Does oncological outcome differ between restorative and nonrestorative low anterior resection in patients with primary rectal cancer?

Dutch Snapshot Res Grp; Roodbeen, Sapho X.; Blok, Robin D.; Borstlap, Wernard A.; Bemelman, Willem A.; Hompes, Roel; Tanis, Pieter J.

Published in:
Colorectal Disease

DOI:
10.1111/codi.15464

Received: 1 August 2020 | Revised: 29 September 2020 | Accepted: 1 November 2020

DOI: 10.1111/codi.15464

ORIGINAL ARTICLE

Does oncological outcome differ between restorative and nonrestorative low anterior resection in patients with primary rectal cancer?

Sapho X. Roodbeen[1] | Robin D. Blok[1,2] | Wernard A. Borstlap[1] | Willem A. Bemelman[1] | Roel Hompes[1] | Pieter J. Tanis[1] | the Dutch Snapshot Research Group*

[1]Department of Surgery, Amsterdam UMC, Cancer Center Amsterdam, University of Amsterdam, Amsterdam, the Netherlands

[2]LEXOR, Center for Experimental and Molecular Medicine, Oncode Institute, Cancer Center Amsterdam, Amsterdam UMC (AMC), University of Amsterdam, Amsterdam, the Netherlands

Correspondence
Pieter J. Tanis, Department of Surgery, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands.
Email: p.j.tanis@amsterdamumc.nl

Funding information
Funding for the initial Snapshot study was received from the Dutch Surgical Colorectal Unit and the Dutch Cancer Society (KWF). This investigator initiated research was performed without influence from the financing parties on data analysis and publication

Abstract

Aim: Nonrestorative low anterior resection (n-rLAR) (also known as low Hartmann's) is performed for rectal cancer when a poor functional outcome is anticipated or there have been problems when constructing the anastomosis. Compared with restorative LAR (rLAR), little oncological outcome data are available for n-rLAR. The aim of this study was to compare oncological outcomes between rLAR and n-rLAR for primary rectal cancer.

Method: This was a nationwide cross-sectional comparative study including all elective sphincter-saving LAR procedures for nonmetastatic primary rectal cancer performed in 2011 in 71 Dutch hospitals. Oncological outcomes of patients undergoing rLAR and n-rLAR were collected in 2015; the data were evaluated using Kaplan–Meier survival analysis and the results compared using log-rank testing. Uni- and multivariable Cox regression analysis was used to evaluate the association between the type of LAR and oncological outcome measures.

Results: A total of 1197 patients were analysed, of whom 892 (75%) underwent rLAR and 305 (25%) underwent n-rLAR. The 3-year local recurrence (LR) rate was 3% after rLAR and 8% after n-rLAR ($P < 0.001$). The 3-year disease-free survival and overall survival rates were 77% (rLAR) *vs* 62% (n-rLAR) ($P < 0.001$) and 90% (rLAR) *vs* 75% (n-rLAR) ($P < 0.001$), respectively. In multivariable Cox analysis, n-rLAR was independently associated with a higher risk of LR (OR = 2.95) and worse overall survival (OR = 1.72).

Conclusion: This nationwide study revealed that n-rLAR for rectal cancer was associated with poorer oncological outcome than r-LAR. This is probably a noncausal relationship, and might reflect technical difficulties during low pelvic dissection in a subset of those patients, with oncological implications.

KEYWORDS
local recurrence, oncological outcome, low anterior resection, rectal surgery

*Dutch Snapshot Research Group members are listed in Appendix 1.

INTRODUCTION

For nonlocally advanced rectal cancer, the reference treatment remains a total mesorectal excision (TME) [1]. If the sphincters can be spared, one may opt for either a restorative low anterior resection (rLAR) or a nonrestorative low anterior resection (n-rLAR) [2,3]. The latter entails cross-stapling of the rectal stump and construction of an end colostomy and is also referred to as a low Hartmann's procedure.

The proportion of n-rLAR procedures in published rectal cancer literature is often relatively small, being <5% in most randomized controlled trials [4,5]. However, in unselected series and population studies, especially those from northern Europe, n-rLAR may be performed in up to 25% of LARs [6]. Despite the fact that the sphincters could be preserved with oncologically satisfactory margins, the rationale for nonrestorative surgery is usually not specified.

Two main reasons to perform n-rLAR are expected poor functional outcome, such as impaired sphincter function and a high risk of mortality should an anastomotic leak occur. Social and cultural factors may also play a role as a result of varied acceptance of a permanent stoma by the patient and reluctance or eagerness on the part of the surgeon to construct an anastomosis. A north-to-south gradient regarding colostomy rates after surgery for primary rectal cancer can be observed in Europe, with relatively high proportions of abdominoperineal excision (APE) and Hartmann's procedures in northern Europe [7]. In the Netherlands, surgeons are carrying out rLAR increasingly more frequently, probably because of subspecialization and auditing [8].

However, n-rLAR may also be unplanned. Dissection in the pelvis can be technically challenging (e.g., male gender, narrow pelvis, obesity, bulky tumour) [9]. A long and difficult TME dissection with inadequate exposure might lead the surgeon to construct an end stoma.

Finally, there may be an oncological cost of carrying out an n-rLAR procedure because circumferential margin positivity rates of up to 31.7% have been reported [10].

The aim of this nationwide comparative cross-sectional cohort study was to compare oncological outcome following rLAR and n-rLAR in patients with primary rectal cancer, focusing primarily on local recurrence (LR).

What does this paper add to the literature?

