Stoma closure and adjuvant therapy

Letteratura di riferimento per un’ipotesi di trial

P. Massucco

Randomized clinical trial

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

A. Alves[1], Y. Panis[1], B. Lelong[2], B. Dousset[3], S. Benoist[4] and E. Vicaut[5]

BJS

2008

2001-2004
5 centri

Retto medio-inf (ben/mal)
Rx transito ansa efferente day7

Early (day8) vs late (day60)

Primary outcome
- morbidity/mortality 90ds

Secondary outcome
- total hosp stay
- QoL 12ms

Assessed → 253
Randomized → 190 (75%)

	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)
Operating time for stoma closure (min)*	94 (32–142)	95 (33–142)
Delay until stoma closure (days)*	8 (8–10)	66 (62–69)

	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)	
Hospital stay (days)*	16 (6–59)	18 (9–262)	0·013#

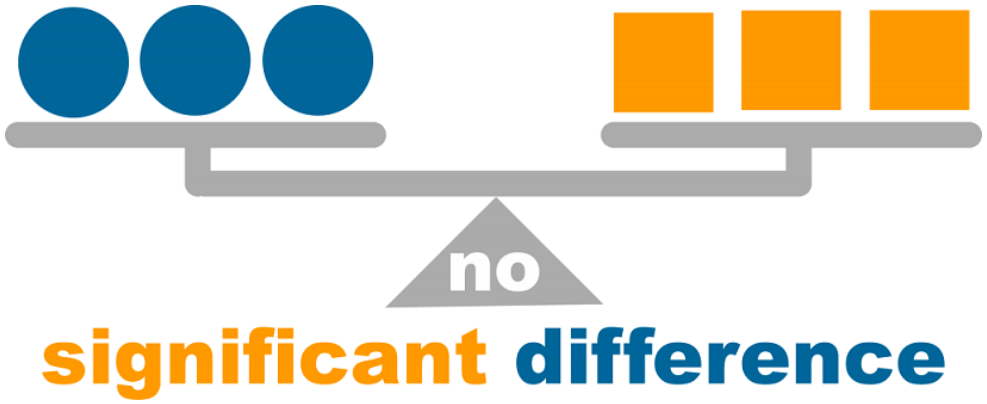
8% both groups

Rx transito
FN 7.5%

Functional results at 90ds and 12ms

- No. bowel movements
- Ability defer
- Discrimination gas/stool
- Nocturnal/daytime continence

QoL (by Gastrointestinal QoL Index) at 12ms



Randomized clinical trial

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

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BJS

2008

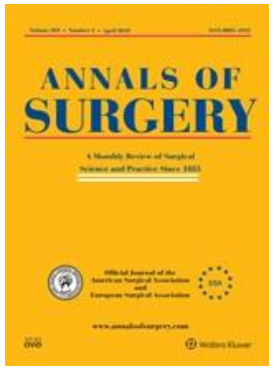
In conclusion, this trial suggests that early stoma closure after proctectomy is possible in selected patients, with some advantages and disadvantages that need to be weighed up by the patient and surgeon.

Early Closure of a Temporary Ileostomy in Patients With Rectal Cancer

A Multicenter Randomized Controlled Trial

EASY trial

Anne K. Danielsen, PhD, MA(Ed), MA(ClN), RN, Jennifer Park, MD,† Jens E. Jansen, MD,‡ David Bock, PhD,† Stefan Skullman, MD, PhD,§ Anette Wedin, RN,† Adiela Correa Marinez, MD,† Eva Haglind, MD, PhD,† Eva Angenete, MD, PhD,† and Jacob Rosenberg, MD, DSc**



2017

2011-2014
8 centri (Dan Swe)

Retto medio-inf (mal)
Enema-CT and/or rectoscopy
day6-8

Early (day8-13) vs late (>12ws)

Primary outcome
- mean n# compl 12ms

Secondary outcome
- % morb Dindo >=IIIa 12ms
- mean n# stoma compl 12ms
- CCI 12ms
- Δ-creat at stoma closure

Assessed → 418
Randomized → 127 (30%)

	Early	Late	
Radiotherapy	29%	28%	
Time to closure	11ds	148ds	
Total hosp stay	14ds	14ds	
Primary			
mean n# compl	1.24	2.88	<0.001
Secondary			
mean Dindo >=IIIa	0.22	0.29	0.32
mean stoma compl	0.30	1.25	<0.001
CCI	8.7	24.4	
Δ-creat (mmol/L)	0.4	9.2	

Details of Loop Ileostomy Closure

	Early Closure (n = 55)	Late Closure (n = 57)*
Hospital stay after closure (days)	4 (2–27)	4 (2–28)
Postoperative complication (number of patients)	4 (7%)	4 (7%)[§]
Type of complication		
Infection	2	0
Fistula/anastomotic leakage	0	1
Bleeding	0	0
Nausea/vomiting	1	2
Cardiopulmonary	0	0
Liver insufficiency	0	0
Pain	1	1
Allergy	0	0
Pancreatitis	0	0
Other (specification)	2[¶]	1[‖]
Cause of reoperation – after loop ileostomy closure		
Failed attempt of stoma closure	1	
Small bowel obstruction	1	1

Classification According to Clavien-Dindo [12,13] (Number of Complications)	Early Closure (n = 55)	Late Closure (n = 57)
3 months	missing n = 1	missing n = 2
Postoperative complication (number of patients)	18/55 (33%)	26/57 (46%)
Grade I	7	11
Grade II	4	11
Grade IIIa	5	9
Grade IIIb	4	2
Grade IVa	1	0
Grade IVb	0	0
Grade V	0	0
6 months		missing n = 3
Postoperative complication (number of patients)	4/55 (7%)	18/57 (32%)
12 months	missing n = 2	missing n = 2
Postoperative complication (number of patients)	8/55 (15%)	19/57 (33%)
Reoperations within 12 months - causes	5/55 (9%)	4/57 (7%)
Small bowel obstruction	1	1
Presacral abscess (leakage of the colo-anal anastomosis)	1	2
Abscess	2	0
Bleeding peptic ulcer	1	0
Stenosis in colo-anal anastomosis	0	1

