



# Subtotal colectomy and ileorectal anastomosis for slow transit constipation: clinical follow-up at median of 15 years

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## Abstract

**Background** Slow transit constipation is characterised by prolonged colonic transit and reliance on laxatives. The pathophysiology is poorly understood and in its most severe form, total colectomy with ileorectal anastomosis is the final treatment option. We present a follow-up study of the long-term function in patients who had surgery for laxative-resistant slow transit constipation.

**Methods** A postal survey was sent to assess bowel frequency, abdominal pain, St Mark's continence score, satisfaction with procedure, likelihood to choose the procedure again, and long-term rates of small bowel obstruction and ileostomy. Longitudinal data from a subgroup studied 23 years previously are reported.

**Results** Forty-two patients (*male* = 2) were available for follow-up out of an initial cohort of 102. Mean time since surgery was 15.9 years (range 1.7–29.7) years. Fifty percent had < 4 bowel motions per day, most commonly Bristol stool 6, mean St Mark's score 7.45. Twenty-one percent had severe incontinence. Satisfaction and likelihood to choose surgery were high (median 10/10). There was a high rate of small bowel obstruction, suggesting pan-intestinal dysmotility in some cases. Conversion to ileostomy occurred in 8 patients. In the longitudinal follow-up in 15 subjects, continence deteriorated ( $p < 0.01$ ), stool consistency softened ( $p < 0.01$ ), and stool frequency fell ( $p < 0.01$ ).

**Conclusions** Satisfactory stool frequency was achieved in the long term, and although 21% had incontinence scores > 12, patient satisfaction was high. This is the longest reported follow-up of colectomy for slow transit constipation, with longitudinal outcomes reported. There was considerable attrition of patients, so larger, longitudinal studies are required to better ascertain the functional outcomes of these patients.

**Keywords** Slow transit constipation · Colectomy · Long-term outcome · Surgery

## Introduction

Constipation is a common gastrointestinal complaint, the reported prevalence varying from 2 to 28% of the population, with western countries clustering around 15% [1]. Slow transit constipation (STC) is a severe form of chronic constipation that occurs more frequently in young females and is characterised by a prolonged colonic transit time [2]. Patients with STC frequently experience abdominal

pain, bloating and distension, and are reliant on laxatives or enemas to produce a bowel action [3]. Patients with this disturbed gastrointestinal function report a significantly impaired quality of life [4].

The pathophysiology of STC is poorly understood. A reduction in the number of the interstitial cells of Cajal and enteric glial neurons has been postulated [5]. However, the normal distribution and density of the cells of Cajal in health are unknown, and observations of depleted cell populations in disease may not be meaningful [6]. Other physiological characteristics of STC have been identified and include a reduced gastro-colic reflex [7] abnormalities of enteric neurotransmitters such as substance-P [8], and degeneration of the myenteric plexus ganglia [9].

Severe laxative-resistant STC is a debilitating condition with few management options. Antegrade colonic lavage via an appendicostomy or caecostomy catheter may be effective

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in some cases [10]. Total colectomy and ileorectal anastomosis offers a definitive surgical solution [11–14]. Unfortunately, as with treatment of other disturbances of function such as rectal prolapse, there are few randomized trials and assessment is obtained from case studies, which have mostly reported medium-term outcomes of bowel frequency, pain, and patient satisfaction [15, 16]. Since a criticism has been that a majority of these papers find favourable outcomes, the aim of the present study was to determine whether there was further information which could be found in longer-term follow-up, and we now sought to assess the long-term functional results, including longitudinal follow-up in a small subgroup of patients who had been assessed 23 years previously.

## Materials and methods

Ethics approval for this study was obtained from the South Eastern Sydney Human Research Ethics Committee ref: 16/263(LNR/16/POWH/508). Patients were given an information sheet via email or post and informed consent was obtained.

