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Title: Sequential assessment of bowel function and anorectal physiology after anterior resection for cancer: A prospective cohort study.

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Abstract

Aim To investigate changes in bowel function and anorectal physiology (ARP) after anterior resection for colorectal cancer.

Methods Patients were recruited from November 2006 to September 2008. Cleveland Clinic Incontinence (CCI) scores and stool frequency were determined by patient questionnaires before surgery (t_0) and at three (t_3), six (t_6), nine (t_9) and 12 (t_{12}) months after restoration of intestinal continuity. ARP measurements were recorded at t_0, t_3 and t_{12}. Endoanal ultrasound was performed at t_0 and t_{12}.

Results Eighty-nine patients were included in the study. CCI score increased post-operatively then normalised, whereas stool frequency did not change. Patients who had neoadjuvant radiotherapy or lower anastomoses had increased incontinence and stool frequency in the post-operative period, whereas those with defunctioning stomas or open surgery had increased stool frequency alone. Maximum resting pressure, volume at first urge and maximum rectal tolerance were reduced throughout the post-operative period. Radiotherapy, lower anastomosis and defunctioning stoma (but not operative approach) altered manometric parameters post-operatively. Maximum tolerance correlated with incontinence and first urge with stool frequency. Anterior internal anal sphincter thickness decreased post-operatively.

Conclusions Incontinence recovers in the first year after anterior resection. Radiotherapy, lower anastomosis, defunctioning stoma and open surgery negatively influence bowel function. ARP may be useful if bowel dysfunction persists beyond 12 months.

What does this paper add to the literature?

This large prospective study documents the link between ARP and incontinence/ stool frequency in the 12 months following anterior resection for colorectal cancer, with subgroup analysis of neoadjuvant radiotherapy, anastomotic height, defunctioning stoma and operative approach.

Introduction

Colorectal cancer survival in the UK has more than doubled in the last 40 years from 22% to 57% (ten-year age standardised survival) [1]. Improvements in preoperative imaging, surgical technique and chemo-radiotherapy have contributed to this [2-4]. Patients expect not only to be cured of bowel cancer but also to have good functional outcome in terms of quality of life and bowel, bladder and sexual function. Unfortunately, a significant proportion of patients experience unwelcome bowel symptoms that impact their quality of life. This constellation of symptoms has been termed low anterior resection syndrome (LARS) and affects 40% of patients have sphincter preserving surgery [5]. A recent international consensus definition describes eight symptoms (e.g., frequency, urgency, incontinence) and consequences (e.g., toilet dependence, preoccupation with bowel function) and recommends that the diagnosis of LARS is dependent on the patient experiencing at least one symptom and one consequence [6]. Importantly, it has been shown that LARS does not only affect patients having low anterior resection, with more than 20% of patients with sigmoid cancer reporting major LARS after surgery [7]. Risk factors for LARS include neoadjuvant radiotherapy [8, 9], low rectal tumours [9-11] and temporary defunctioning stomas [12, 13].

The pathophysiology of LARS has not been fully elucidated and is likely to be multifactorial. It is thought that a combination of altered colonic transit [14], neorectal denervation [15] and internal anal sphincter (IAS) injury [16] may contribute. These pathophysiological processes may manifest as changes in anorectal physiology (ARP). Indeed, studies have shown a reduction in resting anal tone, rectal capacity and rectal sensitivity, which are compounded by neoadjuvant treatment and low anastomoses [17-21].

The objectives of the current study were to: (i) document incontinence and stool frequency after anterior resection for colorectal cancer; (ii) assess postoperative changes in ARP; (iii) determine the effect of neoadjuvant radiotherapy, anastomotic height, defunctioning stoma and operative approach and; (iv) correlate incontinence and stool frequency with ARP.

Methods

This study was given ethical approval by the Southampton and South West Hampshire Local Research Ethics Committee as part of an overarching randomised trial (REC no. 06/Q1704/84). Inclusion criteria were: age ≥18 years, suspected adenocarcinoma within 30 cm of the anal verge (to capture all patients who would have a rectal anastomosis), intention to perform major rectal resection with anastomosis and curative treatment intent. Consecutive patients who met inclusion criteria between November 2006 and September 2008 at University Hospitals Southampton NHS Trust were recruited. Follow up was completed in May 2010. Where the peritoneal reflection was included in the pathological specimen, it was assumed that the patient had had a rectal anastomosis involving the lower third of the rectum (low anastomosis).

Anal incontinence was evaluated using the Cleveland Clinic Incontinence (CCI) score [22] and stool frequency as part of the MSKCC BFI questionnaire [23]. Questionnaires were completed at the following time points: immediately pre-surgery (t_0) and three months (t_3), six months (t_6), nine months (t_9) and 12 months (t_{12}) after surgery (or restoration of intestinal continuity).

Anorectal physiology was recorded at t_0, t_3 and t_{12} using a stationary pull through technique with a 4-channel water-perfused Medtronic catheter. A computerised system (Polygam Lower GI, Synectics Medical, Stockholm, Sweden) was used for data acquisition. Resting pressure and squeeze increment were measured from five stations at 1cm intervals from +6 to +1 cm above the anal verge. Measurement of pressure (resting and squeeze increment) at each station was an average of the pressure recorded by the four channels in the catheter tip. Maximum tolerable rectal volume was assessed by inflating a balloon with water at body temperature, inside the rectum at 5 cm from the anal verge. ARP parameters included mean and maximum resting and squeeze pressures, volume at first urge and maximum tolerable rectal volume.

