

# Overall Survival Associated With Ileostomy Closure in Patients With Rectal Cancer Before and After Adjuvant Therapy

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**Background:** A diverting loop ileostomy is commonly constructed to protect a distal anastomosis after proctectomy for rectal cancer. Little data are available on whether closing the ileostomy before or after adjuvant chemotherapy affects survival.

**Methods:** We conducted a retrospective review of patients with rectal cancer who underwent a low anterior resection with diverting loop ileostomy followed by adjuvant chemotherapy at Ochsner Medical Center. The primary outcome was the long-term survival in patients who had their loop ileostomies closed before chemotherapy (BC) vs after chemotherapy (AC).

**Results:** Seventy-two patients were identified (22 in the BC group vs 50 in the AC group). No difference in mean age (BC 59.5 ± 9.8 vs AC 59.2 ± 12.6,  $P=0.9$ ) or preoperative clinical stage was seen between study groups. The mean interval from ileostomy creation to closure was significantly shorter in the BC group vs AC group (16.9 ± 14.5 weeks vs 33.6 ± 18.1 weeks,  $P=0.0001$ ). Follow-up data revealed a similar mean duration from surgery to last contact (BC 50.6 ± 23.6 months vs AC 43.5 ± 22.1 months,  $P=0.23$ ) and similar overall survival (BC 86% vs AC 70%,  $P=0.23$ ) between groups.

**Conclusion:** Long-term survival was similar in patients who underwent ileostomy closure before and after adjuvant therapy following low anterior resection for rectal cancer. While this study was underpowered, it adds additional insight to an area of surgery lacking significant data. The timing of ileostomy closure should be individualized for each patient.

**Keywords:** Chemotherapy, ileostomy, ileostomy closure, rectal neoplasm, surgical stomas

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## INTRODUCTION

A diverting ileostomy is often created following low anterior resection for rectal cancer to reduce anastomotic complications. However, the construction of an ileostomy is not without complications, and its presence may reduce the quality of life for patients.<sup>1,2</sup> The common clinical scenario for patients with stage II or greater rectal cancer includes preoperative (neoadjuvant) chemoradiation therapy, surgical resection, and ileostomy creation, followed by a 6-month course of postoperative (adjuvant) chemotherapy.<sup>3,4</sup> Typically, the ileostomy is left in place until after completion of the adjuvant therapy, at which time the stoma is closed. This delay in closure for up to 6-8 months following surgery may have significant adverse implications for patients in terms of their quality of life. On the other hand, if the ileostomy is closed prior to adjuvant therapy, the initiation of treatment following surgical resection may be delayed until the patient has recovered from both operations. This delay may affect the patient's survival. The purpose of this study was to compare long-term survival of patients with rectal cancer

who had their ileostomy closed before chemotherapy (BC) vs after chemotherapy (AC).

## METHODS

We conducted a retrospective review of a prospectively collected database of patients with rectal cancer who underwent definitive care at a tertiary care facility. All patients included in this study underwent a low anterior resection with diverting loop ileostomy from 2005-2013. Patients were divided into 2 groups: those who had their ileostomy closed BC and those who had their stoma closed AC. The decision of when to close the ileostomy was made between the surgeon and patient. Neoadjuvant chemotherapy along with radiation therapy is indicated in patients with T3/T4 tumors or evidence of lymph node positivity based on preoperative imaging (pelvic magnetic resonance imaging in this cohort).

Patient demographic information collected from the records included age, preoperative clinical stage (clinical tumor/node/metastasis classification), and postoperative

**Table. Patient Demographics by Ileostomy Closure Timing**

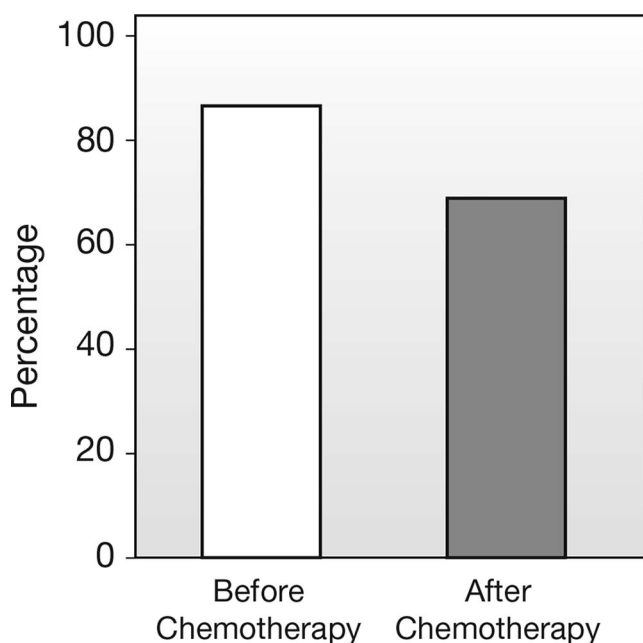
Characteristic	Ileostomy Closure Before Chemotherapy	Ileostomy Closure After Chemotherapy	P Value
	n=22	n=50	
Mean age, years $\pm$ SD	59.5 $\pm$ 9.8	59.2 $\pm$ 12.6	0.9
Postresection pathologic stage, n (%)			0.06
2	7 (32)	30 (60)	
3	14 (64)	17 (34)	
4	1 (5)	3 (6)	
Mean interval to closure, weeks $\pm$ SD	16.9 $\pm$ 14.5	33.6 $\pm$ 18.1	0.0001
Mean follow-up, months $\pm$ SD	50.6 $\pm$ 23.6	43.5 $\pm$ 22.1	0.23

pathologic stage. Neoadjuvant and adjuvant therapies were compared between groups. Time from the initial surgery to the date of ileostomy closure was calculated in weeks. Time from initial surgery to the date of last contact was calculated in months. The vital status (alive vs dead) was recorded at the time of the last contact. Date of last contact was either the date of the last office visit or a telephone inquiry with the patient's family via the tumor registry. The duration in months from the time of surgery to the date of last contact and the vital status were used to calculate the long-term survival for each patient.