Patients who had total colectomy and ileorectal anastomosis for scintigraphically proven STC were identified from a retrospective review of a prospectively maintained database. All patients who had undergone total colectomy and ileorectal anastomosis for laxative-resistant slow transit constipation, proven using either radioisotope scintigraphy or radio-opaque markers, were included. Each patient had a program of management with high-dose laxatives and dietary manipulation, and biofeedback when there were symptoms of pelvic floor dysfunction, prior to being eligible for colectomy. Patients with fecal incontinence were excluded from the procedure. All patients had a positive recto-anal inhibitory reflex demonstrated on anorectal studies to exclude short-segment aganglionosis as part of their preoperative work-up.

The surgical procedure was performed either laparoscopically or by open laparotomy until 2013 and laparoscopically from 2014 on. Patients were sent a postal survey and identified as aligned with St George Hospital and independent from the treating surgeons. Patients who did not respond were contacted by telephone and encouraged to complete the survey. The questions related to bowel function; abdominal pain as measured by visual analogue scale [0–10; 10 is very severe]; stool frequency (number of bowel motions per day); stool consistency on the Bristol stool chart (1–7); continence as measured by St Mark's fecal incontinence score [17] (mild incontinence defined as score of 1–6, moderate incontinence 7–12, severe incontinence > 12) and rectal evacuation assessed incomplete emptying straining, use of enemas, and suppositories and digitation (0–16; 16 = severe

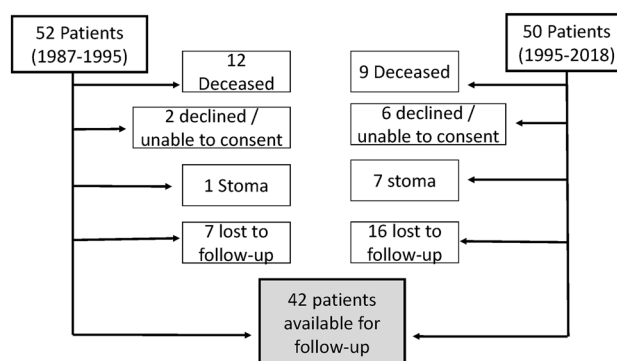
symptoms) which was used in previous study [16]. Patients were asked about satisfaction with the procedure (scale 0–10), and to rate with hindsight their likelihood of choosing to have the surgery, i.e., knowing all they did about their preoperative symptoms, their experience with the surgery, clinical outcome and current function (scale 0–10).

## Statistical analysis

Data were entered in SPSS version 25 (IBM Corp. Armonk, NY, USA). Descriptive statistics were used to identify mean values or medians depending upon the spread of the data and 95% confidence interval was reported in normally distributed continuous data; relationships were calculated using Spearman's correlation coefficient. Chi square was used to identify relationships between categorical data and significance was set at 0.05. Longitudinal data were compared using paired *t* test.

## Results

From 1988 to 2018, 102 patients with STC underwent total colectomy and ileorectal anastomosis. In all cases the anastomosis was carried out to the upper rectum. Twenty-one patients were deceased (unrelated to the surgery), 23 were lost to follow-up, 8 had undergone formation of ileostomy, 4 were unable to complete the survey due to medical incapacity, and 4 declined to participate (flow chart, Fig. 1). This left 42 patients (2 males) available for follow-up. The mean time since surgery was 15.9 years (95% CI 12.81, 19.01), range 1.7–29.7 years. The mean age at surgery was 46.2 years (95% CI 41.97, 50.35), range 22.4–77.6 years. STC was shown in 20 patients with preoperative scintigraphy and in 22 patients with radio-opaque marker studies.



