Original Research Article

EARLY VERSUS CONVENTIONAL CLOSURE OF TEMPORARY ILEOSTOMY – AN OPEN LABELLED PROSPECTIVE RANDOMISED CONTROLLED STUDY

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Abstract

Background: A temporary diversion ileostomy is created to limit the complications of distal anastomotic leaks in colorectal surgeries. The reports on early versus conventional ileostomy closure are conflicting. Hence this study is being done to compare early versus conventional temporary ileostomy closure following colorectal surgeries. **Materials and Methods:** A Prospective randomised controlled trial, consecutive Patients who underwent Rectal cancer surgery with covering ileostomy are included. Patients meeting inclusion criteria and consenting for study are evaluated with a plain CT abdomen with rectal contrast on post operative day 6-7 confirming there is no radiological features suggestive of leak were randomised using computer generated block randomisation sequence using sealed envelops. Early closure was done between Post operative day 8 to 12 in same admission and Late closure defined as at 6 weeks or more. Complications using claviendindo classification, Surgical site infections using CDC definition, Ease of doing stoma closure, time to start adjuvant therapy, Hospital stay, cost analysis, Quality of life were compared. **Result:** Post operative Grade 2 complication(58.3%) are more in early closure group compared to late closure group (8.3%),p-0.017,statistically significant. None of the patients in either group had Grade 3 or above complications. Other parameters like duration of stoma closure surgery, intra operative blood loss were comparable. Mean duration of hospital stay after stoma closure is more in early closure group E:L(9.42 versus 6.25 ,P-0.041)statistically significant. At one month after stoma closure surgery quality of life is better in early closure group than late closure group. Stoma related complications and stoma care costs were significantly high in late closure group. In Early group mean duration to start adjuvant chemotherapy 46.6 days. In Late closure group overall mean duration to start adjuvant therapy is 55.8days but 3(30%) patients had treatment interruption to get stoma closure, 3(30%)patients completed their adjuvant then gone for stoma closure. 4 (40%)patients completed stoma closure then started on adjuvant therapy. **Conclusion:** Early stoma closure at 8-12 days after index surgery is feasible and safe in carefully selected patients and can be done in the same hospital admission. Early closure can have increased risk of Grade 2 Clavien-Dindo complications. Stoma care costs and stoma related complications are more in the late closure group. Quality of life is better in the early closure group. Adjuvant chemotherapy can be started early in the early closure group if it started after stoma closure surgery. Effect on oncological

405

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outcomes due to delay or interruptions in adjuvant chemotherapy due to stoma closure or stoma related complications needs to be evaluated in future studies.

INTRODUCTION

A temporary ileostomy is created to limit the complications of distal anastomotic leaks in colorectal surgeries. A defunctioning stoma is used primarily to protect the anastomosis and prevent pelvic sepsis after bowel surgery.[1,2] Several studies have shown the benefit of a covering stoma in reducing the number of anastomotic leaks requiring reoperation.[2,3] Patients selected to have a defunctioning stoma had an absolute increase of 22% in overall post-operative complications compared to those managed without a stoma.[3]

Temporary stoma remains a major psychological handicap to the patients and causes significant physical stress, leading to an adverse effect on the quality of life.[4,5] A Cochrane review reported that temporary ileostomy is associated with fewer anastomotic leakages.[6] Matthiesen et al reported that defunctioning stoma reduces the need for urgent reoperation.[2]

Evidence surrounding the timing of stoma closure is limited; Delaying stoma closure continues to expose patients to various stoma complications (up to 71%) including poor stoma site, dehydration, acute renal failure, need for parenteral nutrition, peristomal dermatitis, parastomal hernia, prolapse, retraction, and stenosis.[7] Conversely, complications of stoma closure may delay the initiation of chemotherapy. Stoma closure is usually performed after 8-12 weeks. However, quality of life is affected due to stoma related complications during this period with a stoma in a quarter of patients.[4]

