ORIGINAL ARTICLE

Role of transanal irrigation in the treatment of anterior resection syndrome

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Abstract

Background Transanal irrigation(TAI) has been reported to be an inexpensive and effective treatment for low anterior resection syndrome(LARS). The aim of the present prospective study was to evaluate the use of TAI in patients with significant LARS symptoms at a single medical center.

Methods Patients who had low anterior resection for rectal cancer between April 2015 and May 2016 at the Careggi University Hospital were assessed for LARS using the LARS and the Memorial Sloan-Kettering Cancer Center Bowel Function Instrument (MSKCC BFI) questionnaires 30–40 days after surgery or ileostomy closure (if this was done). Quality of life was evaluated using a visual analog scale and the Short Form-36 Health Survey. All patients with LARS score of 30 or higher were included (early LARS) as were all patients with a LARS score of 30 or higher referred 6 months or longer after surgery performed elsewhere (chronic LARS) in the same study period. Study participants were trained to perform TAI using the Peristeen™ System for 6 months, followed by 3 months of enema therapy following a similar protocol.

Results Thirty-three patients were enrolled in the study. Six patients stopped the treatment. The 27 patients (19 early LARS and 8 chronic LARS) who completed the study had a significant decrease in the number of median daily bowel movements [baseline 7 (range 0–14); 6 months 1 (range 0–4); 9 months 4 (range 0–13)]. The median LARS Score fell from 35.1 (range 30–42) (baseline) to 12.2 (range 0–21) after 6 months ($p < 0.0001$) and then rose to 27 (range 5–39) after 3 months of enema therapy. There was no difference in LARS score decrease at 6 months between the patients with early and chronic LARS (22.5 and 23.9 respectively; p=0.7) and there were no predictors of score decrease. Four components of the SF-36 significantly improved during the TAI period. The MSKCC BFI score significantly improved in several domains. Twenty-three patients (85%) asked to continue the treatment with TAI after the study ended.

Conclusions TAI appears to be an effective treatment for LARS and results in a marked improvement of continence and quality of life. Patients may be assessed and treated for LARS early after surgery since the treatment benefit is similar to that observed in patients with LARS diagnosed 6 months or longer after surgery. The potential rehabilitative role of TAI for LARS is promising and should be further investigated.

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Introduction

Many surviving rectal cancer patients experience major problems with bowel function after sphincter-preserving resection. The quality of life of rectal cancer survivors is closely associated with the severity of their symptoms of bowel dysfunction.

After low anterior resection of the rectum (and other rectosigmoid resection procedures), up to 80% of patients report symptoms that include fecal urgency, frequent bowel movements, stool fragmentation, emptying difficulties and

incontinence, and increased gas [1]. Collectively these symptoms are referred to as low anterior resection syndrome (LARS). Even though many of these functional impairments have clinically resolved by 6–12 months after surgery, long-term studies have reported the presence of relevant adverse symptoms up to 15 years after resection in about 50% of patients [2, 3].

Moreover, no specific treatments for LARS have been widely adopted. Management is empirical and symptom based, using existing therapies for fecal incontinence, fecal urgency and rectal evacuatory disorders.

Transanal irrigation (TAI) has been reported to be a cheap and effective treatment for LARS [4, 5].

The aim of the present study was to assess the role of TAI in the treatment of symptoms in patients with LARS, in relation to both impact on quality of life (QoL) and potential rehabilitative effect on colon function.

Materials and methods

From April 2015 to May 2016, all patients undergoing low anterior resection for rectal cancer at the Careggi University Hospital in Florence, Italy, were prospectively evaluated according to the prevention and treatment algorithm previously described [6]. All patients who underwent low anterior resection for rectal cancer were enrolled in an oncological follow-up protocol.

Between 30 and 40 days after rectal surgery (if no stoma) or stoma closure, the functional status and quality of life of all patients were evaluated. Bowel function was assessed using the Memorial Sloan-Kettering Cancer Center Bowel Function Instrument (MSKCC BFI) and the Low Anterior Resection Syndrome Score (LARS score).