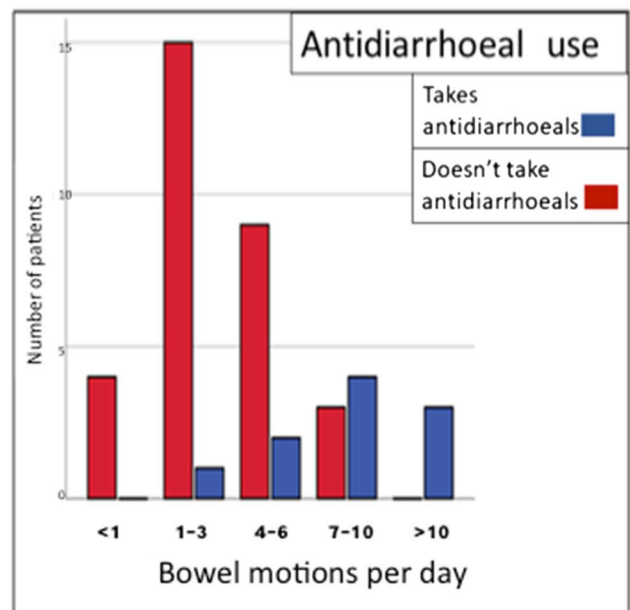
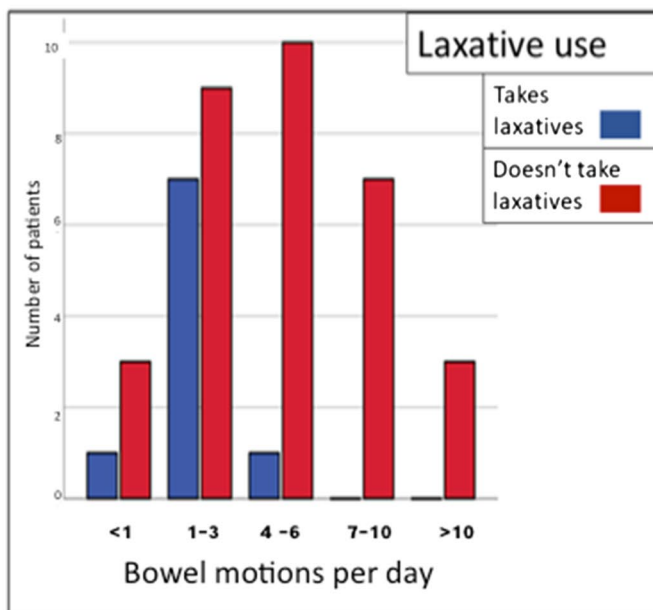
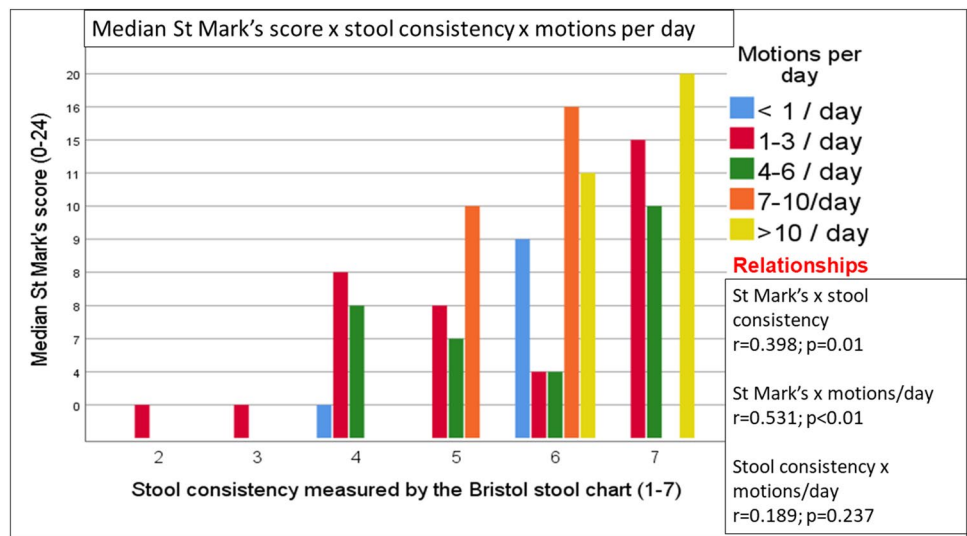
**Fig. 1** Consort flow diagram showing number of patients available for follow-up