While in unselected series and population studies a nonrestorative low anterior resection (n-rLAR) is a frequently performed procedure, there remains little published data on oncological outcomes after this procedure, compared with restorative LAR for primary rectal cancer. We found that n-rLAR was independently associated with a higher risk of local recurrence and worse overall survival.

METHOD

Study design and patients

This was a nationwide, retrospective, cross-sectional study performed by the Dutch Snapshot Research Group. All patients were operated on in 2011, and outcome data were collected in 2015. The study design has been reported previously [11,12]. In short, all resections for primary rectal cancer performed between 1 January 2011 and 31 December 2011 in the Netherlands were identified from the Dutch Colorectal Audit. This is an obligatory nationwide audit of all colorectal cancer resections, for which patient demographics, tumour information, intra-operative details and patient outcomes within 30 days of surgery are collected. Hospitals that participated in this Dutch Snapshot Research Group project were provided with their own Dutch Colorectal Audit data in 2015, and residents completed the dataset, together with additional diagnostic, procedural and outcome data, using an online secured web tool under the supervision of a consultant surgeon. From this database, which contains both short- and long-term outcomes for all rectal cancer resections performed in 71 Dutch Hospitals, patients who had undergone either rLAR or n-rLAR in 2011 were identified. Patients were excluded if they had metastatic disease (cM1), if surgery was noncurative, if they had received a multivisceral resection or if surgery had been carried out as an emergency.

For this study, the following data were analysed: baseline patient demographics; pretreatment tumour characteristics; operative details; histopathological parameters; postoperative complications; and related surgical re-interventions and re-admissions. Oncological follow-up details included date and treatment of recurrence, as well as survival status.

This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [13]. The study received approval from the Medical Ethical Committee of the Amsterdam UMC (Academic Medical Center, Amsterdam, the Netherlands). The local Ethics Committees decided that informed consent was not needed because of the retrospective design of the study and use of anonymized data.

Outcome measures

Primary outcome was 3-year LR rate, including association between type of resection and LR. Secondary outcomes were rates of histopathologically determined circumferential resection margin positivity (pCRM+), overall and surgical complications, pelvic sepsis, 3-year disease-free survival (DFS) and 3-year overall survival (OS).

Definitions

Restorative LAR was defined as a rectal resection with the formation of a stapled or hand-sewn colorectal or coloanal anastomosis, with or without a defunctioning stoma. Nonrestorative LAR was defined as a rectal resection with cross-stapling of the rectal stump

TABLE 1 Patient and tumour characteristics

Characteristic	rLAR (*n* = 892)	%	n-rLAR (*n* = 305)	%	*P*-value
Male	565/891	63.4	181/305	59.3	0.206
Age (years)	65 (58–72)		75 (68–81)		
>70 years	285/892	32.0	212/305	69.5	**<0.001**
ASA ≥ III	116/892	13.0	78/305	25.6	**<0.001**
BMI >30	113/887	12.7	48/302	15.9	0.166
Threatened margin[a]	167/892	18.7	62/305	20.3	0.538
Distance to ARJ ≤3 cm	60/892	6.7	60/305	19.7	**<0.001**
cT-stage					
cT1	38/771	4.9	7/256	2.7	0.161
cT2	244/771	31.6	71/256	27.7	
cT3	463/771	60.1	165/256	64.5	
cT4	26/771	3.4	13/256	5.1	
cTX/missing	121		49		
cN-stage					
cN0	320/743	43.1	125/251	49.8	**0.024**
cN1	292/743	39.3	99/251	39.4	
cN2	131/743	17.6	27/251	10.8	
cNX/missing	149		54		
Neoadjuvant therapy					
None	105/892	11.8	41/305	13.4	0.810
SCRT	502/892	56.3	164/305	53.8	
LCRT	25/892	2.8	10/305	3.3	
CRT	260/892	29.1	90/305	29.5	

Abbreviations: ARJ, anorectal junction, as measured on sagittal MRI; ASA, American Society of Anesthesiologists-Classification; BMI, body mass index; cN-stage, clinical nodal stage; CRT, chemoradiotherapy; cT-stage, clinical tumour stage; LCRT, long-course radiotherapy without concomitant chemotherapy; n-rLAR, nonrestorative low anterior resection; rLAR, restorative low anterior resection SCRT, short-course radiotherapy.

Bold *P*-values are significant.

[a]Threatened margin was defined as presence of tumour or malignant lymph nodes ≤1 mm of the mesorectal fascia on baseline pelvic MRI.

and formation of an end colostomy. Pelvic sepsis, detected at any time during follow-up, was considered to be caused by an anastomotic leakage or pelvic abscess in the rLAR group and a rectal stump abscess in the n-rLAR group. A pCRM+ was defined as the presence of tumour or malignant lymph nodes ≤1 mm from the inked resection plane. Local recurrence was defined as recurrent disease in the pelvis or at the anastomotic site. Distant recurrence was defined as metastatic localizations outside the pelvis, which were not present at the time of rectal resection. The DFS rate was defined as the percentage of patients who were alive without signs of local or distant recurrence, and the OS rate was defined as the percentage of patients who were still alive, independent of disease status.

Statistical analysis

Categorical data were presented as number of patients and percentages, whilst continuous data were shown as either mean ± SD or

median (interquartile range [IQR], depending on the data distribution. Categorical and continuous variables were compared using the chi-square test and the Mann–Whitney *U*-test, respectively.