Restoration of intestinal continuity is generally associated with low mortality.[8] However, stoma reversal may cause major complications ranging from 0% to 7-9% and minor complications varying from 4-5% to 30% requiring reoperation.[9] Early closure of temporary stoma might reduce stoma related morbidity and patient discomfort. Some studies have reported the feasibility of early closure of temporary loop ileostomy following rectal surgery and found encouraging results.[8,10]

Previous studies have shown that early stoma closure was associated with reduced morbidity and mortality. Recently a multicentre randomized trial - EASY trial concluded that early closure helps in significantly reducing stoma related morbidity and they advised to consider early closure if there are no signs of anastomotic leak.[11] Recent Indian studies also showed better outcomes and cost-effectiveness with early stoma closure.[12] Alves et al reported reduced hospital stay, bowel obstruction and medical complications following early stoma closure. However, they found a higher surgical wound complication rates in their series.[13] In a recent meta-analysis, it was mentioned that in select patients early closure of the temporary ileostomy is safe and feasible even as early as 8-12 days after index surgery.[14,15] Recently one randomized trial was stopped due to high complications in early stoma closures and recommended against stoma closure at 30 days.[16]

The reports on early versus conventional stoma closure are conflicting. Studies from India are scarce. Hence this study was done to compare early versus conventional stomaclosure following bowel surgery in terms of postoperative complications, morbidity, mortality, length of hospitalization and quality of life, cost-effectiveness.

MATERIALS AND METHODS

Our aim is to study the morbidity related to the early closure of temporary ileostomy compared with conventional closure after rectal cancer resection surgery.

Selection and Description of Participants

This study was conducted as a prospective, open labelled, randomised controlled trial in the department of GI, Vascular &multivisceral transplant surgery at Amrita institute of medical sciences. After getting Institutional Ethics committee clearance registered with CTRI - CTRI/2019/01/017016. Conducted between January 2019 to December 2019.

Based on the result of the percentage of wound complication rate in early stoma closure group (19%), versus late stoma closure group (5%), observed in an earlier study by Alves et al,[13] and with 80% power and 95 % confidence interval minimum sample size comes to 83 in each group. But because of the expected possibility of an insufficient number of patients, we proceeded with an expected sample size of 40 in each group.

However due to strict inclusion and exclusion criteria and short duration of the study we were able to randomize only 26 patients and finally included only 24 patients in the analysis who completed stoma closure surgery according to protocol.

Inclusion criteria defined as age more than 18yrs and consecutive patients undergoing temporary stoma following Colorectal cancer surgery. Exclusion criteria includes-Emergency surgeries, Clavien Dindo Grade 3A and above complications after index surgery, Radiological signs of an anastomotic leak on POD 7-8,Ultra-low AR/Incomplete donuts/+air leak test during index surgery,Metastatic Disease/Multi visceral resections/Re resections in index surgery, Patients on steroids/immunosuppression/Unwilling to participate in the study

Technical Information

All patients who underwent temporary diverting ileostomy after rectal cancer surgeries between January 2019 and December 2019 were considered for the study. Patients who met the inclusion criteria and consented for the study were prospectively randomized (Computer-generated block randomization) into one of the two study groups after taking a plain CT abdomen with rectal contrast on POD6 to 8, which was assessed by two senior-most radiologists independently and confirmed there were no radiological features suggestive of leak in distal anastomosis. Early stoma closure defined as Ileostomy closure will be done in between 8-12 days following index operation. Conventional stoma closure defined as Closure of the temporary ileostomy usually after 6weeks(42days) or more.

Primary end point was defined as postoperative complications compared between the two groups using standard Clavien-Dindo grading.[17] Patients followed up from index surgery to 3 months after stoma closure surgery and were assessed for complications, quality of life as assessed by health questionnaire of European organization of research and treatment of cancer. Patients' quality of life was assessed by questionnaires of the European Organization for research and treatment of Cancer (EORTC) as follows: just before stoma closure, at one month after stoma closure and at 3 months after stoma closure in both groups. Data Collected in a prescribed Proforma. Secondary end points were defined as Mortality, Intra and Postoperative parameters of stoma closure surgery, Ease of doing stoma closure surgery, Stoma related complications, Time to start adjuvant therapy, Hospital stay, Cost Analysis, Quality of life.