Anal sphincter dimensions were measured at t_0 and t_{12}, using a BK medical endoanal ultrasound (EAS) probe with the patients in left lateral position.

Baseline (t_0) questionnaires, ARP and EAS were completed before commencement of neoadjuvant radiotherapy wherever possible.

Statistics

Graphpad Prism 9 was used for all statistical analyses. Data were tested for normality using the Kolmogorov-Smirnov Test. Non-parametric variables were compared using Wilcoxan (paired) or Mann-Whitney (unpaired) tests, as appropriate. Parametric variables were compared using paired or unpaired t-tests. The strength of correlations was assessed by the Spearman rank method.

Categorical variables were compared by 2x2 contingency tables (Fisher's exact test). Two-tailed tests were used where applicable, with an alpha significance level of 0.05. Non-parametric data are represented as median +/- IQR and parametric data as mean +/- SEM, unless otherwise stated.

Results

Patient demographics

One hundred and twenty-one consecutive patients who had anterior resection for suspected colorectal cancer were prospectively assessed for inclusion, with 89 patients (who completed 12 months follow up) contributing data for the study (**Table 1**). Median age was 68 years (IQR 62-75) and 50 patients were men (56.2%). Twenty-one patients (23.6%) had neoadjuvant radiotherapy (11 short course and 10 long course). No patients had post-operative radiotherapy. Thirty-seven patients had laparoscopic surgery (41.6%) and 38 patients had a defunctioning stoma (42.7%), with median time to stoma closure five months (IQR 3-7). Median height of the tumour above the anal verge was 15 cm (IQR 10-20 cm) and 57 specimens included the peritoneal reflection (64.0%). Seventy-five specimens contained carcinoma (84.3%), with distribution of pathological T- and N-stages as follows: pT0 (4%), pT1 (21%), pT2 (32%), pT3 (33%) and pT4 (9%); and pN0 (57%), pN1 (36%) and pN2 (7%). Questionnaire completion, ARP and EAS rates at different time points are shown in **Figure 1**. In patients having neoadjuvant radiotherapy, baseline (t_0) questionnaires, ARP measurements and sphincter assessment were completed prior to radiotherapy in 17/21 (81%).

Incontinence and stool frequency in the first year after anterior resection

There was a significant increase in the proportion of patients with incontinence (CCI>0) from t_3 onwards (**Table 2**). Median CCI score for the entire cohort increased at t_3 (p=0.0125), t_6 (p=0.0213) and t_9 (p=0.0024) compared to baseline but not significantly at t_{12} (**Figure 2A**). Patients who received neoadjuvant radiotherapy had no difference in baseline CCI score but significantly higher CCI scores at t_3 (p=0.0212) and t_6 (p=0.0295). However, these differences were not sustained at t_9 and t_{12} (**Figure 2B**). Patients with a lower anastomosis (below peritoneal reflection) had no difference in CCI scores at baseline but significantly higher CCI scores at t_3 (p=0.0110) but not thereafter (**Figure 2C**). Defunctioning stoma (**Figure 2D**) and operative approach (**Figure 2E**) had no effect on CCI scores at any time point.

There was no change in stool frequency in the entire cohort at any time point (**Figure 3A**). Patients who had neoadjuvant radiotherapy had no difference in stool frequency at baseline but increased number of stools at t_3 (p=0.0038), t_6 (p=0.0237) and t_{12} (p=0.0403; **Figure 3B**). The increase at t_9 did not quite reach significance (p=0.0615). Patients with a lower anastomosis had no difference in stool frequency at baseline but increased number of stools at t_3 (p=0.0129) and t_6 (p=0.0124) but not thereafter (**Figure 3C**). Patients who had a defunctioning stoma had no difference in stool frequency pre-operatively but increased number of stools at t_3 (p=0.0009), t_6 (p=0.0155) and t_{12} (p=0.0013; **Figure 3D**). Patients who had open surgery had higher number of stools pre-operatively (p=0.0137) and at t_{12} (p=0.0354) but not in the intervening period (**Figure 3E**).

ARP in the first year after anterior resection (entire cohort)

To objectively measure changes in bowel function after anterior resection, anorectal physiology was conducted at baseline, t_3 and t_{12} for the entire cohort. Maximum resting pressure decreased by 13.5 mmHg at t_3 (p<0.0001) and 16.5 mmHg at t_{12} (p<0.0001), compared to baseline (**Figure 4A**). Volume at first urge reduced by 16.4 ml (p=0.0249) and 15.7 ml (p=0.0198; **Figure 4B**). Maximum rectal tolerance reduced by 36.9 ml (p<0.0001) and 18.9 ml (p=0.0125; **Figure 4C**). Maximum squeeze pressure was not significantly changed at t_3 or t_{12} (**Figure 4D**) and was therefore not examined further.

Effect of neoadjuvant radiotherapy, height of anastomosis, defunctioning stoma and operative approach on ARP

The cohort was then grouped by neoadjuvant radiotherapy (**Figure 5A-C**), height of anastomosis (**Figure 5D-F**), defunctioning stoma (**Figure 5G-I**) and operative approach (**Figure 5J-L**) to ascertain the effect of these variables on post-anterior resection ARP.