The MSKCC BFI is the first validated questionnaire designed specifically for evaluating bowel function after sphincter-preserving surgery for rectal cancer [7, 8]. It consists of 18 questions about the frequency of a variety of LARS issues. For each question, the five frequency options range from "never" to "always" (except for one question asking about the number of bowel movements per 24 h). Responses can be summarized into three subscales [frequency, six items (Q1, Q5, Q8–Q11); diet, four items (Q2, Q3, Q13, Q14); and urgency/soiling, four items (Q15–Q18)] by adding the scores of the items in each subscale. Additionally, four single items that do not belong to a subscale relate to incomplete evacuation (Q4), clustering (having another bowel movement within 15 min of the last movement—Q6), knowing the difference between needing to pass gas and a bowel movement (Q7), and incontinence for flatus (Q12). A global score can be calculated as the sum of the subscale scores, and a total score can be calculated by adding all the

item scores (subscale plus single item scores). A higher score is indicative of better bowel function.

The LARS score is a validated questionnaire that assesses five issues: incontinence for flatus, incontinence for liquid stools, frequency, clustering (the number of times the patient has a bowel movement within 1 h from the last bowel movement) and urgency [9]. Each question has three possible answers and each answer has a different point value. The total scores are used to place patients in one of three categories: no LARS (0–20), minor LARS (21–29) and major LARS (30–42).

QoL was evaluated using the Short Form-36 Health Survey [10].

During the study period, a number of patients were referred to the hospital for long-term functional problems after low anterior resection. All these patients had failed conservative measures including lifestyle and dietary counseling, optimal use of loperamide and anal plugs, and postoperative training in pelvic floor muscle exercises.

To all the short-term and long-term patients with a LARS score of 30 or higher (those in the major LARS category), a TAI treatment was proposed, and they were enrolled in this prospective study after detailed informed consent.

In every patient, the integrity of the anastomosis was documented by endoscopy or barium enema.

Additionally, every patient who enrolled in the study was asked to rate the severity of each of their symptoms, using a visual analog scale (VAS scale) from 1 to 10, with 10 = very negative impact on everyday life.

For every patient, the following data were recorded and analyzed: clinical (age, sex, body mass index (BMI), comorbidities), tumor related (distance from the anal verge, stage), surgical (open or laparoscopy, complications), stoma (presence, type, time before closure, complications) and short-term results (morbidity and mortality 30 days after surgery) were recorded and analyzed.

Tumors were considered to be in the low rectum if they started from < 5 cm above the pectineal line, in the mid rectum if between 5 and 10–12 cm (peritoneal reflection), and in the high rectum if > 10–12 cm (above the peritoneal reflection). The distance of the tumor from the anal verge was measured in all cases using a rigid rectoscope. The cancer stage was defined according to the American Joint Commission on Cancer (AJCC) Tumor Node Metastasis (TNM) classification system.

TAI was performed using the Peristeen system (Coloplast, Humblebaek, Denmark). The system components include a bag that is filled with up to 1500 ml of lukewarm tap water, a coated rectal catheter with a retaining balloon that is inserted into the neorectum, a control unit for the regulation of air and water, and a pump for inflating the balloon and irrigating the rectum. All patients were instructed by a specially trained stoma/rehabilitative nurse, who explained

and assisted in the use of the device until they could independently perform the irrigation without difficulty at home.

For the present study, the TAI protocol consisted of irrigation on alternate days (three or four times per week) over the course of 6 months. At the end of this period, the scores were repeated (LARS, MSKCC, SF-36). For all patients, the TAI therapy was then replaced with a 266 ml enema (2 Clisma fleet; Recordati Spa, Milan, Italy) administered according to the same schedule (3–4 times per week on alternate days) for 3 months. Scoring was repeated at the end of the 3 months of enema self administration.

Statistical analysis

Data were prospectively recorded in a dedicated database; statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 17, Chicago, IL,USA). Quantitative data were given as median (range). Comparisons of proportions were performed using the chi-square test for heterogeneity. The difference between pre- and post-treatment data was analyzed by a Wilcoxon signed rank test. Comparisons between the average LARS scores observed in different strata were analyzed according to the Mann–Whitney U test. A difference was considered statistically significant for p values < 0.05.

