Randomized clinical trial

Randomized clinical trial of early *versus* delayed temporary stoma closure after proctectomy

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Background: **Temporary faecal diversion is recommended with a low colorectal, coloanal or ileoanal anastomosis (LA). This randomized study evaluated early (EC; 8 days) *versus* late (LC; 2 months) closure of the temporary stoma.**

Methods: **Patients undergoing rectal resection with LA were eligible to participate. If there was no radiological sign of anastomotic leakage after 7 days, patients were randomized to EC or LC. The primary endpoints were postoperative morbidity and mortality 90 days after the initial resection.**

Results: **Some 186 patients were analysed. There were no deaths within 90 days and overall morbidity rates were similar in the EC and LC groups (31 *versus* 38 per cent respectively; $P = 0{\cdot}254$). Overall surgical complication (both 15 per cent; $P = 1{\cdot}000$) and reoperation (both 8 per cent; $P = 1{\cdot}000$) rates were similar, but wound complications were more frequent after EC (19 *versus* 5 per cent; $P = 0{\cdot}007$). Small bowel obstruction (3 *versus* 16 per cent; $P = 0{\cdot}002$) and medical complications (5 *versus* 15 per cent; $P = 0{\cdot}021$) were more common with LC. Median (range) hospital stay was reduced by EC (16 (6–59) *versus* 18 (9–262) days; $P = 0{\cdot}013$).**

Conclusion: **Early stoma closure is feasible in selected patients, with reduced hospital stay, bowel obstruction and medical complications, but a higher wound complication rate. Registration number: NCT00428636 (http://www.clinicaltrials.gov).**

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Introduction

A defunctioning stoma is used primarily to protect the anastomosis and prevent pelvic sepsis after rectal surgery[1]. Several studies have shown that the particular benefit of a covering stoma was reduction in the number of leaks requiring surgery[2–6]. Peeters and colleagues[7] proposed that absence of a defunctioning stoma was a risk factor for symptomatic anastomotic leakage in patients undergoing total mesorectal excision for rectal cancer. A temporary loop ileostomy is preferred to colostomy by most surgeons because it is easy to construct and close without a risk of injury to the colic vascular arcade, and there are fewer problems with prolapse[8].

Temporary loop ileostomy remains a major psychological handicap and causes significant physical stress, leading to an adverse effect on quality of life[9,10]. Furthermore, patients with rectal cancer are increasingly being offered postoperative adjuvant therapy, which creates uncertainty about the timing of stoma closure[11]. Early closure (EC) of the temporary loop ileostomy might reduce both stoma-related morbidity and patient discomfort. Two prospective non-randomized studies including 27 and 39 patients respectively[12,13] have evaluated the feasibility of EC of the temporary loop ileostomy after rectal surgery. These two pilot studies reported encouraging results, with no deaths and no need for revisional procedures.

This paper reports the results of a randomized trial of EC *versus* late closure (LC) of the temporary stoma after rectal resection with a low colorectal, coloanal or ileoanal anastomosis (LA).

Methods

Between 2001 and 2004, all patients with benign or malignant disease requiring elective rectal resection with a LA (7 cm or less above the anal verge) were eligible to participate in this multicentre study. All patients were over 18 years old but there was no upper age limit. The study was approved by the ethics committee of the coordinating centre and was registered on the trial register (number NCT00428636). Written informed consent was obtained from all patients.

Interventions

If there were no radiological signs of contrast leakage, patients were randomized to EC (stoma closure on day 8) or to LC (stoma closure on day 60). Patients were randomized by telephone from the central randomization office. Randomization was in blocks of eight, stratified by centre.

Closure of the ileostomy was performed under general anaesthesia with a peristomal skin incision (unnecessary in EC), mobilization and a sutured or stapled anastomosis. The fascia was closed and the skin could be left partially open, completely open or was closed primarily, at the surgeon's discretion. In the LC group, a second antegrade contrast radiograph was performed systematically via the stoma after 2 months, just before stoma closure, to assess the integrity of the LA.