At baseline, there was no difference in resting pressure, first urge or maximum tolerance, in patients who did and did not receive radiotherapy (**Figure 5A-C**). Patients who had radiotherapy, had lower resting pressure at t_3 (-13.5 mmHg; p=0.0058) but not t_{12} (**Figure 5A**); reduced first urge at t_3 (-29.1 ml; p=0.0295) but not t_{12} (**Figure 5B**); and lower maximum tolerance at t_3 (-28.8 ml; p=0.0407) but not t_{12} (**Figure 5C**).

At baseline, there was no difference in resting pressure, first urge or maximum tolerance, in patients who had anastomoses above or below the peritoneal reflection (**Figure 5D-F**). Patients who had a lower anastomosis, had no difference in resting pressure at t_3 or t_{12} (**Figure 5D**); reduced first urge at t_3 (-28.0 ml; p=0.0140) but not t_{12} (**Figure 5E**); and lower maximum tolerance at t_3 (-42.5 ml; p=0.0020) and t_{12} (-42.1 ml; p=0.0088; **Figure 5F**).

At baseline, there was no difference in resting pressure, first urge or maximum tolerance, in patients who had a defunctioning stoma (**Figure 5G-I**). Patients who had a stoma, had reduced resting pressure at t_3 (-11.57 mmHg; p=0.0006) but this did not reach significance at t_{12} (-7.6 mmHg; p=0.0535; **Figure 5G**); reduced first urge at t_3 (-26.5 ml; p=0.0174) but not t_{12} (**Figure**

5H); and lower maximum tolerance at t_3 (-33.7 ml; *p*=0.0136) and t_{12} (-34.7 ml; *p*=0.0256; **Figure 5I**).

At baseline, patients who had laparoscopic surgery had lower resting pressure (-8.8 mmHg; *p*=0.0426) but there were no differences at t_3 or t_{12} (**Figure 5J**). There were no differences in first urge or maximum tolerance according to operative approach at any time point (**Figure 5K-L**).

Correlation between anorectal physiology and CCI score

Having documented a change in incontinence/ stool frequency and ARP in the 12 months following anterior resection, the association between these variables was assessed by simple linear regression (**Figure 6A-F**). Selected ARP parameters which changed significantly after anterior resection, were plotted against CCI score or stool frequency at 12 months. Resting pressure did not correlate with CCI (*p*=0.2560; **Figure 6A**) or stool frequency (*p*=0.5977; **Figure 6D**). First urge (*p*=0.0756) seemed to negatively correlate with CCI but did not reach significance (**Figure 6B),** whereas it correlated significantly with stool frequency (*p*=0.0453; **Figure 6E**). Maximum tolerance showed a significant negative correlation with CCI at 12 months (*p*=0.0297; **Figure 6C**) and a negative correlation with stool frequency which did not reach significance (*p*=0.0942; **Figure 6F**).

Changes in anal sphincter dimensions after anterior resection

EAS was used to measure anal sphincter dimensions in 48 patients (**Table 3**). Tumour height, neoadjuvant radiotherapy and defunctioning stoma rates in this group were comparable with the entire cohort (**Table 3a**). Anterior internal anal sphincter length reduced by 1.7 mm post-operatively (*p*=0.032). There were no significant changes in any of the other parameters (**Table 3b**).

Discussion and conclusions

This is the largest prospective study to sequentially document incontinence and stool frequency together with ARP measurements after anterior resection for colorectal cancer. Key findings were as follows: (i) Faecal incontinence increased post-operatively and was greater in patients who had neoadjuvant radiotherapy and lower anastomoses; (ii) Stool frequency did not change post-operatively but was greater in patients who had neoadjuvant radiotherapy, lower anastomoses and a temporary defunctioning stoma; (iii) Resting anal tone, rectal sensation and capacity decreased post-operatively and were negatively influenced by neoadjuvant radiotherapy, lower anastomoses and defunctioning stomas; (iv) Rectal capacity correlated with CCI score and rectal sensation with stool frequency and; (v) anterior IAS length decreased post-operatively.

The present study confirms previous reports that anal incontinence deteriorates after rectal resection but improves in the first 12 months after surgery [24]. This is relevant because a window of one year is usually given before proposing more invasive treatments for LARS. Furthermore, ARP may not be useful or necessary for follow up of LARS in the first year but could be indicated if symptoms persist further, as part of the evaluation of faecal incontinence or stool frequency.

Interestingly, patterns of incontinence and stool frequency after anterior resection were not identical in the present study. In keeping with this, Kim et al. recently defined incontinence-dominant and frequency-dominant LARS, with radiotherapy identified a risk factor for incontinence and low tumours for frequency [25]. Furthermore, the effect of radiotherapy on incontinence in our study was surprisingly short lived (three months). This may represent an initial improvement in acute radiation proctitis [26]. However, studies have shown that patients who had radiotherapy can have persistent incontinence, several years after surgery [27]. This is attributed to establishment of chronic proctitis or radiation-induced fibrosis. Unfortunately, it was not possible in our study to re-evaluate these patients for longer term effects of radiotherapy. Equally, numbers of patients having long-course and short-course radiotherapy were not large enough to perform subgroup analysis, although it has been shown previously that this does not influence LARS symptoms or quality of life [28-30].