### Stool frequency and continence

Of the 42 patients 4 (9.5%) had fewer than 1 bowel motion per day; 17 (40.5%) had 1–3 bowel motions per day; 11 (26.2%) had 4–6 per day; 7 (16.7%) had 7–10 per day and 3 (7.1%) had > 10 per day (Fig. 2). Stool consistency was most commonly type 6 on the Bristol Stool Chart (Fig. 2). Nine patients took laxatives and 8 of these patients passed 1–3 bowel motions per day or less, which was not statistically significant (Fig. 3a). There was no relationship between laxative use and stool consistency, stool frequency or obstructed defecation score. However, those

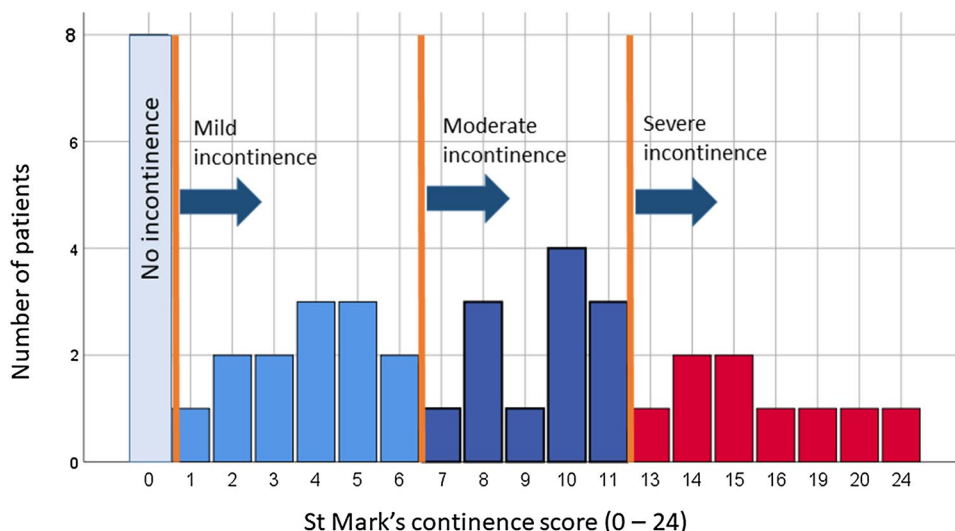
patients with a slower average preoperative transit time had a greater risk of consuming laxatives postoperatively ( $p=0.04$ ). Ten patients used antidiarrheal medication regularly (most commonly loperamide). These patients had a higher stool frequency with nine patients passing 4–6 or more stools per day although this was not statistically significant (Fig. 3b). Twenty-one patients (50%) had normal continence or mild incontinence; 12 patients (28.6%) had moderate incontinence and 9 (21.4%) had severe incontinence (Fig. 4). The majority of patients had no difficulty differentiating between solid stool, liquid stool and gas (Table 1).

**Fig. 2** Bar graph showing maximum St Mark’s continence score × stool consistency × daily stool frequency in 42 patients



**Fig. 3** a Shows bar graph of number of motions per day × laxative use: b shows bar graph of number of motions per day × antidiarrheal medication

**Fig. 4** Bar graph showing the distribution and severity of St Mark’s fecal incontinence score



**Table 1** Summary of 42 patients’ functional results, clinical outcome and satisfaction after total colectomy and ileorectal anastomosis for slow transit constipation

Description	Mean	Min	Max	(95% CI)
Age at surgery (years)	46.2	22.4	77.6	(38.71, 51.96)
Stool consistency as per Bristol stool chart (1–7)	6	2	7	
St Mark’s continence score	7.45	0	24	(5.52, 9.39)
Obstructed defecation score (0–16)	1.85	0	8	(1.20, 2.50)
Abdominal pain (0–10)	1.6	0	8	(0.88, 2.32)
Abdominal pain after bowel motion (0–10)	1.08	0	8	(0.42, 1.73)
Number laxatives per week	0.90	0	14	(0.13, 1.67)