Statistics: Statistical analysis was done using IBM SPSS 20. (SPSS Inc, Chicago, USA). For all the continuous variables, the results are given in Mean ± SD and for categorical variables as a percentage. To test the statistical significance of the difference in the proportion of categorical variables Fisher's exact test was used. To compare the mean of numerical variables between the two groups, an independent sample 't' test was applied and for non- normal data, the Mann Whitney U test was used. A p-value < 0.05 was considered as statistically significant.

RESULTS

Out of 84 patients screened, 58 patients were excluded at various levels, finally, 26 patients were randomized after thorough clinical and radiological evaluation. Two groups after Randomisation. After randomization 24 out of 26 patients completed their stoma closure surgery who were included in the analysis. 12 patients were randomised to early closure group (EC), all completed ileostomy closure surgery. 14 patients were randomized to late closure group (LC), 12 completed ileostomy closure surgery. One patient waiting for stoma closure

hence excluded from the analysis. One patient was excluded from the analysis of ileostomy closure surgery complications, as he underwent emergency laparotomy and stoma closure surgery in a waiting period at 4 weeks after index surgery. Data from 12 in the Early closure group and 12 in the Late closure group were analysed for early versus late ileostomy closure outcomes. No Mortality reported in either group till the following up period. No re-operations after ileostomy closure in either group.

Demographic parameters and primary disease characters and neoadjuvant therapies were comparable between the groups. As mentioned in [Figure 1],All 24 patients received minimal invasive low anterior resection with covering loop ileostomy as primary surgery. None of them underwent open surgery. Total 7 patients i.e 58.33% in early closure group and 6 patients i.e 50% in late closure group underwent laparoscopic low anterior resectionwith covering loop ileostomy. Robotic low anterior resection with covering ileostomy was done in 5 patients i.e 41.66% in early closure group and 6 patients i.e 50% in late closure group. P-value 0.682 not show any statistically significant difference between the two groups.

Our primary endpoint, Grade 1 complications are seen in 3(25%) out of 12 patients in the early closure group and 4 (33.33%) out of 12 patients in the late closure group. Grade 2 complications according to Clavien-Dindo grade are seen in 7(58.33%) patients in the early closure group and one (8.33%) patient in late closure group, Overall percentage of patients with Grade 1 and 2 complications are more in early closure group with statistically significant P-Value of 0.017. Clinically significant complications like grade 3 and above are not seen in either group after stoma closure surgery.