Similarly, the effect of lower anastomosis on incontinence was not demonstrated beyond six months in the present study. The compliance of the neorectum improves after a period of remodelling [31], which may partly explain this. However, large cross-sectional studies with several years post-surgical follow up have shown long lasting effects of low anastomosis on bowel-related quality of life [30].

It should also be mentioned that ARP may be altered, or measurements impaired by fibrosis and scar tissue following a rectal anastomosis, with the balloon not inflating as it would in a surgery-naive patient. This should be considered when interpreting results, as it may influence the relationship between ARP and clinical symptoms.

In keeping with previous studies [17, 18, 20], we showed a sustained reduction in resting anal tone in the first year after surgery. This corresponded with a decrease in anterior IAS length. Damage to sympathetic nerves, which course in the intersphincteric space and supply the internal anal sphincter, may be responsible for LARS symptoms in low anterior resection [32]. However, this mechanism would not necessarily account for the symptoms experienced by patients having high anterior resection [7]. With regard to LARS in patients having sigmoid resections, Elfeki et al. identified 12 bowel symptoms ("excessive straining, fragmentation, bloating, nocturnal defaecation, bowel false alarm, liquid stool incontinence, incomplete evacuation and sense of outlet obstruction"), which include incontinence but not stool frequency, highlighting that patterns of LARS may be different after surgery for sigmoid and rectal cancer [33]. Nonetheless, it has been shown that the IAS can be damaged by insertion of the transanal stapling device and this should also be considered in the pathophysiology of LARS in both high and low anterior resection [34]. Of note, all patients in the present study had stapled transanal anastomoses.

In terms of operative approach, the literature to date is sparse about its impact on LARS. Kang et al. showed that fewer patients having laparoscopic low anterior resection had 'defecatory problems' compared to those having open surgery [35]. However, this study was restricted to patients with mid to low cT3 tumours. In contrast, Andersson et al. showed no difference in health-related quality of life between laparoscopic and open surgery groups in their analysis of the COLOR II trial [36]. In the present study, we showed that at 12-months post-procedure, stool frequency but not CCI score was lower in patients having laparoscopic surgery. In fact, stool frequency was lower at baseline in the laparoscopic group, suggesting that more symptomatic patients may have had open surgery. It should be noted that none of the patients in this study had transanal surgery.

Rather unsurprisingly, pre-operative ARP predicts post-operative ARP [37]. However, pre- or post-operative ARP does not seem to predict LARS and does not feature in the POLARS nomogram [38]. In this study, not all ARP parameters correlated with CCI score and stool frequency and resting anal pressure did not correlate with either. This may reflect the limitation of using individual LARS symptoms or that multiple continence mechanisms are disrupted after anterior resection.

In terms of generalisability, the findings presented here are from a sample of patients which represent a typical urban Western European population, where management of colorectal cancer meets nationally recommended guidelines [39]. CCI scores, stool frequency and ARP parameters are in line with previous studies [17, 19]. However, one of the main limitations is that there has been a significant delay from study completion to data submission. Nonetheless, the sequential recording of ARP measurements after anterior resection, coupled with incontinence and stool frequency data, has not been duplicated in this number of patients. More importantly, there is an ethical duty to the patients who participated and the colorectal research community, to present this data, in line with the AllTrials campaign [40]. Nonetheless, our understanding of LARS has changed significantly in this time. In particular, the study pre-dated the LARS score [41]. As such, the present study focuses on faecal incontinence and stool frequency, as two of the most frequent LARS symptoms [42].

Another point for discussion is the measurement of anastomotic height. This was inferred from the histopathological specimen and whether or not it included the peritoneal reflection. Clearly, this method is unable to distinguish between an anastomosis at 3 cm and 6 cm for example, which may result in different functional symptoms and altered rectal sensation and capacity. The original intention was to perform sigmoidoscopy immediately after the anastomosis was fashioned, to determine an accurate anastomotic height, as studies have shown a direct link between level of anastomosis and functional outcome [12, 43]. However, several surgeons involved in the study did not agree to this. An alternative was to use tumour height as a proxy but distal resection margins vary from procedure to procedure and therefore this was not used. It should also be noted that in this study, which included patients having high and low anterior resections (sigmoid and rectal tumours), radiotherapy, anastomotic height and defunctioning stomas were likely to be confounding factors (as radiation is not used for sigmoid tumours and patients with higher anastomoses are less likely to be defunctioned). Although not our main objective here, future studies aiming to predict LARS based on risk factors should consider stratified or multivariable analyses.

In terms of defunctioning stomas, Vogel and colleagues recently published a systematic review suggesting that increased time to stoma closure was a risk factor for major LARS, with a mean difference of 2.4 months between 'major LARS' and 'no LARS' groups [13]. Time to stoma closure in the present study fell within a narrow range (IQR 3-7 months) but was clearly greater than this threshold, highlighting a potential source of bias.

Questionnaire completion rates ranged between 80-100%. At six and nine months, postal questionnaires were used, which explains lower completion at these time points. ARP rates were 76-100% and EAS 44-54%. Considering that ARP and EAS are invasive and do not form part of routine surgical or oncological follow up, these rates are understandable. However, certain groups of patients may have been more or less likely to attend study follow up due to severity of symptoms, oncological outcome or satisfaction with treatment, which is another potential source of bias.