	Median	Min	Max	IQR
Satisfaction with procedure (0–10)	10	8.0	10	2.0
Likelihood of having surgery (0–10)	10	9.0	10	1.0

Description	Yes n (% of total)	No n (% of total)	Details
Antidiarrheal medication	11 (26%)	31 (74%)	9 × loperamide, 2 × lomotil
Laxatives	9 (22%)	33 (78%)	3 × PEG, 2 × nulax, 2 × bisacodyl 2 × coloxyl with senna
Other bowel medication	7 (17%)	35 (83%)	4 × psyllium, 1 × codeine, 1 × enema, 1 × probiotic
Strain to empty	7 (17%)	35 (83%)	
Differentiate gas	28 (67%)	14 (33%)	
Differentiate liquid stool	30 (71%)	12 (29%)	
Differentiate solid stool	34 (81%)	8 (19%)	
Small bowel obstruction	9 (21%)		Requiring hospital admission

**Abdominal pain and overall satisfaction**

The mean abdominal pain score was 1.60 (95% CI 0.88, 2.32: range 0–8). Pain was not relieved by defecation (mean pain score immediately after defaecation 1.08 (95% CI 0.42, 1.73: range 0–8:  $p=0.101$ ). There was an inverse

correlation between abdominal pain and patient satisfaction ( $r = -0.437, p < 0.01$ ). Overall patient satisfaction with the procedure was high, with a median score of 10 (IQR 2.0: range 8–10). The likelihood of choosing to have the surgery in hindsight had a median score of 10 (IQR 1.0: range 9–10).

## Long-term complications: small bowel obstruction

Nine of the 42 patients (21%) developed small bowel obstruction requiring hospital admission, 4 of whom required a laparotomy.

## Stoma patients

From our original study cohort of 102 patients 8 progressed to end ileostomy. One was due to perforation during dilatation of an anastomotic stricture, 1 due to high stool frequency, 1 due to recurrent constipation, and 5 due to recurrent small bowel obstruction. These 8 patients with stoma are not included in the data collected from the 42 patients in the clinical follow-up (Fig. 1). However, we did follow them separately.

Of these 8 patients with stoma (all female, mean age at stoma formation 46.5 years, range 27–70 years; mean time from colectomy to stoma formation was 4.5 years), 2 had died and 1 was in an aged care facility with dementia, leaving 5 available for follow-up. When asked about satisfaction (on a 0–10 scale) with their result of colectomy prior to undergoing stoma formation, the mean score was 3.8 (range 0–8). When asked if they would still have colectomy with knowledge it would result in a stoma, all 5 answered affirmatively.

## Longitudinal study subgroup

Fifteen of the patients, all female, mean age at surgery 43.8 years ( $SD \pm 10.32$ ), had been surveyed in our previous study [16]. The interval between data collection in the two studies was 23 years. The mean time since surgery in these 15 patients was 25 years (95% CI 23.28, 26.71; range 23.1–29.7 years). Over time, the frequency of bowel motions reduced significantly, stool consistency became significantly looser and there was a significant deterioration in continence over the 23 years (Table 2).

Satisfaction with the procedure was measured in the initial postal questionnaire in 1995 by a binomial “yes” or “no” answer. All 15 patients were satisfied with the procedure and had initially answered “yes”. In the follow-up questionnaire, a VAS (0–10) score was used, with zero being not satisfied and 10 totally satisfied; satisfaction scores ranged from 8 to 10. Two patients reported that stool frequency impaired their quality of life due to disrupted sleep and restricted their ability to travel. Two patients reported needing to restrict their dietary intake. Despite this, all 15 patients reported they would still select to have the procedure knowing what they knew now. One patient who initially demonstrated regret in having procedure was now satisfied (Table 2). Two of the 15 patients had small bowel obstruction, 1 of whom required surgery.