Exclusion criteria

Exclusion criteria included contraindications to EC of the temporary loop ileostomy, such as signs of active infection or organ failure in the postoperative period, or radiological signs of anastomotic leakage evident at a water-soluble contrast examination through the temporary loop ileostomy performed 7 days after surgery. A transanal

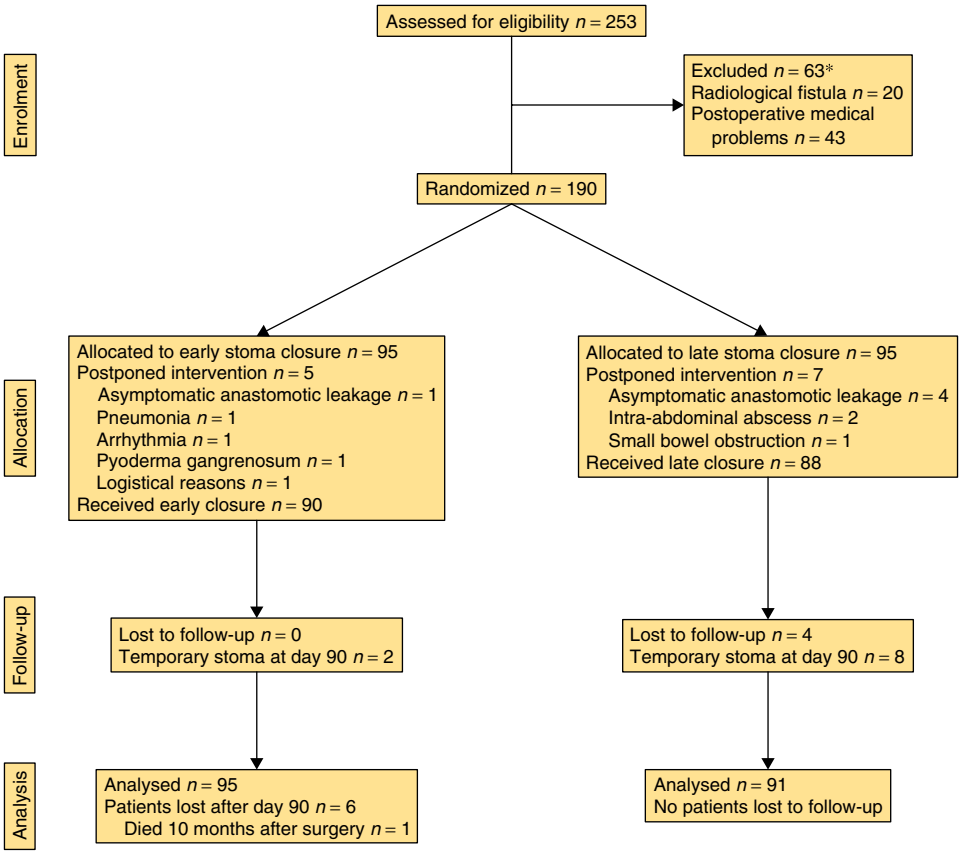

Fig. 1 Profile of randomized clinical trial comparing early *versus* late temporary stoma closure after proctectomy. *Exclusion criteria included contraindications to early closure of the temporary loop ileostomy, such as signs of active infection or organ failure in the postoperative period, or anastomotic leakage seen at antegrade water-soluble contrast examination performed via the loop ileostomy 7 days after operation

approach was not used to avoid any potential anastomotic injury, but this risk is unproven.

Outcomes

All patients were followed up at 1, 2, 3, 6 and 12 months after the rectal resection. The primary endpoints were morbidity and mortality rates within 90 days of proctectomy. The secondary endpoints were total hospital stay for all procedures, functional results and quality of life at 12 months. Functional results were assessed at 3 and 12 months after the first operation in both groups according to criteria reported previously[14,15]. Quality of life was measured using the Gastrointestinal Quality of Life Index[16] before and at 12 months after operation.