Kaplan–Meier survival analysis was used to determine the actual 3-year LR, 3-year DFS and 3-year OS rates from the date of surgery, and the rates from each group were compared using the log-rank test.

Uni- and multivariable Cox regression analyses were used to evaluate the association between type of LAR and LR, DFS and OS. Potential risk factors for these outcomes with a univariate value of $P < 0.1$ were included in the multivariable regression analysis. A value of $P \leq 0.05$ was considered statistically significant. Data were analysed using the Statistical Package for Social Sciences (SPSS) (IBM SPSS Statistics for Windows, version 25.0 (IBM Corp.).

RESULTS

Patients

In 2011, 1400 LAR procedures (998 rLAR and 402 n-rLAR) from 71 hospitals in the Netherlands were registered in the Dutch Snapshot Database. After exclusion of cM1 stage, noncurative intent, multivisceral resection and emergency procedures, 1197 patients were included for analysis. Of those, 892 (74.5%) underwent rLAR and 305 (25.5%) underwent n-rLAR. Median follow-up time of the total cohort was 42 (IQR = 32–47) months.

Table 1 shows the baseline patient- and tumour characteristics for the two procedures. Most patients were male (rLAR: 565 [63.4%]; n-rLAR: 181 [59.3%]). Patients in the n-rLAR group were significantly older (65 [IQR: 58–72] years *vs* 75 [IQR: 68–81] years; $P < 0.001$), presented with higher American Society of Anesthesiologists (ASA) classification (13.0% *vs* 25.6%; $P < 0.001$) and more often had a tumour located ≤3 cm from the anorectal junction (ARJ) (6.7% *vs* 19.7%; $P < 0.001$), than those in the rLAR group. Clinical T-stage was comparable between the groups, while clinical N0-stage occurred slightly more often in the n-rLAR group (43.1% *vs* 49.8%; $P = 0.02$).

Surgical and pathological characteristics

Annual hospital volume did not differ significantly between the groups. A laparoscopic approach was used significantly more often in the rLAR group (54.4% *vs* 42.0%; $P < 0.001$). Laparoscopic procedures were significantly more often converted to midline laparotomy in the n-rLAR group (13.4% *vs* 26.2%; $P < 0.001$). Major intra-operative complications (including bleeding requiring transfusion and visceral injuries to the bowel, ureter/urethra and bladder), occurred in 15 (1.8%) patients from the rLAR group and in nine (3.2%) from the n-rLAR group ($P = 0.16$; Table 2).

There was no significant difference in overall complication rate within 30 days ($P = 0.63$). Pelvic sepsis occurred in a similar percentage of patients at any time during follow-up among the two groups; anastomotic leakage or presacral abscess was reported in 16.5% of patients in the rLAR group, whereas an abscess on top of the rectal stump after n-rLAR was reported in 18.9% of patients ($P = 0.34$). Also, no differences in re-interventions and re-admissions beyond 30 days were observed (Table 2). A secondary anastomosis was constructed in 15 (3.7%) patients from the n-rLAR group.

The pCRM+ rate was 5.7% in the rLAR group and 7.2% in the n-rLAR group ($P = 0.76$). Overall, the (y)pT-stages were significantly higher in the n-rLAR group ($P = 0.007$). There were no significant differences in pathological nodal stage, total number of lymph nodes examined and presence of extramural vascular invasion. Adjuvant chemotherapy was administered significantly more often in the rLAR group (13.4% [rLAR group] *vs* 5.6% [n-rLAR group]; $P < 0.001$; Table 3).

Oncological outcomes

The 3-year LR rate was 3% after rLAR and 8% after n-rLAR, as evaluated using univariate Kaplan–Meier survival analysis (log-rank: $P < 0.001$; Figure 1A). Table 4 shows the results of uni- and multivariable Cox regression analyses for LR. In addition to type of procedure (rLAR and n-rLAR), tumour height from ARJ, neoadjuvant therapy and pathological tumour and nodal stages were found to have $P < 0.1$ in univariable analyses. Multivariable Cox regression analyses revealed that n-rLAR was independently associated with higher odds of LR (OR = 2.950; 95% CI: 1.559–5.581; $P = 0.001$). Another independent risk factor for LR was (y)pN1-2 stage (OR = 2.608; 95% CI: 1.402–4.849; $P = 0.002$), while neoadjuvant therapy lowered the risk of LR (OR = 0.328; 95% CI: 0.161–0.666; $P = 0.002$).

Univariate Kaplan–Meier survival analysis demonstrated that 3-year DFS was significantly ($P < 0.001$) better after rLAR (77%) than after n-rLAR (62%). Data from uni- and multivariable Cox regression analyses for any recurrence (LR and/or distant metastasis [DM]) or death are provided in Table S1. Classification as ASA ≥III (OR = 2.582; 95% CI: 1.171–5.691; $P = 0.02$) and adjuvant therapy (OR = 0.043; 95% CI: 0.003–0.544, $P = 0.02$) were independently associated with DFS, while type of procedure (rLAR and n-rLAR) was not. Univariate Kaplan-Meier survival analysis demonstrated that 3-year OS was significantly ($P < 0.001$) higher after rLAR (90%) than after n-rLAR (75%) (Figure 1B). Multivariable Cox regression analyses showed that n-rLAR was an independent risk factor for death (OR = 1.720; 95% CI: 1.210–2.444; $P = 0.003$), as were male gender (OR = 0.64), age ≥70 years (OR = 2.54), ASA ≥III (OR = 2.54), tumour height from ARJ (OR = 1.60) and (y)pN1-2 stage (OR = 2.11) (Table S2).