**Table 2** Longitudinal data showing functional results in 15 patients in 1995 and 2018

Longitudinal data	1995				2018				
	Mean	Min	Max	95% CI	Mean	Min	Max	95% CI	<i>p</i>
Length of follow-up (years)	10.9	1.7	28.2	7.4, 14.3	25.0	23.1	29.7	23.3, 26.7	
Motions per day	4.93	1	7	4.79, 5.08	2.57	1	5	1.98, 3.16	< 0.01
Stool consistency	3.71	2	5	3.14, 4.29	5.07	2	7	4.15, 5.99	< 0.01
Continence score	1.14	0	16	– 1.326, 3.61	6.21	0	19	2.82, 9.61	< 0.01
OD score	3.0	1	5	2.25, 3.75	1.86	0	6	0.68, 3.03	0.104
					No. pts in 1995				No. pts in 2017
Takes laxatives					1 (7%)				3 (20%)
Strains					1 (7%)				4 (27%)
Cannot differentiate solid					3 (20%)				2 (13%)
Cannot differentiate liquid					3 (20%)				3 (20%)
Cannot differentiate gas					4 (27%)				5 (33%)
Abdominal pain					5 (33%)				8 (53%)
Persisting abdominal pain post-defaecation					5 (33%)				3 (20%)
Satisfaction with procedure					Yes: 14 (93%)				Median 10 Min 8 Max 10
Likelihood of having procedure					Yes: 14 (93%)				Median 10 Min 9 Max 10

OD obstructed defaecation, *Pts* patients

## Discussion

Total colectomy with ileorectal anastomosis is performed as the final step in a series of escalating management strategies for patients with severe idiopathic slow transit constipation. As with most surgical procedures that address function, long-term outcomes are important and especially where there is a relatively young cohort (mean age 47 years). This paper is the longest follow-up of the functional results of colectomy for slow transit constipation with a mean time 15.9 years [18]. The main weakness of the study is the high attrition of patients during the follow-up period, and hence potential sample bias. However, 23 of the initial 102 patients were lost to follow-up which we feel is a reasonable number after such a long period of time, and it should be noted that there were only 4 patients who refused to participate in the follow-up study. Although there were only 15 patients remaining from the earlier study 23 years previously, nonetheless, this is the only longitudinal follow-up of patients over an extended period of time. The finding that continence deteriorated during that time should be a reason for further studies to be done where larger numbers are available.

Excluding the patients whose surgery progressed to an ileostomy, the remaining 42 patients in this study reported a high level of overall satisfaction with total colectomy. When asked if they would undergo the procedure again, armed with their retrospective knowledge and experience, all answered affirmatively with a median likelihood score of 10/10.

Although some patients underwent a program of biofeedback pre-operatively, it is uncertain whether this provided any benefit to long-term outcomes. We do not use proctography other than to assess anterior and posterior rectoceles, since we do not exclude patients with pelvic floor weakness from colectomy as long as they have proven STC. Some reports show that patients with STC who also have rectal evacuation disorders have poorer outcomes after colectomy [19], while other studies have shown that patients with STC, with and without obstructed emptying symptoms have similar outcomes [20] and that the surgery results in resolution of the obstructed defecation [21, 22]. Our longitudinal data demonstrated a reduction in the obstructed defecation score over time although this was not statistically significant (Table 2).

We did not treat any patients with sacral neuromodulation since our randomized double blind crossover trial did not show a long-term benefit in patients with severe STC [23].

The majority of patients had fewer than 4 bowel movements per day and only 24% had more than 6 bowel

movements (Table 1), which is similar to previously reported results [11, 13, 24, 25]. Only 2 patients found that the frequency of bowel motions significantly impacted on their quality of life, specifically with sleep and ability to travel. The reported stool consistency was commonly loose and 26% took medication to firm up the stool.