Another consideration is the use of CCI/ Wexner score to measure incontinence symptoms. This is a quick, easy-to-complete and easy-to-score tool, which has been validated and used extensively since 1993 [22]. However, it uses vague quantifiers (e.g., "sometimes"), which means that severity is influenced by patients' personal experience. In addition, incontinence to solid, liquid or gas, use of pads and effect on lifestyle are given equal weighting in determining severity [44]. Nonetheless, it has been shown by Vaizey et al. that CCI score correlates well with the clinical impression of incontinence [45]. A bowel diary could have been used to supplement this, for better discrimination of episodes of incontinence per day or week [46].

The primary outcome measures of this study were incontinence/ stool frequency and ARP. However, as already discussed, LARS encompasses a number of symptoms and effects which include but are not limited to incontinence and frequency [6]. Quality of life after rectal resection is an equally important set of outcomes and a number of tools have been employed to assess these, including global quality of life assessment tools (e.g. EORTC QLQ C30) and the faecal incontinence quality of life (FIQOL) instrument [30, 47]. Quality of life has repeatedly been shown to correlate with LARS symptoms [48, 49] and future studies should include quality of life assessment as standard.

Overall, this study highlights patterns of bowel dysfunction and changes in ARP after anterior resection, with respect to specific risk factors (radiotherapy, anastomotic height, stoma and operative approach). Our hope is that these prospectively collected data, from a significant number of patients, will add to the body of literature which informs clinicians and patients about the functional effects of major rectal resection.

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Table 1. Demographic and clinical characteristics of study cohort (n=89).

Gender	**Male**	50 (56%)
	Female	39 (44%)
Age (years)	*Median (IQR)*	68 (62-75)
Neoadjuvant radiotherapy	**No**	68 (76%)
	Yes	21 (24%)
Tumour height (cm)	*Median (IQR)*	15 (10-20)
Anastomosis	**Low**	57 (64%)
	High	32 (36%)
Defunctioning stoma	**No**	52 (58%
	Yes	37 (42%)
Stoma closure (months)	*Median (IQR)*	5 (3-7)
Operative approach	**Open**	52 (58%)
	Laparoscopic	37 (42%)

Table 2. Proportion of patients with and without incontinence in the first year after anterior resection.

Time point	**CCI=0 Perfect Continence**	**CCI>0 Some Incontinence**	***n***	***P****
t_0	40 (45%)	48 (55%)	88	
t_3	21 (26%)	61 (74%)	82	0.0102
t_6	14 (19%)	59 (81%)	73	0.0004
t_9	8 (11%)	63 (89%)	71	0.0001
t_{12}	19 (21%)	70 (79%)	89	0.0008

* Comparison of proportions (perfect continence/ some incontinence) at different time points with those at t_0. *P* value determined by Fisher's exact test.

Table 3. Changes in anal sphincter dimensions after anterior resection (n=48).

(a)

Clinal parameters of subgroup		
	n	48
Tumour height (cm)	*Median (IQR)*	15 (10.5-20)
Neoadjuvant radiotherapy	**No**	37 (77%)
	Yes	11 (23%)
Defunctioning stoma	**No**	30 (63%)
	Yes	18 (38%)

(b)

	Mean change (mm)	**95% CI (mm)**	***P****
TSL	+0.9	[-1.34 - 3.24]	0.620
$\mathbf{EAS_{max}}$	+0.6	[-2.17 - 3.46]	0.802
$\mathbf{EAS_{ant}}$	+0.8	[-1.98 - 3.65]	0.490
AV to IAS	+0.8	[-0.92 - 2.43]	0.246
IAS	-0.4	[-2.79 - 2.01]	0.151
$\mathbf{IAS_{ant}}$	-1.7	[-3.35 - -0.01]	**0.032**
$\mathbf{IAS_{post}}$	-1.2	[-2.95 - 0.47]	0.116
$\mathbf{IAS_{left}}$	+0.5	[-2.68 - 1.60]	0.610
$\mathbf{IAS_{right}}$	-0.5	[-2.37 - 1.33]	0.210
AV to end	+1.6	[-0.75 - 3.90]	0.167

**P* value determined by unpaired t-test.

TSL – total sphincter length; EAS – external anal sphincter; EASant – length of EAS forming a complete ring; AV – anal verge; IAS – internal anal sphincter; IASant – anterior aspect IAS; IASpost – posterior aspect IAS; IASleft – left aspect IAS; IASright – right aspect IAS.

Figure 1

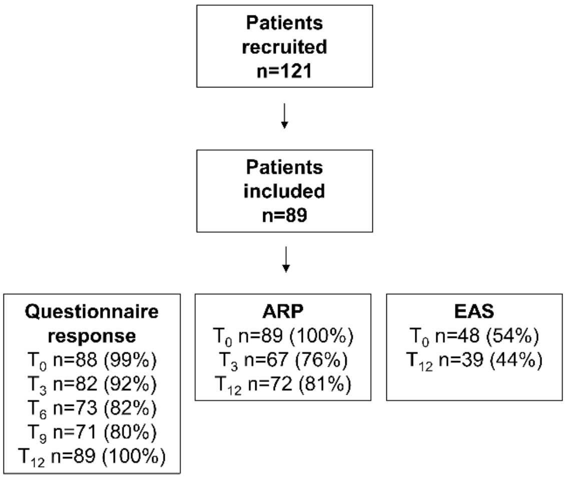

Figure 1. Patient recruitment and data capture. Flow diagram to show number of patients contributing data at different time points during the study. *ARP* – anorectal physiology; *EAS* – endoanal ultrasound.