Table S3 shows treatment of LR and DM and the locations of DM. Approximately one-third of patients with LR in both rLAR and n-LAR groups could be treated with curative intent, while in the presence of DM, 55.2% of patients in the rLAR group were treated with curative intent compared with 35.1% in the n-rLAR group ($P = 0.01$).

TABLE 2 Operative details and postoperative outcomes

Variable	rLAR (*n* = 892)	%	n-rLAR (*n* = 305)	%	*P*-value
Annual hospital volume (no. of patients)					
<25	184/892	20.6	71/305	23.3	0.408
25–50	470/892	52.7	163/305	53.4	
>50	238/892	26.7	71/305	23.3	
Approach					
Open	407/892	45.6	177/305	58.0	**<0.001**
Laparoscopic	485/892	54.4	128/305	42.0	
Conversion	62/463	13.4	32/122	26.2	**0.001**
Of which early	31/463	6.7	17/122	13.9	**0.003**
Diverting stoma	588/812	72.4	NA	NA	
Major intra-operative complications	15/850	1.8	9/284	3.2	0.155
Bleeding requiring transfusion	7/850	0.8	6/284	2.1	
Visceral injury[a]	7/850	0.8	2/284	0.8	
Other	1/850	0.1	1/284	0.4	
Complications <30 days					
Overall	329/863	38.1	116/292	39.7	0.627
Surgical	191/863	22.1	62/292	21.2	0.748
Requiring re-intervention	127/863	14.7	42/292	14.4	0.889
Re-intervention >30 days	110/888	12.4	38/305	12.5	0.974
Re-admission >30 days	172/889	19.3	62/305	20.3	0.710
Pelvic sepsis[b]	144/871	16.5	48/254	18.9	0.378

Abbreviation: NA, not applicable.

Bold *P*-values are significant.

[a]Restorative low anterior resection (r-LAR): bowel (*n* = 5), ureter/urethra (*n* = 1), bladder (*n* = 1); nonrestorative LAR (n-rLAR): bowel (*n* = 1), ureter/urethra (*n* = 1).

[b]Pelvic sepsis was considered an anastomotic leakage or pelvic abscess in the rLAR group and a rectal stump abscess in the n-rLAR group, being detected at any time during follow-up.

DISCUSSION

In this nationwide cross-sectional comparative study of 1197 elective sphincter-saving primary rectal cancer resections from 71 Dutch hospitals, continuity was not restored in 25% of patients. Comparison of baseline characteristics revealed that this decision was mainly driven by patient-related factors. Patients who underwent n-rLAR were a median of 10 years older than those who underwent rLAR (and more than twice as many patients who underwent n-rLAR were over 70 years of age), and twice as many patients who underwent n-rLAR were classified as ASA grade 3. By contrast, cT-stage, cN-stage, proportion of threatened CRM on MRI, and percentage and type of neoadjuvant therapy were remarkably similar between patients undergoing rLAR and those undergoing n-rLAR. The only tumour-related factor that differed significantly between patients in rLAR and n-rLAR groups was distance from the ARJ. The pathological CRM+ rate was not significantly different, while (y)pT-stages were significantly higher in patients from the n-rLAR group. Considering these characteristics and after correction for distance from the ARJ, multivariable analysis demonstrated that n-rLAR with end colostomy was independently associated with a higher risk of LR than rLAR with primary anastomosis. Uncorrected 3-year DFS and OS were significantly lower after n-rLAR, probably reflecting the elderly frail patient group, but n-rLAR remained independently associated with worse OS after correction for confounding variables.

The observed 3-year LR rates after rLAR (3%) and non-rLAR (8%) are in line with other published data on rates of LR following LAR. A Swedish study analysing 114 rLAR and 58 n-rLAR procedures performed in the Stockholm region between 1995 and 2003, showed a 5-year cumulative LR rate of 5% and 10%, respectively [14]. In contrast to the present study, this could be explained by the percentage of positive margins which, similarly to those in the present study (5% [rLAR] *vs* 14% [n-rLAR]), was also significantly higher in the n-rLAR group. Another analysis of 2333 rLAR and 248 n-rLAR procedures registered in the Spanish rectal cancer project between 2006 and 2010 showed LR rates of 3.7% and 11.3%, respectively, after a median follow-up of 37 months [15]. Perforation (2.3% *vs* 12.6%) and CRM+ (6.6% *vs* 16.6%) were also significantly higher in

TABLE 3 Histopathological parameters and oncological follow-up

Variable	rLAR (*n* = 892)	%	n-rLAR (*n* = 305)	%	*P*-value
(y)pT-stage					
pT0	49/871	5.6	22/297	7.4	**0.007**
pT1	75/871	8.6	18/297	6.1	
pT2	316/871	36.3	88/297	29.6	
pT3	396/871	45.4	149/297	50.2	
pT4	14/871	1.6	14/297	4.7	
pTx	21/871	2.4	6/297	2.0	
(y)pN-stage					
pN0	561/871	64.4	187/297	63.0	0.086
pN1	216/871	24.8	81/297	27.3	
pN2	83/871	9.5	20/297	6.7	
pNx	11/871	1.3	9/297	3.0	
pCRM					
≤1 mm	39/689	5.7	16/222	7.2	0.400
No. of lymph nodes examined					
Median (IQR)	12 (9–12)		12 (8–16)		0.072
>10	563/869	64.8	177/298	59.4	0.095
EMVI	80/817	9.8	28/274	10.2	0.838
Adjuvant chemotherapy	119/889	13.4	17/304	5.6	**<0.001**
FU time (months)					
Median (IQR)	43 (36–47)		38 (15–45)		**<0.001**
Actual 3-year LR		3.0		8.0	**<0.001**
Actual 3-year DFS		77.0		62.0	**<0.001**
Actual 3-year OS		90.0		75.0	**<0.001**

Abbreviations: CRM, circumferential resection margin; DFS, disease-free survival; EMVI, extramural vascular invasion; FU, follow-up; IQR, interquartile range; LR, local recurrence; n-rLAR, nonrestorative low anterior resection; OS, overall survival; pN-stage, pathological nodal stage; pT-stage, pathological tumour stage; r-LAR, restorative low anterior resection.