Classification According to Clavien-Dindo[12,13] (Number of Complications)	Early Closure (n = 55)	Late Closure (n = 57)
Stoma related complications		
Number of patients	13/55 (24%)	44/57 (77%)
Grade I	13	63
Grade II	3	3
Grade IIIa	0	2
Grade IIIb	0	3†
Grade IVa	1*	0
Grade IVb	0	0
Grade V	0	0
Type of stoma related complications		
Skin irritation	3	16
Stomal ulcer	2	18
Parastomal infection	1	0
Leakage outside appliance bag	3	17
High volume output	5	9
Parastomal hernia	0	2
Stenosis	2	2
Prolaps	0	1
Retraction	0	2
Other	1	4

Although stoma related complications may seem less severe than complications > IIIa in the Clavien-Dindo classification, these complications can be tiresome, distressing, and embarrassing for the patient

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EASY trial

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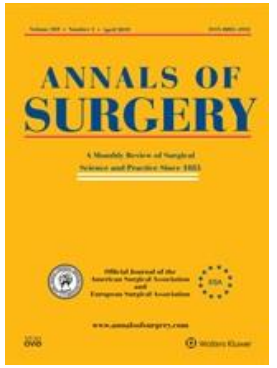


2017

This clinical trial provides evidence of the safety, efficacy, and feasibility of early closure of a temporary ileostomy

early closure resulted in a significantly lower mean number of complications

patients should be considered for early closure of an ileostomy if they have no signs of anastomotic leakage in the postoperative period after rectal resection

Original article

Quality of life in a randomized trial of early closure of temporary ileostomy after rectal resection for cancer (EASY trial)

J. Park[1], A. K. Danielsen[3], E. Angenete[1], D. Bock[1], A. C. Marinez[1], E. Haglind[1], J. E. Jansen[4], S. Skullman[2], A. Wedin[1] and J. Rosenberg[3]

BJS

2018

2011-2014
8 centri (Dan Swe)

Retto medio-inf (mal)
Enema-CT and/or rectoscopy
day6-8

Early (day8-13) vs late (>12ws)

Secondary outcome
- HRQoL at 3, 6 and 12ms

Table 2 SF-36® scores at 3, 6 and 12 months after rectal resection

	3 months			6 months			12 months		
	Median (i.q.r.)	H–L*	*P*†	Median (i.q.r.)	H–L*	*P*†	Median (i.q.r.)	H–L*	*P*†
Physical functioning									
Early	90 (75–95)	0 (–5, 5)	0·646	90 (81·7–100)	0 (–5, 5)	0·630	95 (70–100)	0 (0, 5)	0·322
Late	90 (80–95)			90 (80–95)			95 (90–100)		
Role physical									
Early	75 (50–96·9)	12·5 (0, 18·8)	0·025	81·3 (50–100)	6·3 (0, 18·8)	0·140	81·3 (56·3–100)	0 (–6·3, 6·3)	0·718
Late	62·5 (43·8–75)			75 (50–93·8)			87·5 (75–100)		
Bodily pain									
Early	80 (52–100)	0 (–10, 0)	0·858	74 (62–100)	0 (–16, 0)	0·264	79 (51–100)	0 (0, 20)	0·035
Late	74 (62–100)			84 (63–100)			100 (74–100)		
General health									
Early	71·6 (52–88·5)	–5 (–15, 2)	0·139	77 (56–87)	0 (–10, 5)	0·820	74·5 (45–92)	5 (–5, 16·8)	0·279
Late	77 (67–87)			77 (65–87)			82 (72–87)		
Vitality									
Early	62·5 (43·8–81·3)	4·2 (–6·3, 12·5)	0·441	68·8 (50–81·3)	0 (–12·5, 6·3)	0·796	68·8 (50–81·3)	6·3 (0, 12·5)	0·196
Late	68·8 (56·3–81·3)			68·8 (56·3–81·3)			75 (62·5–87·5)		
Social functioning									
Early	75 (62·5–100)	0 (–12·5, 0)	0·468	87·5 (62·5–100)	0 (0, 0)	0·976	87·5 (62·5–100)	0 (0, 12·5)	0·415
Late	87·5 (75–100)			87·5 (62·5–100)			100 (75–100)		
Role emotional									
Early	83·3 (58·3–100)	0 (0, 8·3)	0·345	87·5 (66·7–100)	0 (0, 0)	0·923	95·8 (66·7–100)	0 (0, 0)	0·697
Late	83·3 (50–100)			83·3 (75–100)			95·8 (75–100)		
Mental health									
Early	80 (55–90)	5 (–5, 10)	0·217	80 (60–90)	–5 (–10, 5)	0·291	80 (60–90)	10 (0, 15)	0·020
Late	85 (65–90)			85 (70–95)			85 (75–95)		
Mental component score									
Early	52·5 (40·7–58·6)	1 (–2·6, 5)	0·588	54·4 (42·8–58·6)	0·2 (–3, 3·9)	0·939	54·1 (42·6–58·5)	2·5 (–0·7, 6·3)	0·105
Late	53 (44·8–57·8)			54·6 (46·9–57·5)			56·6 (52·9–59·2)		
Physical component score									
Early	51·8 (40·9–58·2)	–0·5(–3·8, 3·4)	0·823	53·3 (43·3–57·1)	–0·2 (–3·6, 3)	0·900	54·1 (44·5–59)	1·6 (–1, 6·1)	0·281
Late	51·2 (46·9–54·8)			52·2 (45·8–57·9)			56·8 (51–59·4)		

O'Leary DP, Fide CJ, Foy C, Lucarotti ME.
Quality of life after low anterior resection with total mesorectal excision and temporary loop ileostomy for rectal carcinoma.
Br J Surg 2001.

Stoma vs no stoma → better QoL

Tsunoda A, Tsunoda Y, Narita K, Watanabe M, Nakao K, Kusano M.
Quality of life after low anterior resection and temporary loop ileostomy.
Dis Colon Rectum 2008

Danielsen AK, Soerensen EE, Burcharth K, Rosenberg J.
Impact of a temporary stoma on patients' everyday lives: feelings of uncertainty while waiting for closure of the stoma.
J Clin Nurs 2013

- closure seen as crucial event
- importance of knowing the date

Camilleri-Brennan J, Steele RJ.
Prospective analysis of quality of life after reversal of a defunctioning loop ileostomy.
Colorectal Dis 2002

Stoma closure → improved QoL

Siassi M, Hohenberger W, Lösel F, Weiss M.
Quality of life and patient's expectations after closure of a temporary stoma.
Int J Colorectal Dis 2008

Siassi M, Weiss M, Hohenberger W, Losel F, Matzel K.
Personality rather than clinical variables determines quality of life after major colorectal surgery.
Dis Colon Rectum 2009

Stoma closure → no improvement QoL (LARS)

EASYtrial → early closure safe and advantageous in patients with no clinical or radiological signs of anastomotic leakage. However, the present study did not find a link between this clinical advantage and patients' HRQOL.

