 years of follow-up, they reported LR, DFS, and OS rates comparable to

those in patients who underwent immediate low anterior or abdominoperineal resection with TME. None of the patients developed pelvic LR. The reported 5-year DFS of 71 cCR patients was 92%, compared with the 83% for patients with radical surgery-confirmed pCR ($P = 0.09$). Patients who underwent observation had better functional outcomes than those who received surgery. The difference was larger in terms of control over flatus and the change in bowel habits, since all the patients with a pCR after surgery had changed bowel habits.

Disadvantages of surgery which are advantage to patients in wait and watch:

Aggressive TME surgery is a significant associated risk factor of morbidity, including anastomotic leakage, pelvic autonomic nerve injury, and mortality. Moreover, a proportion of patients who underwent rectal cancer surgery will require either a temporary or permanent stoma.

Selection of patients for wait and watch:

Strong will for sphincter-saving or could not tolerate radical surgery because of poor physical condition.

Predictive factors of pCR:

Improving the rate of pCR is also a major task in neoadjuvant therapy for rectal cancer. It is commonly believed that different neoadjuvant therapeutic regimens and intervals between neoadjuvant CRT and surgery significantly affect the pCR rate. Other factors that predict a pCR after neoadjuvant treatment of rectal cancers include absence of circumferential involvement and signet ring cell histology, primary tumor size, histological type, and pretreatment clinical stage.

Neoadjuvant therapy regimen and pCR The Polish study compared short- and long-course preoperative pelvic radiotherapies for T3/T4 mid to low rectal cancer, and found higher rates of pCR in the LC (16%) than in the SC (1%) group.¹¹ Short-course radiotherapy does not include administration of sensitizing chemotherapy. Long-course radiotherapy includes administration of sensitizing therapy, most commonly 5-fluorouracil (5-FU).

The interval between neoadjuvant therapy and Surgery:

It is recommended by the National Comprehensive Cancer Network (NCCN) guidelines that surgery should be implemented within 5-10 weeks after neoadjuvant therapy.

CONCLUSIONS

Pathological complete response after neoadjuvant therapy for rectal cancer is associated with significantly improved long-term outcomes. Intensified neoadjuvant therapy and delayed surgery are likely to increase the pCR rate. Owing to the limited accuracy of clinical imaging in predicting pCR, radical surgery remains the standard of care for patients downstaged by neoadjuvant therapy. LE or the "wait and see" strategy should be recommended with caution in selected cCR patients who have a strong will for sphincter-saving or could not tolerate radical surgery.

REFERENCES:

1. Belluco C, De Paoli A, Canzonieri V, et al. Long-term outcome of patients with complete pathologic response after neoadjuvant chemoradiation for cT3 rectal cancer:

- implications for local excision surgical strategies. *Ann Surg Oncol.* 2011;18:3686e3693.
2. Jayanand SB, Seshadri RA, Tapkire R. Signet ring cell histology and non-circumferential tumors predict pathological complete response following neoadjuvant chemoradiation in rectal cancers. *Int J Colorectal Dis.* 2011;26:23e27.
3. Zorcolo L, Rosman AS, Restivo A, et al. Complete pathologic response after combined modality treatment for rectal cancer and long-term survival: a meta-analysis. *Ann Surg Oncol.* 2012;19:2822e2832.
4. de Campos-Lobato LF, Stocchi L, da Luz Moreira A, et al. Pathologic complete response after neoadjuvant treatment for rectal cancer decreases distant recurrence and could eradicate local recurrence. *Ann Surg Oncol.* 2011;18:1590e1598.
5. Habr-Gama A, Perez RO, Nadalin W, et al. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. *Ann Surg.* 2004;240:711e717; discussion 717e718.
6. Pomerri F, Pucciarelli S, Maretto I, et al. Prospective assessment of imaging after preoperative chemoradiotherapy for rectal cancer. *Surgery.* 2011;149:56e64.
7. Barbaro B, Vitale R, Leccisotti L, et al. Restaging locally advanced rectal cancer with MR imaging after chemoradiation therapy. *Radiographics.* 2010;30:699e716.
8. Tong T, Sun Y, Gollub MJ, et al. Dynamic contrast-enhanced MRI: use in predicting pathological complete response to neoadjuvant chemoradiation in locally advanced rectal cancer. *J Magn Reson Imaging.* 2015;42:673e680.
9. Callender GG, Das P, Rodriguez-Bigas MA, et al. Local excision after preoperative chemoradiation results in an equivalent outcome to total mesorectal excision in selected patients with T3 rectal cancer. *Ann Surg Oncol.* 2010;17:441e447.
10. Rullier E, Vendrely V. Can mesorectal lymph node excision be avoided in rectal cancer surgery? *Colorectal Dis.* 2011;13 Suppl 7:37e42.
11. Bujko K, Nowacki MP, Nasierowska-Guttmejer A, Michalski W, Bebenek M, Kryj M. Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer. *Br J Surg.* 2006;93:1215e1223.