For statistical analysis, *t* test and chi-square analysis were used to compare discrete and continuous variables, respectively, and  $P < 0.05$  was considered statistically significant. A Kaplan-Meier curve was calculated to compare survival between groups. Statistical analysis was performed with SPSS statistical software, v.20 (IBM Corp).

## RESULTS

A total of 72 patients were included in this analysis: 22 patients who underwent ileostomy closure BC and 50 patients

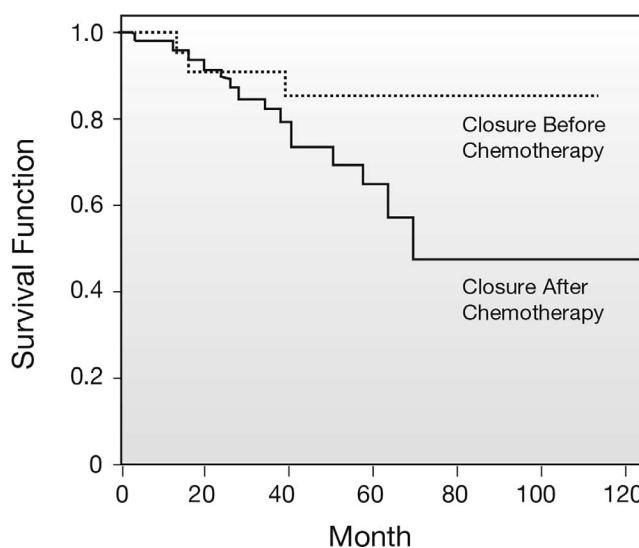


**Figure 1. Overall survival of ileostomy closure before chemotherapy vs after chemotherapy,  $P=0.23$ .**

with closure AC. Study participants were similar in age in both groups (BC group mean age of 59.5  $\pm$  9.8 years vs 59.2  $\pm$  12.6 years in the AC group,  $P=0.9$ ) (Table). The pathologic stage following resection was similar between groups. Neoadjuvant therapy was given to the majority of patients in each study group. Twenty-one of 22 patients (95%) in the BC group and 47 of 50 patients (94%) in the AC group received neoadjuvant therapy,  $P=0.9$ . The mean interval from ileostomy creation to closure was significantly shorter in the BC group vs AC group (16.9  $\pm$  14.5 weeks vs 33.6  $\pm$  18.1,  $P=0.0001$ ). The mean duration from surgery to last contact was similar between the study groups (BC 50.6  $\pm$  23.6 months vs AC 43.5  $\pm$  22.1 months,  $P=0.23$ ). Additionally, the number of patients alive at the date of last contact was similar between groups (BC 19 [86%] vs AC 35 [70%],  $P=0.23$ ) (Figure 1). The Kaplan Meier curve favored closure BC, but the results failed to reach statistical significance (Figure 2).

## DISCUSSION

This analysis demonstrates that overall survival was similar between patients who underwent ileostomy closure before vs after adjuvant chemotherapy. Ileostomy-related complications are not insignificant and may occur in 10%-75% of patients.<sup>1,5,6</sup> Complications include parastomal hernia, ob-



**Figure 2. Kaplan-Meier curve: Closure before chemotherapy=1, closure after chemotherapy=0,  $P=0.124$ .**

struction, high output with excessive fluid loss, and skin rash and are more prevalent in patients who receive neoadjuvant or adjuvant therapy. On the other hand, ileostomy closure is also associated with complications. Ileostomy closure is associated with a complication rate of 17.2%, with small bowel obstruction being the most common complication.<sup>7</sup> The optimal timing of ileostomy closure in regard to morbidity remains unknown. Perez et al demonstrated an increase in ileostomy closure complications when the stoma was closed <8.5 weeks following ileostomy creation.<sup>7</sup> However, a randomized clinical trial of early ileostomy closure (8 days) vs late ileostomy closure (2 months) demonstrated similar rates of morbidity for each study group.<sup>8</sup> Consequently, whether the timing of ileostomy closure relative to adjuvant chemotherapy has an impact on complications or survival for the patient remains unclear. While the quality of life for the patient may be improved with closure prior to the start of adjuvant chemotherapy, a complication related to the closure will likely delay treatment.

Our study specifically looked at the long-term survival in patients with rectal cancer in relation to the timing of ileostomy closure. These results add to the current data about diverting loop ileostomy closure in relation to adjuvant chemotherapy. This important clinical issue is currently underrepresented in the surgical literature. Further studies are needed to evaluate the optimal timing of ileostomy closure for disease-free survival and overall survival for patients with rectal cancer.

One of the limitations of this analysis is that it was underpowered to demonstrate a difference >20%. Therefore, whether there is any real difference in survival is unclear, but for this cohort of patients, survival appears to be similar. In addition, the interval between ileostomy creation and the start of chemotherapy is an important consideration. However, because of limitations in the dataset and the fact that a significant number of patients received adjuvant chemotherapy at outside facilities following surgical resection, this interval could not be calculated with any level of accuracy.

## CONCLUSION

The results of this study demonstrate similar overall survival in patients who underwent ileostomy closure before vs after adjuvant therapy following low anterior resection for rectal cancer. While this study was underpowered, it adds insight to an area of surgery lacking significant data. Until such data are available, the timing of ileostomy closure should be individualized for each patient.

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