ORIGINAL CONTRIBUTION

Quality of Life and Timing of Stoma Closure in Patients With Rectal Cancer Undergoing Low Anterior Resection With Diverting Stoma: A Multicenter Longitudinal Observational Study

Florian Herrle, M.D., M.Sc.[1] • Flavius Sandra-Petrescu, M.D.[1] • Christel Weiss, Ph.D.[2]
Stefan Post, Ph.D., M.D.[1] • Norbert Runkel, Ph.D., M.D.[3] • Peter Kienle, M.D., Ph.D.[1]

1 Surgical Department, University Medical Centre Mannheim, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
2 Department for Medical Statistics, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
3 Schwarzwald-Baar Hospital, Department of General and Visceral Surgery, Villingen-Schwenningen, Germany

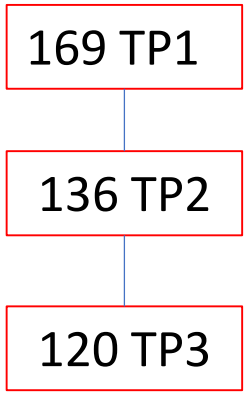
2016

16 centers
2009 – 2011

Rectal cancer with ileostomy

QoL EORTC C30 – CR29

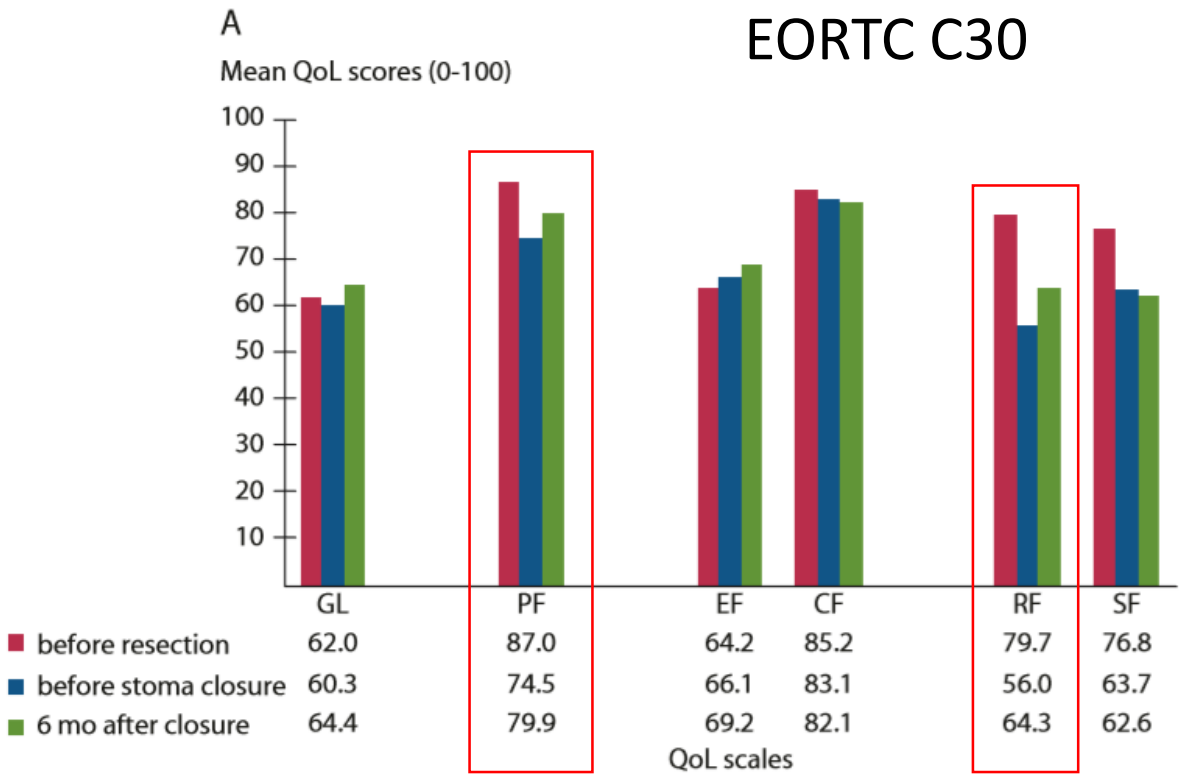
TP1 before rectal resection
TP2 before stoma closure
TP3 3 ms after stoma closure