Bold *P*-values are significant.

the n-rLAR group. In multivariable analysis, n-rLAR was an independent predictor for LR and survival. However, in our study, pCRM+ was comparable between the groups and cannot explain the differences observed in LR rate and survival, in contrast to the Swedish and Spanish studies.

An important factor which has been linked to LR is pelvic sepsis, with a relatively recent meta-analysis suggesting that anastomotic leakage after rLAR can adversely affect the oncological outcome [16]. Leaving a rectal stump after n-rLAR may also lead to formation of pelvic abscess as a result of infected pelvic haematoma or staple-line disruption. Published data based on the Dutch Colorectal Audit 2009–2013 has reported that n-rLAR was associated with significantly fewer 30-day abdominal infective complications than rLAR [17]. The present study reveals that with longer follow-up (beyond 1 year postoperatively) the pelvic sepsis rates in both groups are substantially higher and not significantly different. Pelvic sepsis might have contributed to the high LR rate observed after n-rLAR, but does not explain the increased rate of LR observed after rLAR.

More patients received adjuvant therapy after rLAR. A meta-analysis showed that adjuvant fluorouracil-based chemotherapy did not improve oncological outcome in rectal cancer patients after preoperative (chemo)radiotherapy [18]. As preoperative radiotherapy was given to almost 90% of patients in both rLAR and n-rLAR groups, the difference in adjuvant chemotherapy does not seem to (fully) explain the observed difference in oncological outcome.

Other factors to consider are the impact of intra-operative technical issues and subspecialization. In a proportion of patients in the n-rLAR group, the decision not to restore bowel continuity might have been made intra-operatively following a difficult TME dissection with inadequate exposure. This is suggested by the observation that n-rLAR was converted more frequently than rLAR from an open to a laparoscopic procedure. In the n-rLAR group, 20% of tumours were located within 3 cm from the ARJ. Visualization of the distal rectum from an abdominal approach can be difficult, thereby complicating TME dissection, cross-stapling and construction of a coloanal anastomosis.