Figure 2

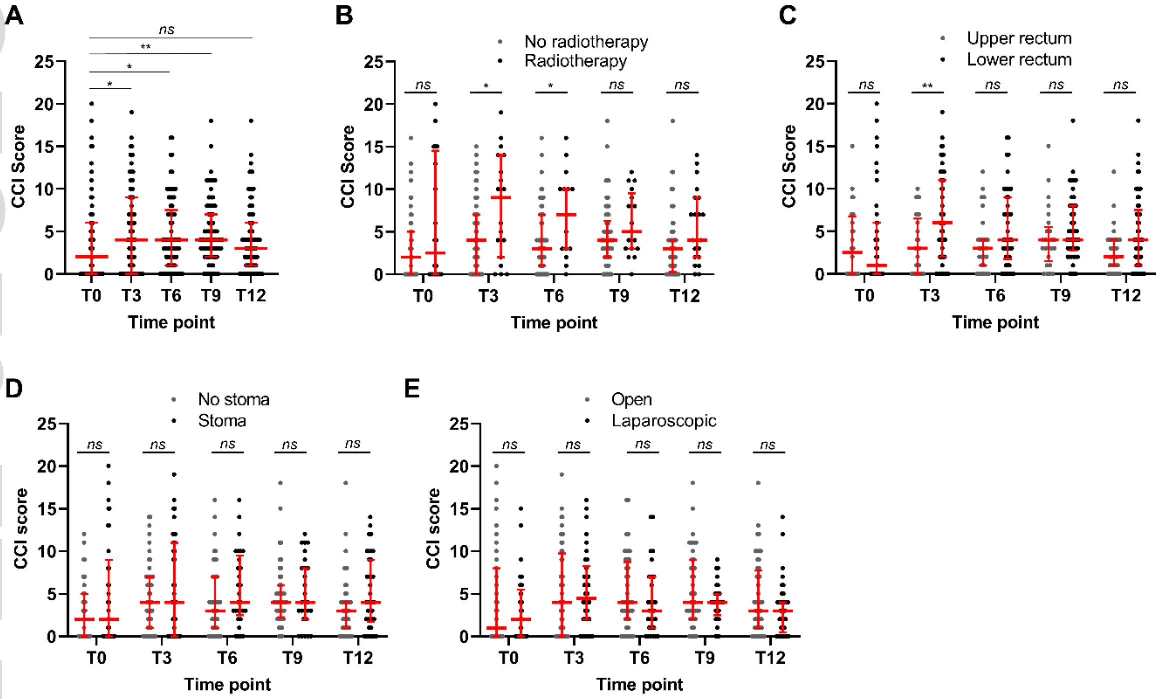

Figure 2. CCI scores in the 12 months following anterior resection. (A) CCI scores in the entire cohort at baseline (T0), 3 months (T3), 6 months (T6), 9 months (T9) and 12 months (T12). (B) CCI scores in patients who did and did not have neoadjuvant radiotherapy. (C) CCI scores in patients who had anastomoses above (upper) and below (lower) the peritoneal reflection. (D) CCI scores (after restoration of continuity) in patients who did and did not have a defunctioning stoma. (E) CCI scores in patients who had open and laparoscopic surgery. Median +/- IQR indicated in red. Comparisons by Mann Whitney Test. * p<0.05, ** p<0.01, ns-not significant.