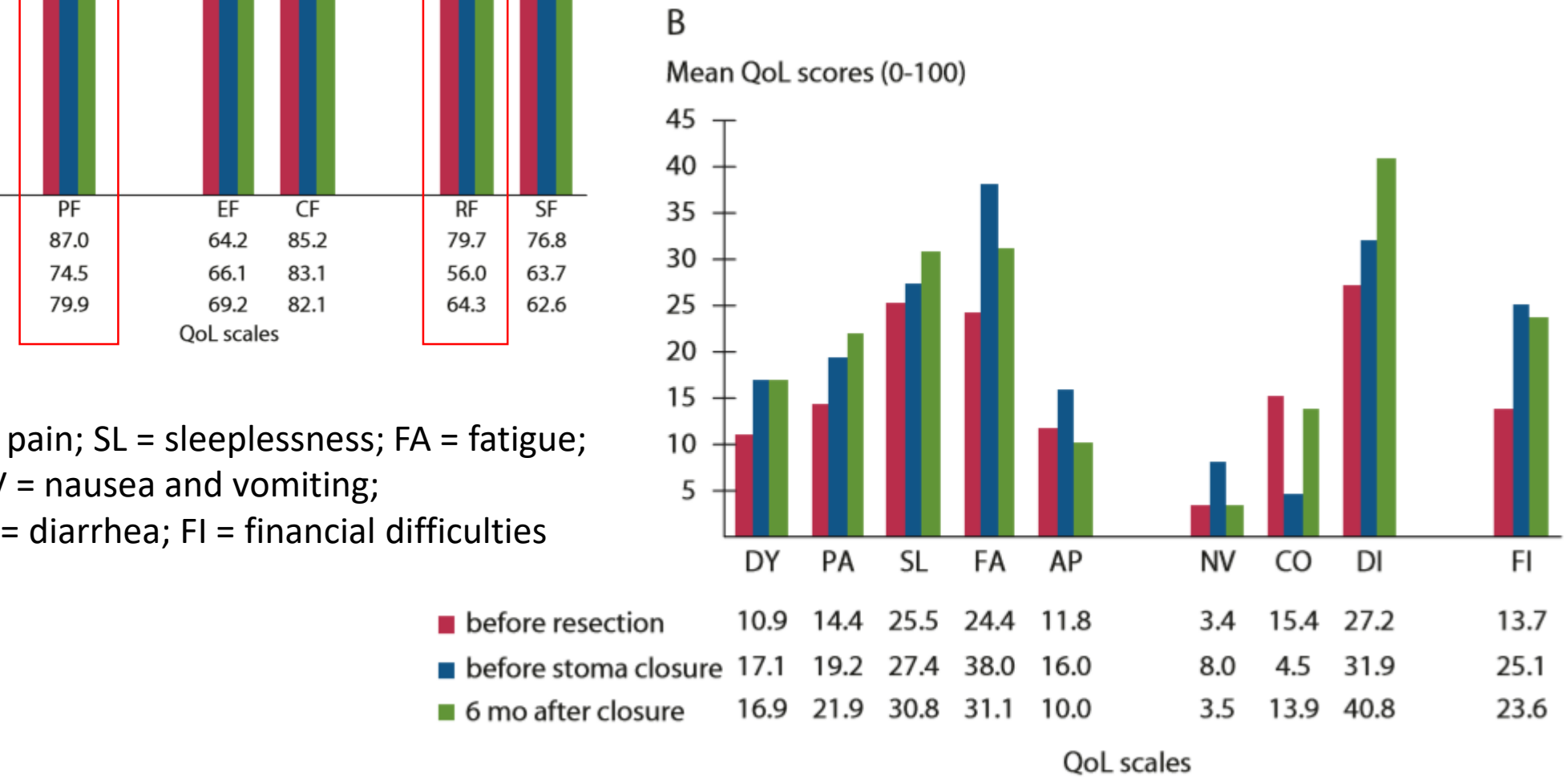
63% neoadj cht
57% adj cht

Interval to closure → 5 ms
- very early (<1m) 3%
- adj cht → yes 5.6ms vs no 3.4 ms

EORTC C30

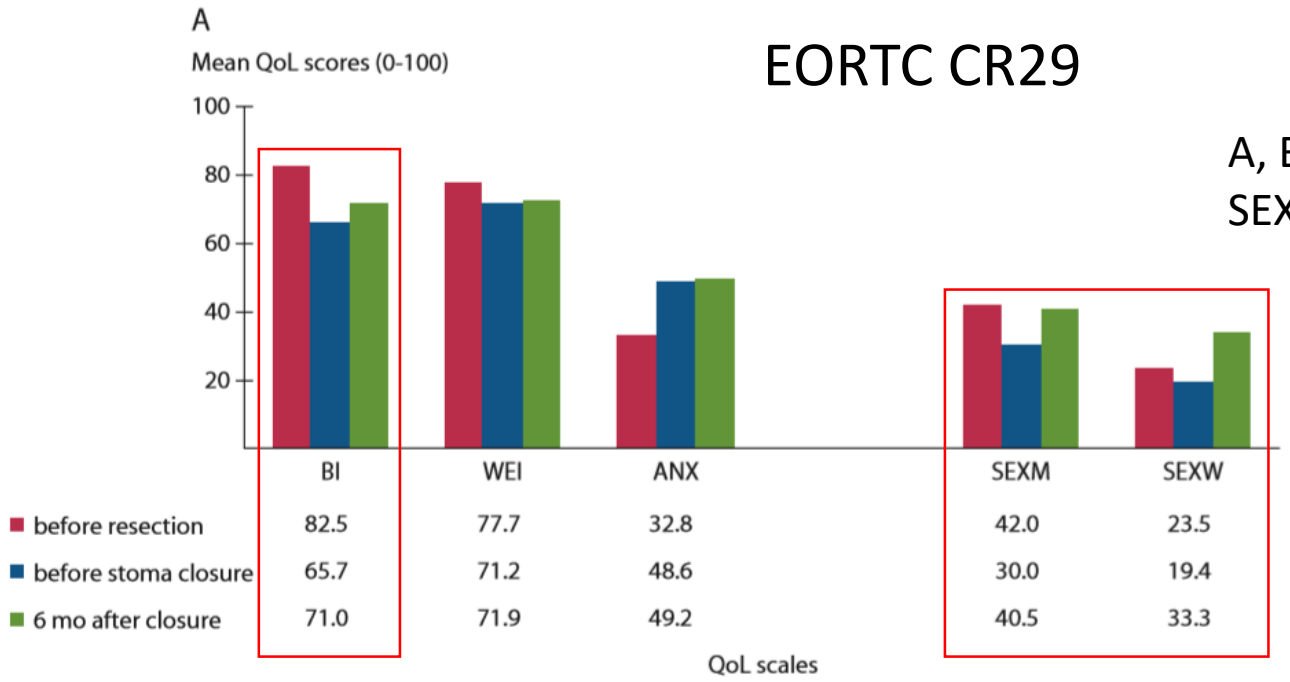


A, Global QoL and function scales.
GL = global quality of life; PF = physical functioning;
EF = emotional functioning; CF = cognitive functioning;
RF = role functioning; SF = social functioning.