Statistical analysis

It was calculated that 90 patients would be needed in each group to give the study a power of 80 per cent to detect (by χ^2 test with a 5 per cent two-sided significance level) a difference in primary outcome of 30 *versus* 13 per cent for groups LC *versus* EC (odds ratio (OR) 0·35). Early stoppage of the trial was planned if severe abdominal complications arose in over 20 per cent of patients in either group.

Analysis was performed according to the intention-to-treat principle. Primary endpoints in the two groups were compared by means of the χ^2 test and by calculation of ORs with 95 per cent confidence intervals. Secondary endpoints were compared using the χ^2 test for discrete variables, and Student's *t* test for Gaussian or Mann–Whitney *U* test for non-Gaussian continuous variables. All *P* values were two sided and $P < 0{\cdot}050$ was considered significant. SAS® version 9.13 was used for statistical analysis (SAS Institute, Cary, North Carolina, USA).

Results

Of 253 eligible patients, 63 did not participate in study (*Fig. 1*). Reasons for exclusion included signs of active infection or organ failure in first 7 days after rectal surgery. Therefore, 190 patients originating from four university centres were randomized. Four patients were withdrawn from analysis because they withdrew their consent immediately after randomization. The final analysis included 186 patients, 95 in the EC group and 91 in the LC group. Preoperative and intraoperative characteristics of the two groups were comparable (*Table 1*). Carcinoma was the most frequently encountered disease (65 per cent).

Table 1 Preoperative and peroperative characteristics of early- and late-closure groups

	Early closure ($n = 95$)	Late closure ($n = 91$)
Sex ratio (M : F)	44 : 51	42 : 49
Age (years)*	58 (18–89)	56 (20–82)
Body mass index (kg/m^2)†	23(3) (17–37)	24(4) (17–39)
Cardiopulmonary co-morbidity	36 (38)	39 (43)
Neurological co-morbidity	0 (0)	0 (0)
History of smoking	6 (10)	11 (20)
History of alcohol use	6 (10)	7 (13)
Diabetes mellitus	3 (5)	1 (2)
Stomach ulcer	3 (5)	3 (6)
Previous blood transfusion	2 (3)	1 (2)
Previous surgical procedure	50 (56)	50 (57)
Preoperative treatment		
Radiotherapy	37 (39)	37 (41)
Chemotherapy	18 (19)	14 (15)
Steroid use (< 3 months)	3 (3)	4 (4)
Immunosuppressive agents	0 (0)	1 (1)
Bowel disease		
Rectal carcinoma	61 (64)	60 (66)
Familial adenomatous polyposis	3 (3)	2 (2)
Inflammatory bowel disease	6 (6)	5 (5)
Endometriosis	20 (21)	20 (22)
Other	5 (5)	4 (4)
Quality of life score*	99 (32–142)	102 (22–142)
Operating time for first procedure (min)*	300 (140–643)	300 (120–565)
Anastomosis		
Ileal pouch–anal	11 (12)	8 (9)
Low colorectal‡	66 (69)	66 (73)
Coloanal	18 (19)	17 (19)
Peroperative morbidity		
Vaginal injury	1 (1)	0 (0)
Colonic ischaemia	0 (0)	1 (1)
Operating time for stoma closure (min)*	94 (32–142)	95 (33–142)
Delay until stoma closure (days)*	8 (8–10)	66 (62–69)

Values in parentheses are percentages (per cent of total no. of patients in group) unless indicated otherwise; *values are median (range); †values are mean(s.d.) (range). ‡Anastomosis 7 cm or less above anal verge.

In the EC group, reasons for postponing ileostomy closure included asymptomatic anastomotic leakage (one patient; although water-soluble contrast enema was considered normal, anastomotic leakage was recognized by digital examination under general anaesthesia just before stoma closure), pneumonia and small bowel obstruction (one), cardiac arrhythmia (one), pyoderma gangrenosum (one) and logistical problems (one). Reasons in the LC group included asymptomatic anastomotic leakage discovered at the second water-soluble contrast enema (four), intra-abdominal abscess requiring percutaneous computed tomography (CT)-guided drainage or transanal drainage (two) and small bowel obstruction (one). These patients were analysed in their randomization group (*Fig. 1*). Ten patients still had a stoma at 90 days after operation.