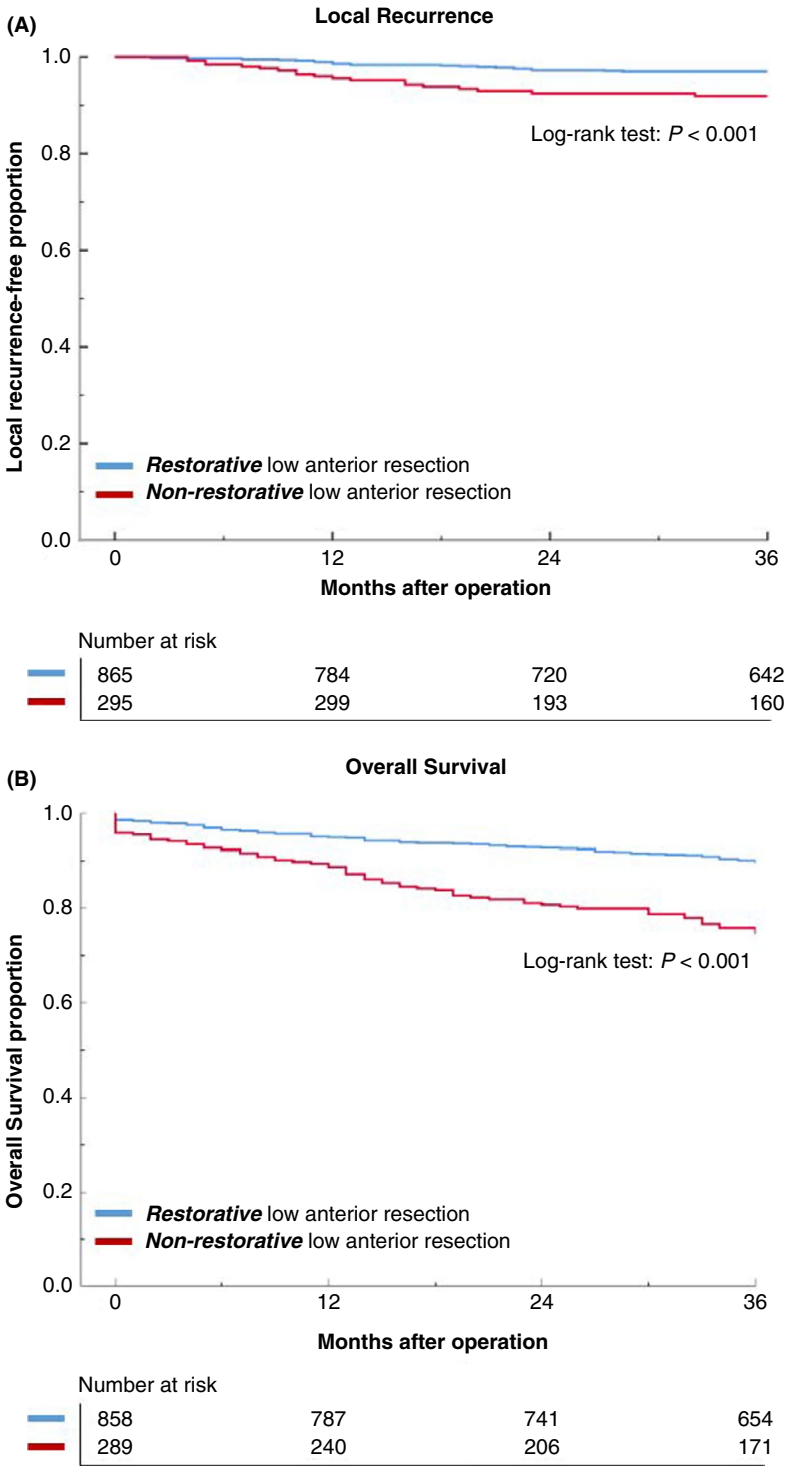

FIGURE 1 (A) Kaplan-Meier survival curves of 3-year local recurrence-free (A) and 3-year overall survival (B) proportion of the totale groups. n-rLAR, nonrestorative low anterior resection; rLAR, restorative low anterior resection

Hypothetically, n-rLAR might correlate with incomplete TME specimen with residual mesorectum, which potentially still consists malignant lymph nodes, leading to the development of LR. This would explain the discrepancy between the pCRM+ rate and the LR rate because residual mesorectum does not impact on pCRM+. Bondeven et al. [19] demonstrated that inadvertent residual mesorectum was commonly found on postoperative MRI, supporting this hypothesis. Unfortunately, quality of the specimen obtained following TME, data on distal resection margin length and postoperative imaging were not available in this dataset.

Hospital volume was equally distributed between groups. Data on surgeon seniority and experience in low rectal surgery were

TABLE 4 Uni- and multivariable Cox regression analyses for risk factors of local recurrence (LR)

	Univariable analysis		Multivariable analysis	
Variable	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Gender				
Male	1.238 (0.682–2.248)	0.483		
Female	Ref			
BMI				
<30	Ref			
≥30	1.393 (0.648–2.997)	0.396		
MRF threatened				
No	Ref			
Yes	1.072 (0.516–2.231)	0.851		
Distance ARJ				
<4 cm	**1.964 (0.913–4.225)**	**0.084**		NS
≥4 cm	Ref			
NAT				
None	Ref			
Yes	**0.347 (0.175–0.687)**	**0.002**	**0.328 (0.161–0.666)**	**0.002**
Procedure				
rLAR	Ref			
n-rLAR	**3.173 (1.755–5.735)**	**<0.001**	**2.950 (1.559–5.581)**	**0.001**
Approach				
Open	Ref			
Lap.	1.389 (0.765–2.522)	0.280		
Tumour stage				
(y)pT0-3	Ref			
(y)pT4	3.551 (1.097–11.497)	**0.034**		NS
Nodal stage				
(y)pN0	Ref			
(y)pN1-2	**2.342 (1.286–4.265)**	**0.005**	**2.608 (1.402–4.849)**	**0.002**
Adjuvant chemotherapy				
Yes	20.347 (0.000–1.319E+15)	0.853		
No	Ref			

Abbreviations: ARJ, anorectal junction; BMI, body mass index; Lap., laparoscopic; MRF, mesorectal fascia; NAT, neoadjuvant therapy; n-rLAR, nonrestorative low anterior resection; Ref, reference; rLAR, restorative low anterior resection.

Bold *P*-values are significant.

unavailable. Therefore, we cannot contradict the suggestion that different levels of expertise within high-volume hospitals may have influenced the choice of procedure. Against this is the fact that Dutch colorectal cancer care is provided in community hospitals only by certified and specialized gastrointestinal surgeons with obligatory auditing, including continuous feedback; service review is performed if there is evidence of underperformance. There are no low-volume centres and no 'general' surgeons performing rectal cancer resections in the Netherlands. Any surgeon carrying out rectal cancer surgery must perform a minimum of 20 rectal resections per year (including APE and surgery for benign disease). Finally, rectal cancer surgery is often performed by two consultants, so this makes analyses on an individual surgeon basis difficult.

What are the clinical implications of our findings? We suggest that when nonrestoration of continuity is being considered (for example, if poor bowel function is expected, or restoration appears to be technically difficult), an intersphincteric APE (iAPE) might be an option. This has a potentially lower risk of residual mesorectum but might also reduce the risk of diversion proctitis and pelvic sepsis. Our group has previously reported that iAPE and n-rLAR have an equal risk of pelvic abscess formation and have a similar need for re-intervention and re-admission [20]. Caution is needed because an

iAPE can also be challenging, requiring experience and subspecialist training. A currently ongoing multicentre randomized controlled trial comparing iAPE and n-rLAR should reveal data on the optimal non-restorative technique [21].

A further option to avoid a permanent stoma when intra-operative difficulties are encountered could be use of the n-rLAR procedure to carry out a delayed coloanal anastomosis. This might facilitate better quality of the specimen obtained by TME if combined with an intersphincteric approach from below. A randomized multicentre trial (46 patients in each arm) compared delayed hand-sewn coloanal anastomosis with immediate hand-sewn coloanal anastomosis with diverting ileostomy [22]. The composite 30-day complication rate (including stoma reversal) was 35% (delayed coloanal anastomosis) *vs* 45% (immediate coloanal anastomosis plus ileostomy), and not statistically significant, leading the authors to conclude that delayed anastomosis is a safe alternative.