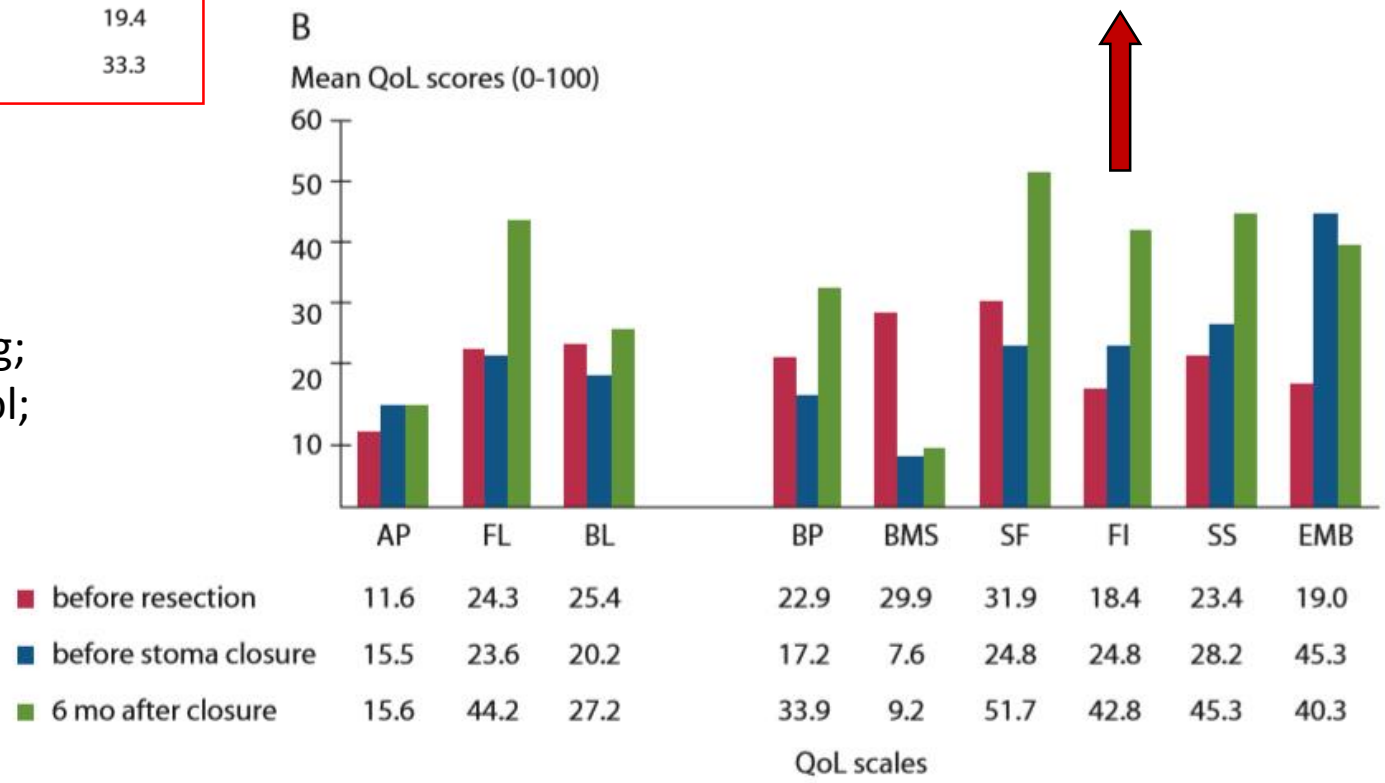
B, DY = dyspnea; PA = pain; SL = sleeplessness; FA = fatigue;
AP = appetite loss; NV = nausea and vomiting;
CO = constipation; DI = diarrhea; FI = financial difficulties

EORTC CR29



A, BI = body image; WEI = weight; ANX = anxiety;
SEXM = sexual interest (men); SEXW = sexual interest (women).

Wexner >10 → 54%
>15 → 18%



B, CR29 longitudinal symptom scales.
AP = abdominal pain; FL = flatulence; BF = bloating;
BP = buttock pain; BMS = blood and mucus in stool;
SF = stool frequency; FI = fecal incontinence;
SS = sore skin; EMB = embarrassment

ORIGINAL CONTRIBUTION

Quality of Life and Timing of Stoma Closure in Patients With Rectal Cancer Undergoing Low Anterior Resection With Diverting Stoma: A Multicenter Longitudinal Observational Study

Florian Herrle, M.D., M.Sc.[1] • Flavius Sandra-Petrescu, M.D.[1] • Christel Weiss, Ph.D.[2]
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1 Surgical Department, University Medical Centre Mannheim, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
2 Department for Medical Statistics, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
3 Schwarzwald-Baar Hospital, Department of General and Visceral Surgery, Villingen-Schwenningen, Germany

2016

…the presence of a diverting stoma after rectal cancer resection had a negative impact on role, social, and physical functioning and GI symptoms… an early stoma-closure strategy may therefore be beneficial for patients and should be addressed in future randomized controlled trials.

Ochsner Journal 17:328–330, 2017

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

Table. Patient Demographics by Ileostomy Closure Timing

Characteristic	Ileostomy Closure Before Chemotherapy n=22	Ileostomy Closure After Chemotherapy n=50	*P* Value
Mean age, years ± SD	59.5 ± 9.8	59.2 ± 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 ± SD	16.9 ± 14.5	33.6 ± 18.1	0.0001
Mean follow-up, months ± SD	50.6 ± 23.6	43.5 ± 22.1	0.23