Table 2 Postoperative outcome at day 90

	Early closure ($n = 95$)	Late closure ($n = 91$)	P
Deaths	0 (0)	0 (0)	
Overall morbidity†	29 (31)	35 (38)	0·254§
Surgical complications	14 (15)	14 (15)	1·000§
Not requiring reoperation			
Enterocutaneous fistula	5 (5)	1 (1)	
Intra-abdominal abscess	0 (0)	2 (2)	
Anastomotic leakage	1 (1)	4 (4)	
Requiring reoperation			
Intraperitoneal bleeding	1 (1)	1 (1)	
Intestinal injury	0 (0)	1 (1)	
Anastomotic leakage‡	5 (5)	4 (4)	
Anastomotic stenosis	2 (2)	0 (0)	
Ureteral injury	0 (0)	1 (1)	
Wound complications	18 (19)	5 (5)	0·007§
Small bowel obstruction	3 (3)	15 (16)	0·002§
Medical complications	5 (5)	14 (15)	0·021§
Stoma-related complications	1 (1)	11 (12)	
Lymphangitis	2 (2)	0 (0)	
Deep vein thrombosis	0 (0)	1 (1)	
Urinary tract infection	0 (0)	1 (1)	
Pneumonia	1 (1)	0 (0)	
Other	1 (1)	1 (1)	
Hospital stay (days)*	16 (6–59)	18 (9–262)	0·013#

Values in parentheses are percentages unless indicated otherwise; *values are median (range). †Number of patients with at least one severe complication (note that one patient may have had several complications). ‡Including rectovaginal fistula. §χ^2 test; #Mann–Whitney U test.

Table 3 Functional results at 90 days and 12 months

	Early closure ($n = 95$)	Late closure group ($n = 91$)	P
Functional results at 90 days			
No. of bowel movements*	$n = 72$	$n = 74$	
Nocturnal	0·5 (0–7)	0·0 (0–3)	0·156‡
Diurnal	3 (0–8)	3·5 (0–11)	0·036‡
Ability to defer evacuation for > 15 min	48 of 72 (67)	41 of 73 (56)	0·233§
Discrimination between gas and stool	$n = 72$	$n = 73$	0·297§
Excellent	54 (75)	46 (63)	
Good	15 (21)	22 (30)	
Poor	3 (4)	5 (7)	
Nocturnal continence	$n = 73$	$n = 73$	0·179§
Excellent	61 (84)	57 (78)	
Good	7 (10)	14 (19)	
Poor	5 (7)	2 (3)	
Daytime continence	68 of 73 (93)	71 of 73 (97)	0·441§
Functional results at 12 months			
No. of bowel movements*	$n = 76$	$n = 76$	
Nocturnal	0·5 (0–11)	0·5 (0–7)	0·939‡
Diurnal	2·0 (0–6)	2·0 (0–13)	0·678‡
Ability to defer evacuation for > 15 min	58 of 81 (72)	58 of 78 (74)	0·797§
Discrimination between gas and stool	$n = 82$	$n = 79$	0·760§
Excellent	66 (80)	67 (85)	
Good	15 (18)	11 (14)	
Poor	1 (1)	1 (1)	
Nocturnal continence	$n = 83$	$n = 78$	0·268§
Excellent	70 (84)	61 (78)	
Good	9 (11)	15 (19)	
Poor	4 (5)	2 (3)	
Daytime continence score	82 of 83 (99)	76 of 78 (97)	0·611
Quality of life at 12 months	$n = 63$	$n = 70$	
Score*†	111 (43–141)	108 (37–139)	0·566‡

Values in parentheses are percentages unless indicated otherwise; *values are median (range). †Quality of life was measured using the Gastrointestinal Quality of Life Index[16]; an overall score of 0 represents the worst and a score of 144 the best possible result. ‡Mann–Whitney U test; §χ^2 test.