The regular use of laxatives was seen in 22% of the 42 patients and in 20% of patients in the longitudinal study. The reasons for taking the laxatives were not specifically assessed in this study, but it was interesting to note that those patients who had slower colon transit on preoperative study were more likely to take laxatives and none of the patients who required laxatives exceeded 4–6 bowel motions per day (Fig. 3a).

Most patients who experienced fecal incontinence reported that this was only occasional and mild. Patients were able to discriminate between flatus, liquid feces and solid stool but despite this there was a moderate correlation between loose stool and incontinence. In the time during the two follow-up periods, continence scores deteriorated. The majority of patients were women who had prior vaginal deliveries, so the extent to which impaired continence could be attributed entirely to the colectomy or to progressive age-related pelvic floor weakness with age is not quantifiable. The observed deterioration is worth noting, so that multiparous patients can be informed of this possible long-term outcome.

Pain and bloating are symptoms commonly reported by patients with STC [26]. Our data showed that pain scores were low with a mean of 1.7 out of 10.

There was a high rate of small bowel obstruction, with 9 patients (21%) developing at least 1 episode of obstruction, 4 of whom required surgery. This is in keeping with other studies, and is higher than the rate of obstruction seen in patients who have undergone total colectomy for colitis or cancer [27]. A review of 22 studies found the median incidence of small bowel obstruction was 18% (range 2–71%) and reoperation 14% (range 0–50%) [15]. Eight patients had an ileostomy, 5 due to recurrent small bowel obstruction causing repeated hospitalisation. It is unclear how frequently patients undergoing surgery for chronic idiopathic constipation have a generalized motor disorder of the gastrointestinal tract and slow small intestinal transit which may contribute to developing small bowel obstruction. Indeed, small bowel pseudo-obstruction can be misdiagnosed as a true mechanical obstruction, in some cases even leading to laparotomy.

Since the procedure was carried out laparoscopically only in the last few years of the study, there were insufficient numbers to provide a meaningful comparison with the open laparotomy cohort.



## Conclusions

We found that overall patient satisfaction was high even in those patients whose final outcome was ileostomy. However, in the cohort of patients within the longitudinal follow-up we found significant deterioration in continence. We suggest that women should be informed about this possibility when considering colectomy for slow transit constipation.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** Ethics approval for this study was obtained from the South Eastern Sydney Human Research Ethics Committee ref: 16/263(LNR/16/POWH/508).