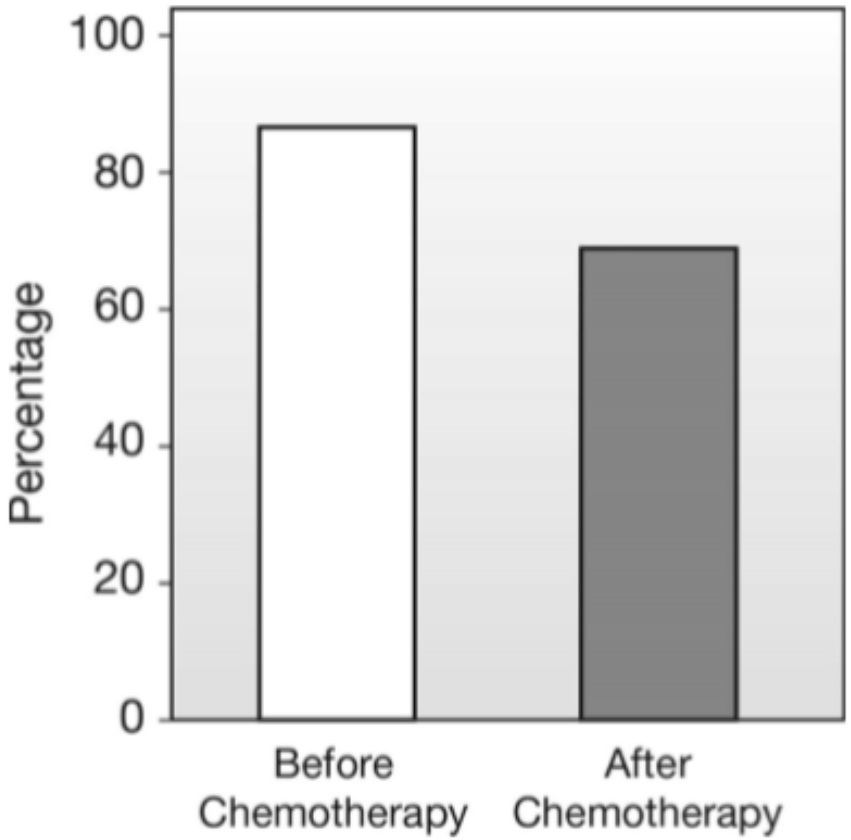


Figure 1. Overall survival of ileostomy closure before chemotherapy vs after chemotherapy, *P*=0.23.

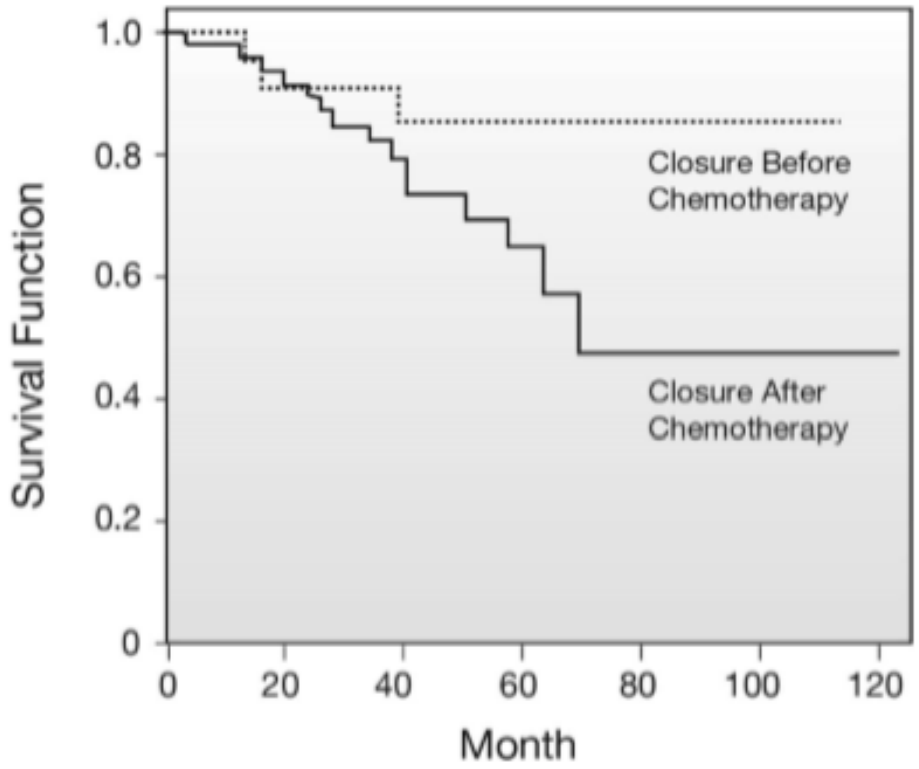


Figure 2. Kaplan-Meier curve: Closure before chemotherapy=1, closure after chemotherapy=0, *P*=0.124.

Should a Loop Ileostomy Closure in Rectal Cancer Patients Be Done During or After Adjuvant Chemotherapy?

HAGIT TULCHINSKY, MD,[1,2]* EINAT SHACHAM-SHMUELI, MD,[3] JOSEPH M. KLAUSNER, MD,[2] MOSHE INBAR, MD,[3] AND RAVIT GEVA, MD[3]