Outcomes

Postoperative complications in each group are shown in *Table 2*. The overall morbidity rate was similar in the EC and LC groups (31 *versus* 38 per cent; $P = 0·254$, OR 0·725, 95 per cent confidence interval 0·394, 1·333). Although overall surgical complication rates (both 15 per cent; $P = 1·000$) and reoperation rates (both 8 per cent; $P = 1·000$) were similar in both groups, wound complications were more frequent in the EC group (19 *versus* 5 per cent; $P = 0·007$). However, small bowel obstruction (3 *versus* 16 per cent; $P = 0·002$) and medical complications (including stoma-related complications) (5 *versus* 15 per cent; $P = 0·021$) were more frequent in the LC group.

The antegrade contrast study failed to show anastomotic leakage in 14 (7·5 per cent) of 186 patients and nine of these needed reoperation. Ileostomy closure was postponed in the remaining patients. Although antegrade water-soluble contrast enema examination was considered normal, three patients (two EC and one LC) suffered from a rectovaginal fistula after closure of the ileostomy. In these patients a new temporary ileostomy was created during relaparotomy. Eight patients (five EC and three LC) were reoperated by a transanal approach because of colorectal anastomotic leakage (six) and/or stenosis (two). One other patient in the LC group with a ureteral injury was reoperated by an endoscopic approach.

After closure of the ileostomy, six patients developed an enterocutaneous fistula (five EC and one LC), and all were managed conservatively without reoperation. Two patients in the LC group developed a postoperative intra-abdominal abscess that was drained percutaneously under CT guidance. One required transanal drainage owing to recurrence of pelvic abscess.

Median duration of hospital stay was significantly shorter in the EC group (*Table 2*).

Functional results and quality of life

Functional results at 90 days were similar in both groups, except for the median number of diurnal bowel movements which was higher in the LC group (*Table 3*). Eighteen patients were not followed up for 12 months because of death (six), loss to follow-up (eight) and patient choice (four). Functional results and quality of life at 12 months were similar in both groups (*Table 3*).

Discussion

This randomized clinical trial demonstrated that EC of the temporary loop ileostomy was feasible in patients who had an uneventful recovery during the first week after rectal resection. Despite the higher rate of wound complications, EC was associated with lower rates of medical complications (including stoma-related morbidity) and small bowel obstruction. These results are in accordance with the morbidity rate reported in the literature during the 2–3-month period before stoma closure[11].

Restoration of intestinal continuity is usually performed after 8–12 weeks. However, during this time, stoma-related complications occur in a quarter of patients, with adverse effects on quality of life[9–11].

According to two randomized trials[17,18], preoperative chemoradiotherapy did not increase early postoperative mortality and morbidity significantly. Early stoma closure could be considered in selected patients even following preoperative chemoradiotherapy.

Two non-randomized[12,13] studies reported that EC of the stoma (by day 11 after operation) was possible in only one- to two-thirds of patients. Closure was delayed in a minority of patients in the present study owing to anastomotic leakage, small bowel obstruction and medical complications, or for logistical reasons. However, unlike the previous studies, 15 patients (8·1 per cent) required reintervention. The antegrade contrast study failed to show anastomotic leakage in 7·5 per cent of the patients.

Total hospital stay was significantly longer in the LC group than in the EC group, as noted previously[13]. This may be explained in part by the logistics of two hospital admissions. The difference was not dramatic and streamlined admission protocols may have negated this potential advantage.

EC of the stoma had no adverse effect on functional results or quality of life. Although 18 patients were not available for follow-up at 12 months, quality of life was investigated in more than two-thirds of the population and the results were similar in the two groups.

In conclusion, this trial suggests that early stoma closure after proctectomy is possible in selected patients, with some advantages and disadvantages that need to be weighed up by the patient and surgeon.

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