Mean number of stoma related complications in Late randomized group was 1.28+1.43, In Early randomized group was 0.083+ 0.288 significantly more in late closure group with a p- value 0.008, [Figure 1] described these findings.
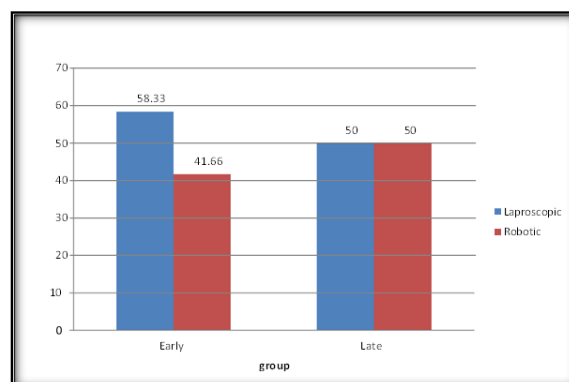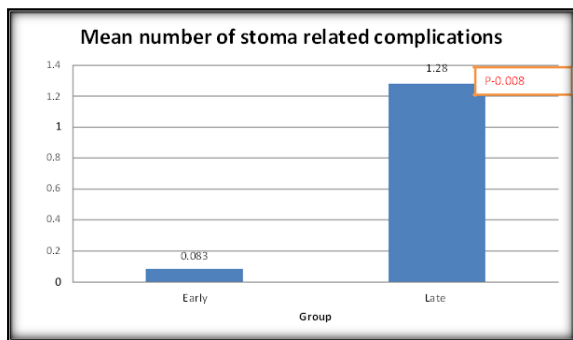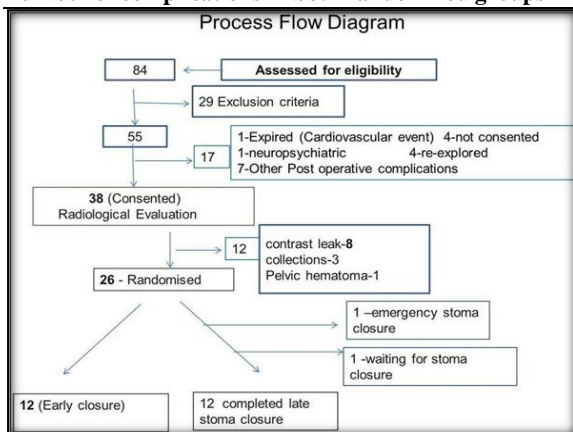

Figure 1: Type of index surgery

407

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Figure 2: Comparison of stoma related Complications in all randomized (26) patients, comparing the mean number of complications in both randomized groups

Appendix 1:

Mean Total hospital stay duration [Table1] related to surgery combining index surgery and stoma closure surgery significantly more in early closure group i.e 20.50+4.275 days compared to late closure group i.e 15.08+5.230days with a p-value of 0.011. Cost analysis overall hospital expenditure for both the index surgery and stoma closure surgery was statistically not significantly different between both the groups with a p-value 0.557, Early group Rs 2,98,418+57911, late group Rs 2,95,627 +52,878. Mean Stoma care cost spent by late closure group was Rs 4201.66+1885.45 compared to the early closure group who spent Rs 586.66+164.33 is significantly more with a p-value of 0.001, as naturally, they were having stoma for more time.

Table 1: Comparison of Hospital stay and Cost analysis between two study groups

Parameter	Group (24)				P-value
	Early (12)		Late (12)		
	Mean	SD	Mean	SD	
Length of Hospital stay after Stoma closure	9.42	4.078	6.25	2.927	0.041
Total Hospital stay in days (after index surgery+ Stoma closure)	20.50	4.275	15.08	5.230	0.011
Total mean Hospital Expenditure (in-hospital stay)	Rs 2,98,418	57,911	Rs2,95,627	52,878	0.526
Stoma care cost	586.66	164.33	4201.66	1885.45	0.001

Table 2: Comparing Quality of life between two groups using EORTC QLQ CR-29

EORTC QLQ CR-29 Scale	Timepoint	Group				P-Value
		Early(10)		Late(11)		
		Mean	SD	Mean	SD	
Urinary Frequency	Before stoma closure	14.44	15.75	16.16	14.36	0.742
	At 1 month	8.88	8.76	11.11	7.02	0.486
	At 3 months	2.22	4.684	1.01	3.35	0.486
Body Image	Before stoma closure	21.10	13.30	15.15	15.12	0.311
	At 1 month	2.22	4.68	7.07	8.98	0.175
	At 3 months	00.00	00.00	2.02	4.94	0.167
Embarrassment score	Before stoma closure	18.30	1.76	21.10	13.30	0.007
	At 1 month	14.70	2.83	16.45	2.50	0.132
	At 3 months	10.70	2.214	10.36	2.157	0.691

Appendix 2: Distribution of comorbidities in the study population

Co-Morbidity	Group(24)			
	Early(12)		Late(12)	
	n	%	n	%
No Comorbidities	07	58.3	02	16.7
Diabetes mellitus	02	16.7	02	16.7
Hypertension	00	00	06	50
DM, HTN, and CAD	03	25	02	16.7