2014

Tel Aviv University
2000 – 2012

Rectal cancer after neoadj therapy

234 pats

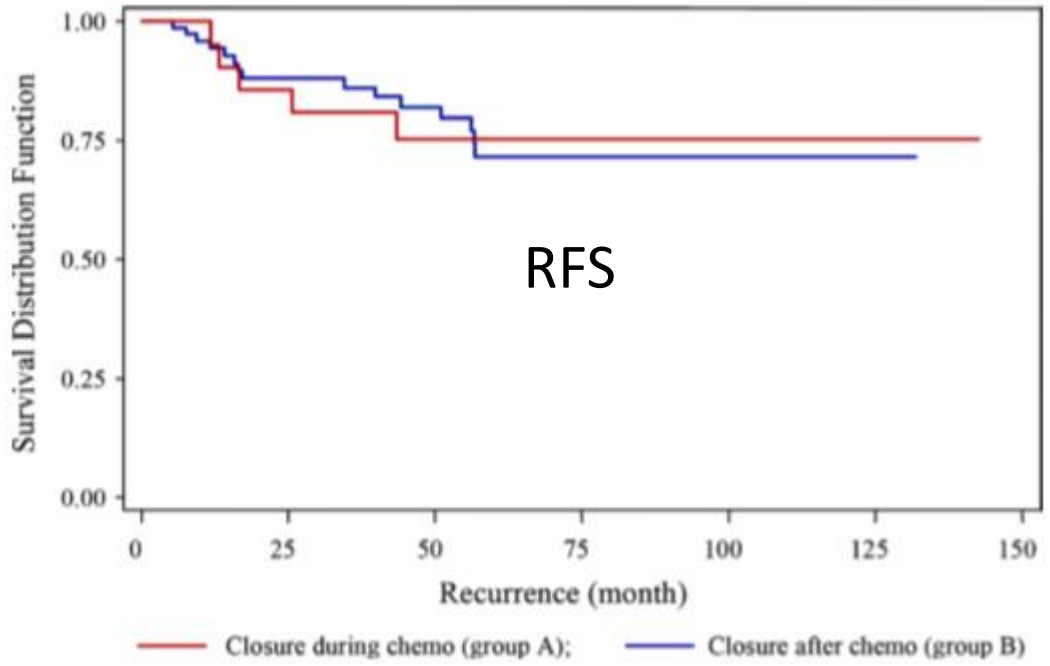
141 ileostomy

124 closed

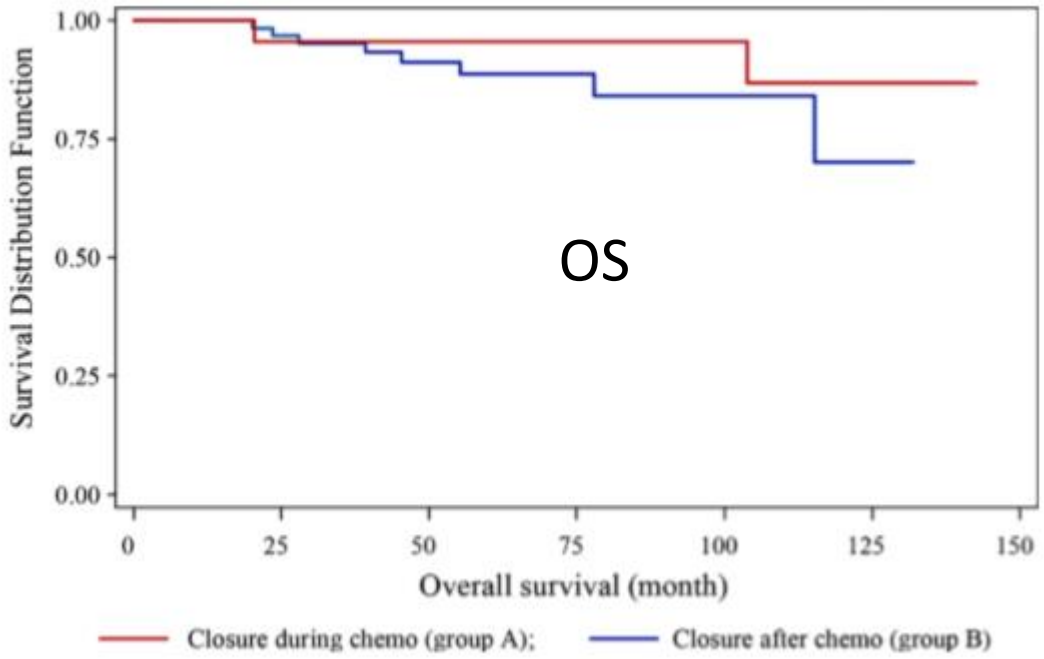
104 adj therapy

Group A
during the course
25 pats

Group B
after completion
79 pats



RFS



OS

	morb	II-III stage	follow-up
Group A	16%	36%	79.5 ms
Group B	15%	61%	55.2 ms

Should a Loop Ileostomy Closure in Rectal Cancer Patients Be Done During or After Adjuvant Chemotherapy?

HAGIT TULCHINSKY, MD,[1,2]* EINAT SHACHAM-SHMUELI, MD,[3] JOSEPH M. KLAUSNER, MD,[2] MOSHE INBAR, MD,[3] AND RAVIT GEVA, MD[3]

2014

Our findings suggest that timing of ileostomy closure appear not to change both short- and long-term results and that performing the procedure while during chemotherapy can be potentially offered to patients who have compelling impairment in their quality of life as a result of the stoma.

ORIGINAL CONTRIBUTION

Effect of Diversion Ileostomy on the Occurrence and Consequences of Chemotherapy-Induced Diarrhea

Jason P. Robertson, M.B.Ch.B. • Cameron I. Wells • Ryash Vather, M.B.Ch.B.
Ian P. Bissett, M.B.Ch.B., M.D., F.R.A.C.S.

Department of Surgery, University of Auckland, Auckland, New Zealand

2015

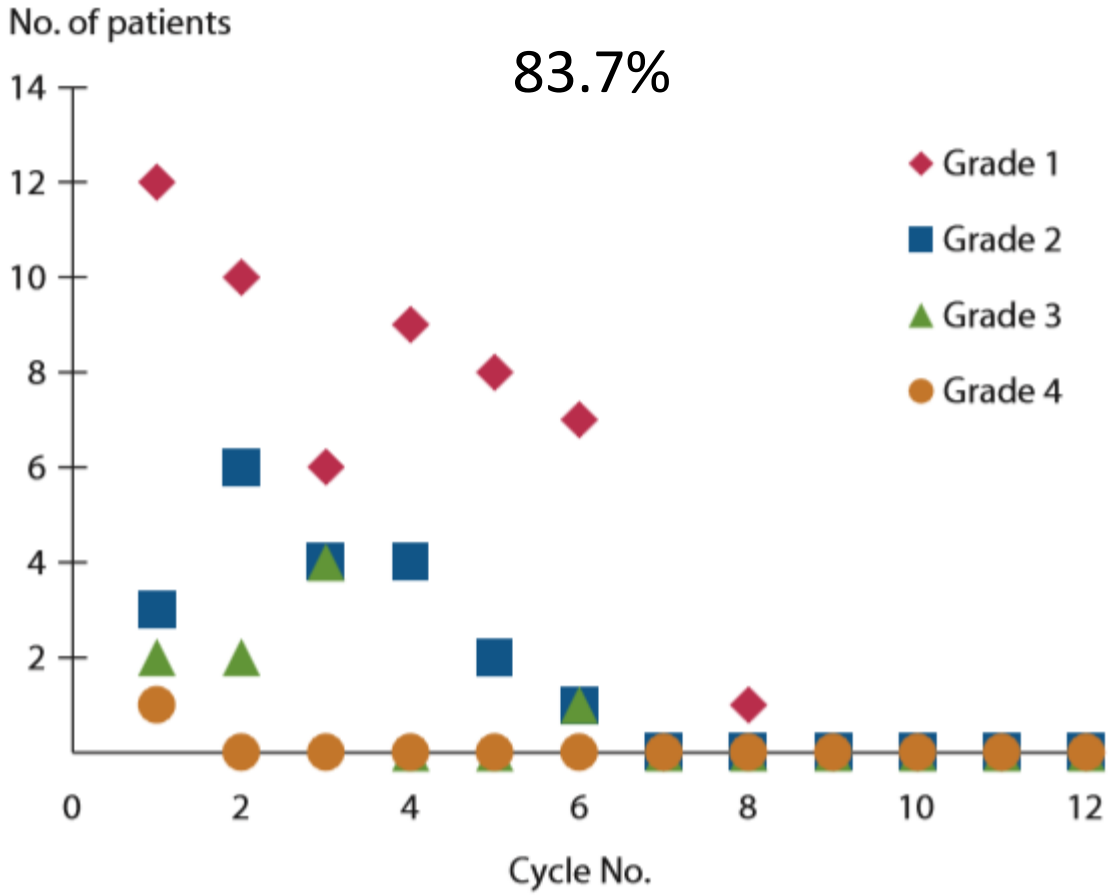
2002-2013

109 adj treat after anterior resection
43 stoma vs 66 no stoma

Primary outcome
- Occurrence of CID
- Modif of cht because of CID
- Hospitalization for CID