**Informed consent** Patients were given an information sheet via email or post and informed consent was obtained.

## References

- Krogh K, Chiarioni G, Whitehead W (2017) Management of chronic constipation in adults. *United Eur Gastroenterol J* 5(4):465–472
- Andromanakos NP, Pinis SI, Kostakis AI (2015) Chronic severe constipation: current pathophysiological aspects, new diagnostic approaches, and therapeutic options. *Eur J Gastroenterol Hepatol* 27(3):204–214
- Dinning PG, Jones M, Hunt L, Fuentealba SE, Kalanter J, King DW et al (2011) Factor analysis identifies subgroups of constipation. *World J Gastroenterol* 17(11):1468–1474
- Tillou J, Poylin V (2017) Functional disorders: slow-transit constipation. *Clin Colon Rectal Surg* 30(1):76–86
- He CL, Burgart L, Wang L, Pemberton J, Young-Fadok T, Szurszewski J et al (2000) Decreased interstitial cell of cajal volume in patients with slow-transit constipation. *Gastroenterology* 118(1):14–21
- Knowles CH, Farrugia G (2011) Gastrointestinal neuromuscular pathology in chronic constipation. *Best Pract Res Clin Gastroenterol* 25(1):43–57
- Bassotti G, Roberto GD, Sediari L, Morelli A (2004) Toward a definition of colonic inertia. *World J Gastroenterol* 10(17):2465–2467
- Uemura S, Hurley MR, Hutson JM, Chow CW (1998) Distributions of substance P- and VIP-immunoreactive nerve fibres in the colonic circular muscle in children. *Pediatr Surg Int* 14(1):66–70
- Wedel T, Spiegler J, Soellner S, Roblick UJ, Schiedeck TH, Bruch HP et al (2002) Enteric nerves and interstitial cells of Cajal are altered in patients with slow-transit constipation and megacolon. *Gastroenterology* 123(5):1459–1467
- Patton V, Lubowski DZ (2015) Clinical outcome and efficacy of antegrade colonic enemas administered via an indwelling cecostomy catheter in adults with defecatory disorders. *Dis Colon Rectum* 58(4):457–462
- Piccirillo MF, Reissman P, Wexner SD (1995) Colectomy as treatment for constipation in selected patients. *Br J Surg* 82(7):898–901
- Fitzharris G, Garcia-Aguilar J, Parker S, Bullard K, Madoff R, Golberg S et al (2003) Quality of life after sub-total colectomy for slow transit constipation. *Colon Rectum* 46(4):433–440
- Yoshioka K, Keighley MR (1989) Clinical results of colectomy for severe constipation. *Br J Surg* 76(6):600–604
- Nyam DC, Pemberton JH, Ilstrup DM, Rath DM (1997) Long-term results of surgery for chronic constipation. *Dis Colon Rectum* 40(3):273–279
- Knowles CH, Scott M, Lunniss PJ (1999) Outcome of colectomy for slow transit constipation. *Ann Surg* 230(5):627–638
- Lubowski DZ, Chen FC, Kennedy ML, King DW (1996) Results of colectomy for severe slow transit constipation. *Dis Colon Rectum* 39(1):23–29
- Vaizey CJ, Carapeti E, Cahill JA, Kamm MA (1999) Prospective comparison of faecal incontinence grading systems. *Gut* 44:77–80
- Knowles CH, Grossi U, Chapman M, Mason J (2017) Surgery for constipation: systematic review and practice recommendations: results I: colonic resection. *Colorectal Dis* 19(Suppl 3):17–36
- Kuijpers HC (1990) Application of the colorectal laboratory in diagnosis and treatment of functional constipation. *Dis Colon Rectum* 33(1):35–39
- Reshef A, Alves-Ferreira P, Zutshi M, Hull T, Gurland B (2013) Colectomy for slow transit constipation: effective for patients with coexistent obstructed defecation. *Int J Colorectal Dis* 28(6):841–847
- Ding W, Jiang J, Feng X, Ni L, Li J, Li N (2015) Clinical and pelvic morphologic correlation after subtotal colectomy with colorectal anastomosis for combined slow-transit constipation and obstructive defecation. *Dis Colon Rectum* 58(1):91–96
- Duthie GS, Bartolo DC (1992) Anismus: the cause of constipation? Results of investigation and treatment. *World J Surg* 16(5):831–835
- Patton V, Stewart P, Lubowski DZ, Cook IJ, Dinning PG (2016) Sacral nerve stimulation fails to offer long-term benefit in patients with slow-transit constipation. *Dis Colon Rectum* 59(9):878–885
- Kamm MA, Hawley PR, Lennard-Jones JE (1988) Outcome of colectomy for severe idiopathic constipation. *Gut* 29(7):969–973
- Platell C, Scache D, Mumme G, Stitz R (1996) A long-term follow-up of patients undergoing colectomy for chronic idiopathic constipation. *Aust N Z J Surg* 66(8):525–529
- Dinning PG, Hunt L, Lubowski DZ, Kalantar JS, Cook IJ, Jones MP (2011) The impact of laxative use upon symptoms in patients with proven slow transit constipation. *BMC Gastroenterol* 11:121
- Ghosh S, Papachrysostomou M, Batool M, Eastwood MA (1996) Long-term results of subtotal colectomy and evidence of noncolonic involvement in patients with idiopathic slow-transit constipation. *Scand J Gastroenterol* 31(11):1083–1091

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