Appendix 3: Distribution of variations in starting and interrupting Adjuvant chemotherapy between two groups				
Variations in starting adjuvant chemotherapy	Group (24)			
	Early (10/12)		Late (10/12)	
	n	%	n	%
Adjuvant chemo started after stomaclosure	10	100	04	40
Adjuvant chemo was completed thenunderwent Stoma closure	00	00	03	30
Adjuvant chemo was interrupted forstoma closure	00	00	03	30

Quality of life was analyzed by using EORTC QLQ C-30 questionnaires. Just before stoma closure and then at 1 month after stoma closure, then at 3 months after stoma closure. 10(83.33%) out of 12 patients in the early closure group and 11(91.66%) out of 12 in the late closure group completed the questionnaires.

At one month after the stoma closure global quality of life(GQL) and physical functioning(PF), Role functioning(RF) were significantly better in the early closure group. At three months after the stoma closure surgery, there is no significant difference between the two groups in global quality of life or the five functional scales according to EORTC QLQ-30 Questionnaire.

Comparing EORTC QLQ CR-29 scales before stoma closure and at 1 month and 3 months after stoma closure did not show any statistically significant difference between the groups except for Embarrassment score before stoma closure, which was higher in late closure group and statistically significant with a p-value of 0.007, as mentioned in [Table 2] which represents the low quality of life for the late closure group before stoma closure.

DISCUSSION

Covering ileostomy stoma closure surgery conventionally performed at our institute between 6-8 weeks following the index operation. This duration of 6-8 weeks following the index operation is given so that it allows the patient to recover fully from the index surgery, reduce bowel friability.

In our study early stoma closure is performed between 8-12 days following index operation in this study. Some Studies that compared the early closure carried out the stoma closure within the same hospital admission following index operation.[11,18]

In the present study, the demographics, comorbidities and diseased parameters between the two randomized groups are comparable. All patients underwent the index surgery low anterior resection with covering loop ileostomy for rectal cancer(100%).

In a previous study from Spain, the most common indication for index surgery was colorectal cancer which accounted for 56% of the study population. The majority of the patients in their study were operated electively.[19]In the present study, All patients in both groups underwent index operation as minimally invasive low anterior resection with covering ileostomy.

In the present study, there is no significant difference in the operating time between the early stoma closure group and the conventional stoma closure group. This implies that the early stoma closure does not involve added operative difficulties.

Comparable mean intraoperative blood loss and no conversion to laparotomy in both the groups confirm the technical feasibility of early stoma closure and prove that early stoma closure can be undertaken without additional operative morbidity. Similar findings were recorded by a previous study from France wherein the operating time and intraoperative bleeding did not vary significantly between the early and late closure groups.[13] In a study by lasithiotakis et al they documented early reversal was significantly superior in terms of ease of abdominal wall closure and ease of reversal and even duration of the operation.[18]

In the present study, the most common postoperative surgical complication is superficial surgical site infection at stoma closure site which came under Clavien Dindo grades 1 and 2, comparatively higher in the early stoma closure group(58.33%). Alves et al showed that surgical site infection was significantly more common in the early stoma closure group (19%) than delayed stoma closure group(5%).

In present study, none of the patients in either group developed anastomotic leaks, deep or organ space surgical site infections, intestinal obstruction, burst abdomen, incisional hernias, postoperative pneumonias, deep vein thrombosis, pulmonary embolism, etc which can amount to Clavien Dindo grade 3 and above complications in the follow-up period of 3 months after the stoma closure surgery. Bausy et al stopped their randomizedstudy due to significant complications like anastomotic leaks in the early closure group, of course, their early closure was defined at 30 days from index surgery.[16]

In a recent systematic review, reduced incidence of overall complications such as small bowel obstruction/ ileus and stoma related complications was observed in the early ileostomy closure group compared to the delayed closure group. However, wound infections had higher incidence among early ileostomy closure groups.[20]

Menegaux et al showed that the median hospital stay was significantly longer in the delayed stoma closure group (36 (14-84) days) than in the early closure group (22 (18-29) days).[21] However in our study overall mean hospital stay and mean hospital stay after stoma closure surgery were significantly more in early stoma closure group. This is due to probably more surgical site infection rate and early closure was done in the same admission, partially

due to bias as it is an open-labelled study and surgeons tend to discharge the patients in early closure a little late. However overall cost analysis did not show any statistically significant difference between the two groups in hospital expenditure for both the surgeries.