Stoma

83.7%



No stoma

47%

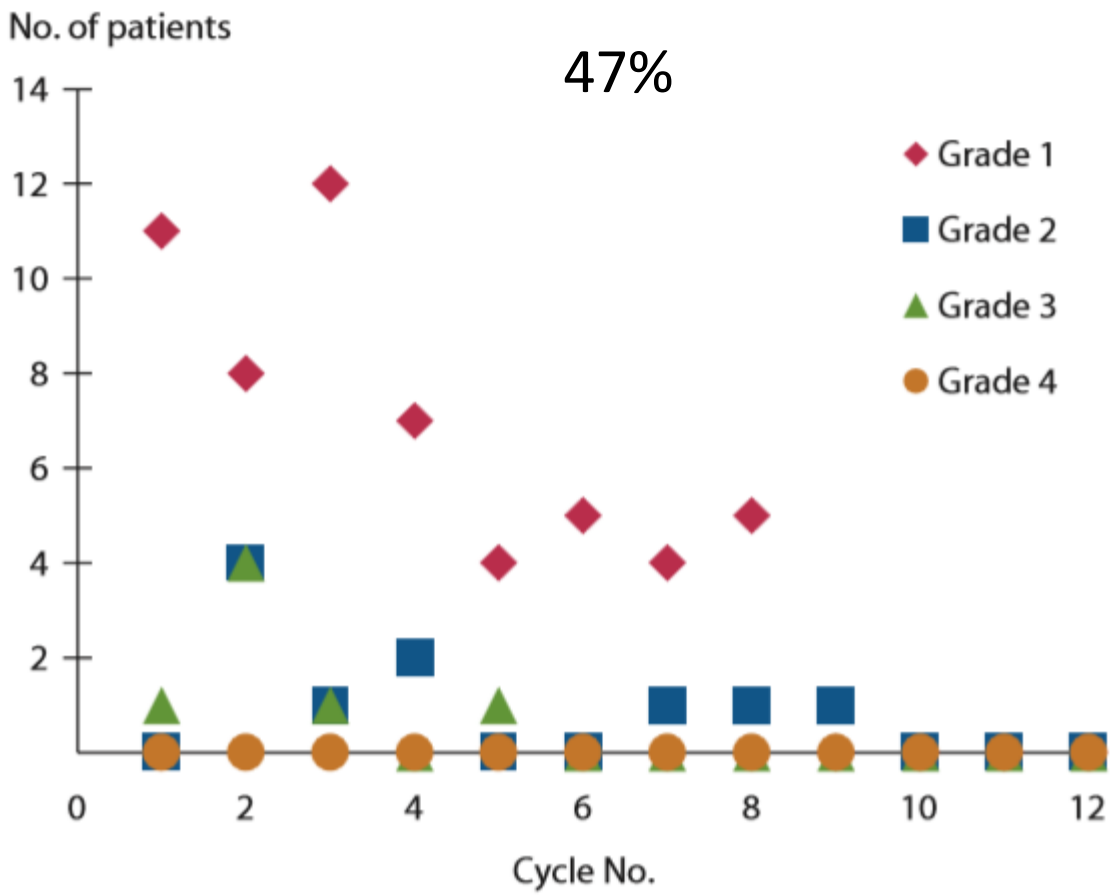


TABLE 3. CID grades and consequences in patients with and without an ileostomy during chemotherapy

CID grade	No. of cycles (%) (N = 691)	Dosing delay (N = 12)	Dosing reduction (N = 35)	Treatment change (N = 1)	Treatment cessation (N = 5)	Hospital admission (N = 7)
0	535 (77.4)	–/–	–/–	–/–	–/–	–/–
1	109 (15.8)	–/1	1/5	–/–	1/–	1/–
2	30 (4.3)	2/3	9/4	–/–	2/–	–/–
3	16 (2.3)	2/4	7/7	–/1	2/–	3/2
4	1 (0.1)	–/–	1/–	–/–	–/–	1/–

Data showing the consequences of CID are presented as $n_{ileostomy}/n_{no\ ileostomy}$.
CID = chemotherapy-induced diarrhea.

TABLE 4. Outcomes related to presence of an ileostomy during chemotherapy on multivariate logistic regression analysis

Outcome	OR	95% CI	p
Grade 3 or higher diarrhea	13.6	1.2–150.9	0.03*
Dose delay			NS
Dose reduction	4.0	1.3–12.4	0.02*
Treatment change			NS
Treatment stop			NS
Hospital admission			NS
Any modification	3.4	1.2–9.6	0.02*

NS = not significant
*P value is significant.

…this is the first study to identify the presence of a loop ileostomy as a significant independent predictor of grade 3 or higher CID, the need for a dosing reduction, and the need for any treatment modification.

ORIGINAL CONTRIBUTION

Effect of Diversion Ileostomy on the Occurrence and Consequences of Chemotherapy-Induced Diarrhea

Jason P. Robertson, M.B.Ch.B. • Cameron I. Wells • Ryash Vather, M.B.Ch.B.
Ian P. Bissett, M.B.Ch.B., M.D., F.R.A.C.S.

Department of Surgery, University of Auckland, Auckland, New Zealand

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…operative planning to ensure the timely delivery of optimal adjuvant chemotherapy is a key consideration for surgeons and an important factor when considering not only the type of stoma formed but also the timing of stoma closure.

Closure before adjuvant therapy may also potentially serve to improve optimal chemotherapy delivery.