We acknowledge that our study has limitations. Some data were missing and some were inaccurately recorded. In addition, the decision to perform a nonrestorative procedure may reflect an expected difficult procedure, a notion supported by the higher conversion rate and other intra-operative major complications in this group. This, in itself, introduces selection bias, even after correcting for several measured confounders using multivariable analyses. Finally, some important information was not collected in the dataset, such as the surgeon's reason for not carrying out a restorative procedure, the quality of the TME specimen and the level of experience of the operating surgeon(s). Information on quality of the TME specimen could have provided insight into the association between n-rLAR and LR but, as an outcome measure itself, would not have been included in the multivariable model as an independent variable.

CONCLUSION

This nationwide study reports that elective n-rLAR for primary rectal cancer is independently associated with a significantly higher risk of LR and worse OS than rLAR with a primary anastomosis but that this is likely to be a noncausal relationship. The higher recurrence rate in n-rLAR may relate to a more technically difficult rectal dissection leading to a damaged or incomplete TME specimen.

ACKNOWLEDGEMENTS

The Dutch Snapshot Research Group provided the data used for this study.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

WAA, RH, and PJT developed the concept and design of the study. SXR and RD performed the analyses of the data, and interpreted the results together with WAA, WAB, RH and PJT. SXR and RD made the first draft of the article, and made subsequent drafts after review by WAA, WAB, RH and PJT. All authors critically revised the manuscript and approved the final version. All authors agree to be accountable for all aspects of the work.

ETHICAL APPROVAL

The study received approval from the Medical Ethical Committee of the Amsterdam UMC, location Academic Medical Center in Amsterdam, the Netherlands.

CONSENT TO PARTICIPATE AND FOR PUBLICATION

The local Ethics Committee decided that informed consent was not needed due to the retrospective design of the study using anonymized data.

DATA AVAILABILITY STATEMENT

The Dutch Colorectal Audit (DCRA).

ORCID

Pieter J. Tanis https://orcid.org/0000-0002-3146-3310

REFERENCES

1. Heald RJ, Moran BJ, Ryall RD, Sexton R, MacFarlane JK. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978–1997. Arch Surg. 1998;133:894–9.
2. Desai DC, Brennan EJ Jr, Reilly JF, Smink RD Jr. The utility of the Hartmann procedure. Am J Surg. 1998;175:152–4.
3. Seah DW, Ibrahim S, Tay KH. Hartmann procedure: is it still relevant today? ANZ J Surg. 2005;75:436–40.
4. Bujko K, Nowacki MP, Kepka L, Oledzki J, Bebenek M, Kryj M. Postoperative complications in patients irradiated pre-operatively for rectal cancer: report of a randomised trial comparing short-term radiotherapy vs chemoradiation. Colorectal Dis. 2005;7:410–6.
5. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. Lancet. 2009;373:811–20.
6. Rutegard M, Haapamaki M, Matthiessen P, Rutegard J. Early postoperative mortality after surgery for rectal cancer in Sweden, 2000–2011. Colorectal Dis. 2014;16:426–32.
7. Elferink MA, Lamkaddem M, Dekker E, Tanis PJ, Visser O, Essink-Bot ML. Ethnic inequalities in rectal cancer care in a universal access healthcare system: a nationwide register-based study. Dis Colon Rectum. 2016;59:513–9.
8. de Neree tot Babberich MPM, Detering R, Dekker JWT, Elferink MA, Tollenaar RAEM, Wouters MWJM, et al. Achievements in colorectal cancer care during 8 years of auditing in The Netherlands. Eur J Surg Oncol. 2018;44:1361–70.
9. Cecil TD, Taffinder N, Gudgeon AM. A personal view on laparoscopic rectal cancer surgery. Colorectal Dis. 2006;8:30–2.
10. Tekkis PP, Heriot AG, Smith J, Thompson MR, Finan P, Stamatakis JD. Comparison of circumferential margin involvement between restorative and nonrestorative resections for rectal cancer. Colorectal Dis. 2005;7:369–74.
11. Borstlap WAA, Westerduin E, Aukema TS, Bemelman WA, Tanis PJ, Dutch Snapshot Research Group. Anastomotic leakage