Patients in early stoma closure group spent significantly less money towards the stoma care than conventional stoma closure group. This is contributed by the fact that patients with a stoma for a longer period need a change of stoma appliances regularly. Also, longer the duration of stoma leads to peri-stomal skin excoriations and other stoma related complications hence requiring frequent dressing and further expenses towards the stoma care.

In the present study in the early closure group, the adjuvant chemotherapy was started after the stoma closure with a mean duration to start is 46.60+11.384 days. In the late closure group, the mean duration to start adjuvant chemotherapy from the index surgery is 55.80+30.34 days. In the late closure group, 40% of the patients were started on adjuvant chemotherapy after completing stoma closure surgery at 6 to 8 weeks. 30% of the patients underwent stoma closure surgery after completing their adjuvant chemotherapy due to which their stoma closure was delayed. In another 30% of the late closure group patient adjuvant chemotherapy cycles were interrupted after 2 or 3 cycles then they underwent stoma closure after that remaining adjuvant chemotherapy cycles were restarted. Even though some studies suggested stoma closure complications may be more in patients started on chemotherapy, Studies are lacking about the effect of ileostomy on delay or interruptions in adjuvant chemotherapy completion and its effect on overall survival and recurrence, cancer-related outcomes.[22,23]

It was proven in many studies the quality of life of the patients with covering ileostomy was impaired compared to the patients without a stoma.[10,24–26] In our study, the patients in the late closure group were with diversion ileostomy significantly for more duration andreported more stoma related complications compared to early closure group who got their stomas reversed within 8-12 days of index surgery.

At 1 month after stoma closure, Global quality of life, physical functioning, role functioning were significantly better in early closure group than late closure group this maybe because most of the late closure group patients were already on chemotherapy by this time and some of the early closure patients not at started chemotherapy by this time.

Early stoma closure improves the patients' psychosocial well being . Longer duration for stoma closure leads to limitations in social behavior and at times depression. These factors also should be considered in the decision of stoma closure and early closure hence could help in alleviating the possible psychological impact in these patients as seen by the improvement in the quality of life scores.[10]

Strengths and Limitations

It is a well-designed prospective randomized controlled trial. The study population is homogenous. All are rectal cancer patients and preoperative characteristics in both groups are comparable. The sample size was calculated. Primary and secondary endpoints are well defined using standard definitions like clavien Dindo grading for postoperative complications, visual analog scales, time points are defined well, Standardised questionnaires are used for quality of life assessment. Uniformity in all surgical interventions with standard protocol for both index and stoma closure surgery.

Our limitations include short follow up period after stoma closure surgery i.e. 3 months. We did not meet the expected sample size probably due to highly selective strict inclusion and exclusion criteria. In the quality of life assessment most of the patients on adjuvant chemotherapy by that time, which can also affect the quality of life.

CONCLUSION

Early stoma closure at 8-12 days after index surgery is feasible and safe in carefully selected patients and can be done in the same hospital admission. Early closure can have increased risk of Grade 2 Clavien Dindo complications. Stoma care costs and stoma related complications are more in the late closure group. Quality of life is better in the early closure group. Adjuvant chemotherapy can be started early in the early closure group if it started after stoma closure surgery. Effect on oncological outcomes due to delay/interruptions in adjuvant chemotherapy due to stoma closure or stoma related complications needs to be evaluated in future studies.

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