Figure 3

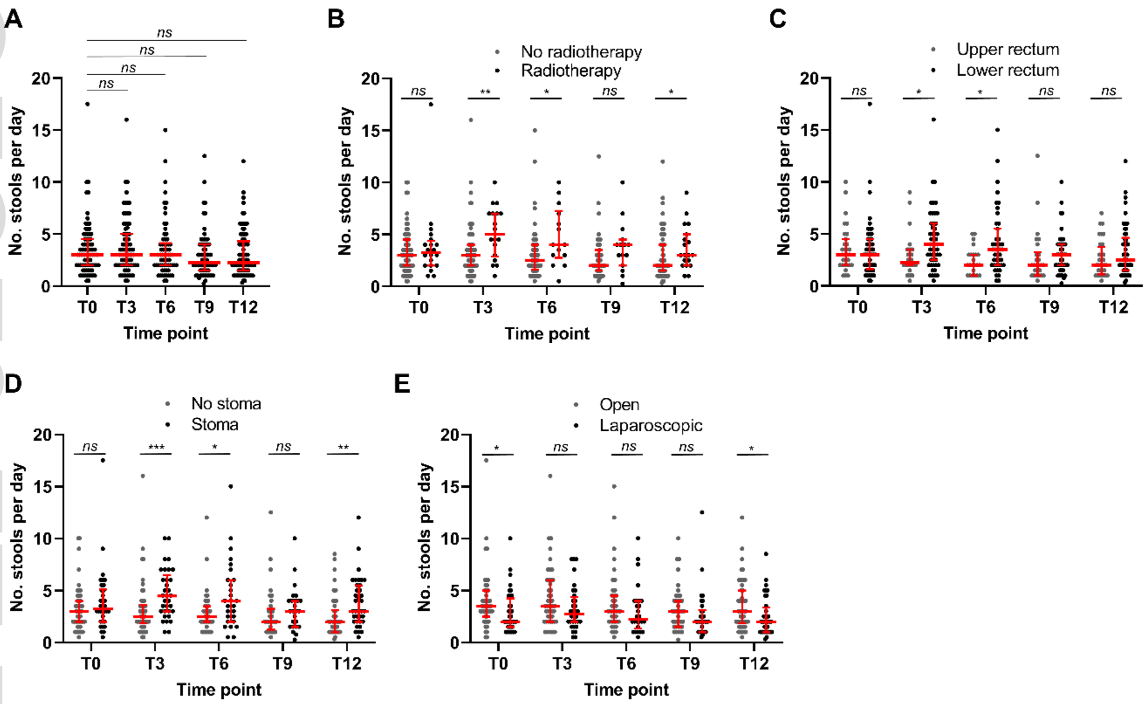

Figure 3. Stool frequency in the 12 months following anterior resection. (A) Stool frequency in the entire cohort at baseline (T0), 3 months (T3), 6 months (T6), 9 months (T9) and 12 months (T12). (B) Stool frequency in patients who did and did not have neoadjuvant radiotherapy. (C) Stool frequency in patients who had anastomoses above (upper) and below (lower) the peritoneal reflection. (D) Stool frequency (after restoration of continuity) in patients who did and did not have a defunctioning stoma. (E) Stool frequency in patients who had open and laparoscopic surgery. Median +/- IQR indicated in red. Comparisons by Mann Whitney Test. * $p<0.05$, ** $p<0.01$, ns-not significant.

Figure 4

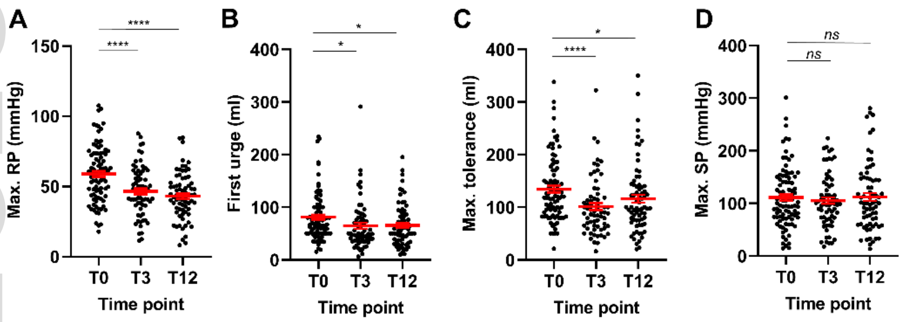

Figure 4. Changes in anorectal physiology after anterior resection. (A) Maximum resting pressure in the entire cohort at baseline (T0), three months (T3) and 12 months (T12). (B) Volume at first urge. (C) Maximum tolerance. (D) Maximum squeeze pressure. Mean +/- SEM show in red. Comparisons by paired t-test. * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001, ns-not significant.

Figure 5

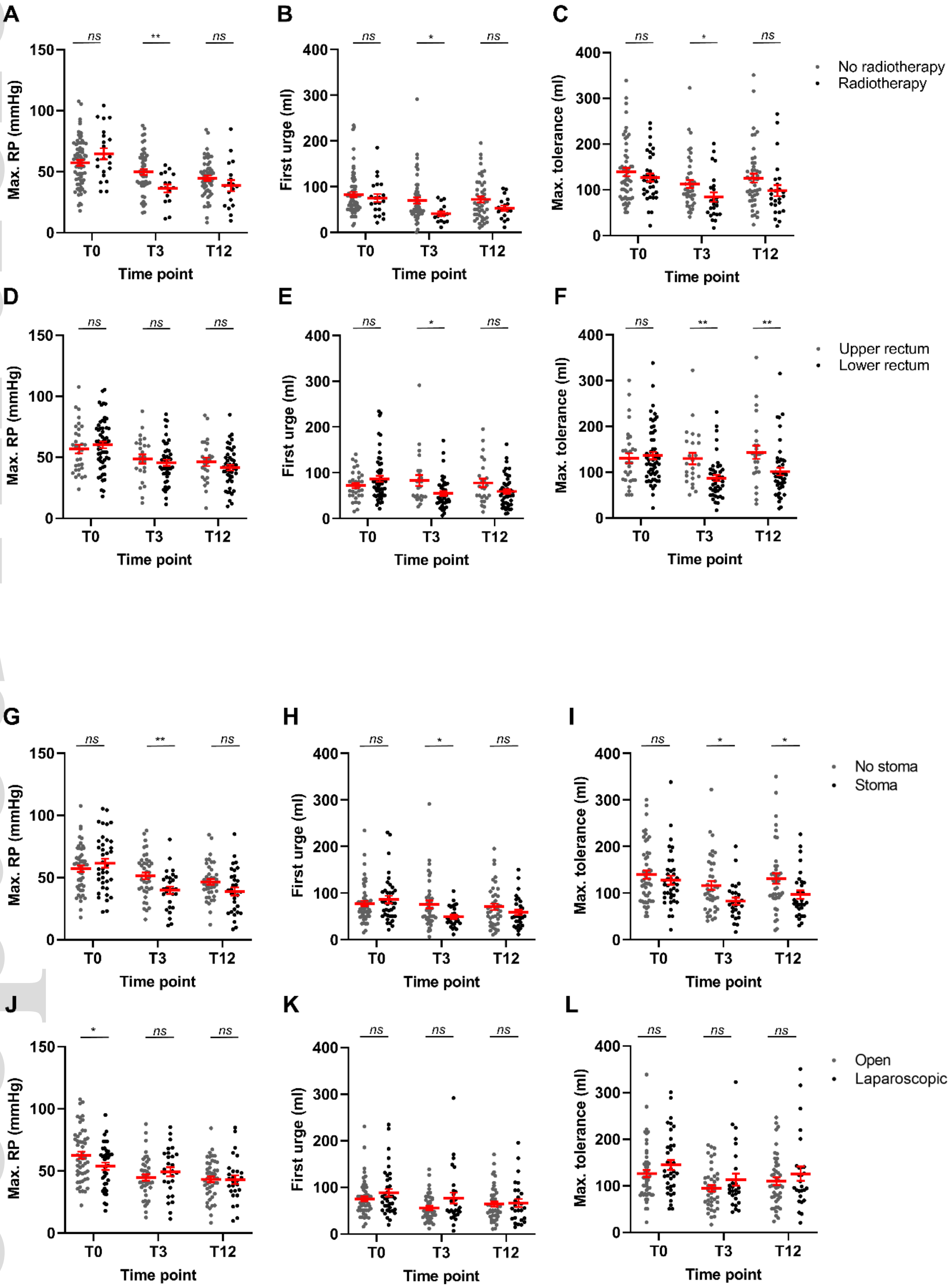
A
B
C
D
E
F
G
H
I
J
K
L
Max. RP (mmHg)
First urge (ml)
Max. tolerance (ml)
Time point
T0
T3
T12
ns
*
**
No radiotherapy
Radiotherapy
Upper rectum
Lower rectum
No stoma
Stoma
Open
Laparoscopic