and chronic presacral sinus formation after low anterior resection: results from a large cross-sectional study. Ann Surg. 2017;266:870–7.
12. Dutch Snapshot Research Group. Benchmarking recent national practice in rectal cancer treatment with landmark randomized controlled trials. Colorectal Dis. 2017;19:O219–31.
13. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Epidemiology. 2007;18:805–35.
14. Anderin C, Martling A, Hellborg H, Holm T. A population-based study on outcome in relation to the type of resection in low rectal cancer. Dis Colon Rectum. 2010;53:753–60.
15. Ortiz H, Wibe A, Ciga MA, Kreisler E, Garcia-Granero E, Roig JV, et al. Multicenter study of outcome in relation to the type of resection in rectal cancer. Dis Colon Rectum. 2014;57:811–22.
16. Lu ZR, Rajendran N, Lynch AC, Heriot AG, Warrier SK. Anastomotic leaks after restorative resections for rectal cancer compromise cancer outcomes and survival. Dis Colon Rectum. 2016;59:236–44.
17. Jonker FH, Tanis PJ, Coene PP, Gietelink L, van der Harst E, Audit Dutch Surgical Colorectal Group. Comparison of a low Hartmann's procedure with low colorectal anastomosis with and without defunctioning ileostomy after radiotherapy for rectal cancer: results from a national registry. Colorectal Dis. 2016;18:785–92.
18. Breugom AJ, Swets M, Bosset JF, Collette L, Sainato A, Cionini L, et al. Adjuvant chemotherapy after preoperative (chemo)radiotherapy and surgery for patients with rectal cancer: a systematic review and meta-analysis of individual patient data. Lancet Oncol. 2015;16:200–7.
19. Bondeven P, Hagemann-Madsen RH, Laurberg S, Pedersen BG. Extent and completeness of mesorectal excision evaluated by postoperative magnetic resonance imaging. Br J Surg. 2013;100:1357–67.
20. Westerduin E, Aukema TS, van Geloven AAW, Bemelman WA, Tanis PJ, Dutch Snapshot Research Group. What to do with the rectal stump during sphincter preserving rectal cancer resection with end colostomy: a collaborative snapshot study. Colorectal Dis. 2018;20:696–703.
21. Smedh K, Sverrisson I, Chabok A, Nikberg M, HAPIrect Collaborative Study Group. Hartmann's procedure vs abdominoperineal resection with intersphincteric dissection in patients with rectal cancer: a randomized multicentre trial (HAPIrect). BMC Surg. 2016;16:43.
22. Biondo S, Trenti L, Espin E, Bianco F, Barrios O, Falato A, et al. Two-Stage Turnbull-Cutait pull-through coloanal anastomosis for low rectal cancer: a randomized clinical trial. JAMA Surg. 2020;155:e201625.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Roodbeen SX, Blok RD, Borstlap WA, et al. Does oncological outcome differ between restorative and nonrestorative low anterior resection in patients with primary rectal cancer?. *Colorectal Dis*. 2021;23:843–852. https://doi.org/10.1111/codi.15464

APPENDIX 1

Collaborators: AGJ Aalbers, Y Acherman, GD Algie, B Alting von Geusau, F Amelung, TS Aukema, IS Bakker, SA Bartels, S Basha, AJNM Bastiaansen, E Belgers, W Bleeker, J Blok, RJI Bosker, JW Bosmans, MC Boute, ND Bouvy, H Bouwman, A Brandt-Kerkhof, DJ Brinkman, S Bruin, ERJ Bruns, JPM Burbach, JWA Burger, CJ Buskens, S Clermonts, PPLO Coene, C Compaan, ECJ Consten, T Darbyshire, SML de Mik, EJR de Graaf, I de Groot, RJ de Vos tot Nederveen Cappel, JHW de Wilt, J van der Wolde, FC den Boer, JWT Dekker, A Demirkiran, M Derkx-Hendriksen, FR Dijkstra, P van Duijvendijk, MS Dunker, QE Eijsbouts, H Fabry, F Ferenschild, JW Foppen, EJB Furnee, MF Gerhards, P van Gerven, JAH Gooszen, JA Govaert, WMU Van Grevenstein, R Haen, JJ Harlaar, E van der Harst, K Havenga, J Heemskerk, JF Heeren, B Heijnen, P Heres, C Hoff, W Hogendoorn, P Hoogland, A Huijbers, P Janssen, AC Jongen, FH Jonker, EG Karthaus, A Keijzer, JMA Ketel, J Klaase, FWH Kloppenberg, ME Kool, R Kortekaas, PM Kruyt, JT Kuiper, B Lamme, JF Lange, T Lettinga, DJ Lips, F Logeman, MF Lutke Holzik, E Madsen, A Mamound, CC Marres, I Masselink, M Meerdink, AG Menon, JS Mieog, D Mierlo, GD Musters, GAP Nieuwenhuijzen, PA Neijenhuis, J Nonner, M Oostdijk, SJ Oosterling, PMP Paul, KCMJ Peeters, ITA Pereboom, F Polat, P Poortman, M Raber, BMM Reiber, RJ Renger, CC van Rossem, HJ Rutten, A Rutten, R Schaapman, M Scheer, L Schoonderwoerd, N Schouten, AM Schreuder, WH Schreurs, GA Simkens, GD Slooter, HCE Sluijmer, N Smakman, R Smeenk, HS Snijders, DJA Sonneveld, B Spaansen, EJ Spillenaar Bilgen, E Steller, WH Steup, C Steur, E Stortelder, J Straatman, HA Swank, C Sietses, HA Groen, HG ten Hoeve, WW ter Riele, IM Thorensen, B Tip-Pluijm, BR Toorenvliet, L Tseng, JB Tuynman, J van Bastelaar, SC van Beek, AWH van de Ven, MAJ van de Weijer, C van den Berg, I van den Bosch, JDW van der Bilt, SJ van der Hagen, R van der Hul, G van der Schelling, A van der Spek, N van der Wielen, E van Duyn, C van Eekelen, JA van Essen, K van Gangelt, AAW van Geloven, C van Kessel, YT van Loon, A van Rijswijk, SJ van Rooijen, T van Sprundel, L van Steensel, WF van Tets, HL van Westreenen, SC Veltkamp, T Verhaak, PM Verheijen, L Versluis-Ossenwaarde, S Vijfhuize, WJ Vles, SC Voeten, FJ Vogelaar, WW Vrijland, E Westerduin, ME Westerterp, M. Wetzel, KP Wevers, B Wiering, CDM Witjes, MW Wouters, STK Yauw, ES van der Zaag, EC Zeestraten, DDE Zimmerman, T Zwieten.