Figure 5. Changes in anorectal physiology after anterior resection categorised by radiotherapy, height of anastomosis, defunctioning stoma and operative approach. (A) Maximum resting pressure, (B) Volume at first urge and (C) Maximum tolerance at baseline, three months (T3) and 12 months (T12) in patients who did and did not have neoadjuvant radiotherapy. (D) Maximum resting pressure, (E) Volume at first urge and (F) Maximum tolerance in patients who had anastomoses above (upper) and below (lower) the peritoneal reflection. (G) Maximum resting pressure, (H) Volume at first urge and (I) Maximum tolerance in patients who did or did not have a defunctioning stoma. (J) Maximum resting pressure, (K) Volume at first urge and (L) Maximum tolerance in patients who had open or laparoscopic surgery. Mean +/- SEM show in red. Comparisons by unpaired t-test. * $p<0.05$, ** $p<0.01$, ns-not significant.

Figure 6

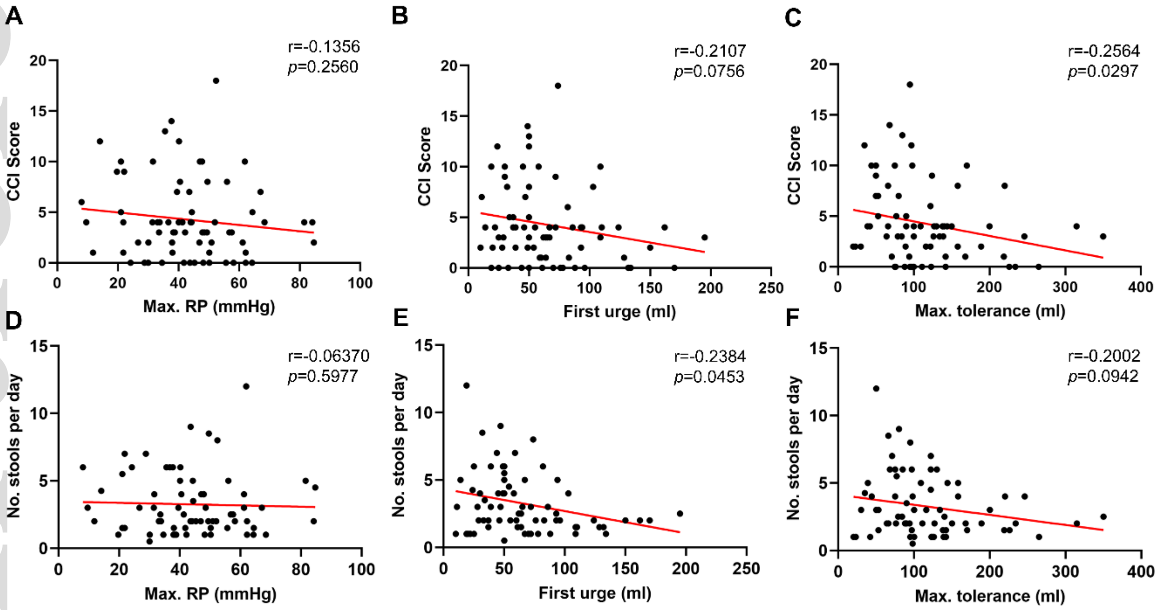

Figure 6. Correlation between anorectal physiology and incontinence/ stool frequency. (A) Maximum resting pressure, (B) Volume at first urge, (C) Maximum tolerance vs. CCI score at 12 months. (D) Maximum resting pressure, (E) Volume at first urge, (F) Maximum tolerance vs. stool frequency at 12 months. Correlation by Spearman Rank method.