Results

During the study period, a total of 41 patients were evaluated at 30–40 days after primary surgery (if no diversion) or the same interval after stoma closure. LARS symptoms were reported in 32 patients (78%), and 23 of them (56%) had scores that placed them in the major LARS category. Moreover, during the study period 10 additional patients with major LARS after previous rectal cancer resection were recruited after outpatient evaluation. For those 10 patients, the median duration of functional impairment was 21 months (range 6–102 months).

TAI treatment protocol was proposed to 33 patients (Fig 1). There were no statistically significant differences between the early post-surgical and long-term patients with LARS regarding sex, age, indications for TAI, functional alterations or median LARS score (Table 1).

Median baseline self-reported functional impairment scores for every symptom are shown in Fig. 2.

One patient refused to participate. Five others initially enrolled but subsequently stopped TAI. Of those five, three had cancer recurrence that contraindicated continuing the procedure, one suspended the treatment due to proctitis and one suspended the treatment citing general dissatisfaction with the protocol.
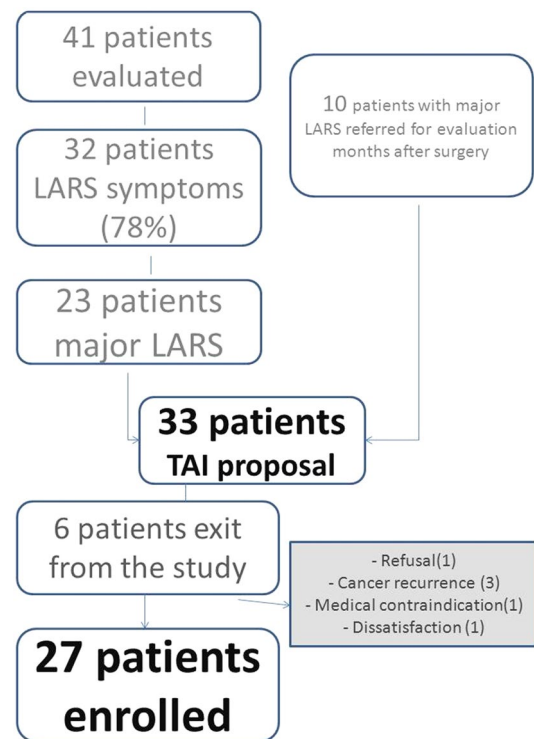
Fig. 1 Study flow chart; *LARS* low anterior resection syndrome, *TAI* transanal irrigation
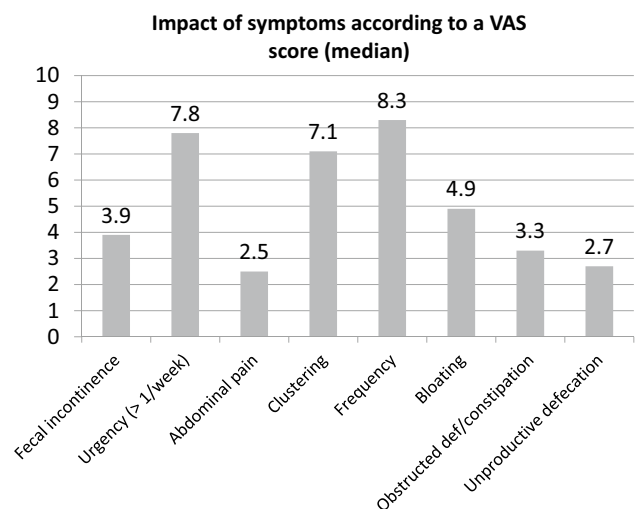
Fig. 2 Baseline median self-reported functional impairment score for every symptom; *VAS* visual analog scale

Ultimately, 27 patients completed the study. Their median age was 61 years (range 29–83 years) and 17 were male (63%) (Table 1). Twenty-one patients had a protective colostomy. The median time between low anterior resection and closure of the stoma was 5 months (range 1–13 months). Twenty-five patients had surgery for rectal cancer (1 had a

Table 1 Patient data

	All patients 27	Early LARS 19	Chronic LARS 8	p
Sex				
Male	17 (63%)	13 (68%)	4 (50%)	0.4
Female	10 (37%)	6 (32%)	4 (50%)	
Age (years)	61 (range 29–83)	60 (range 29–83)	64 (range 42–79)	
Procedure				
TME	21 (78%)	16 (84%)	5 (63%)	0.2
PME	3 (11%)	2 (10%)	1 (12%)	
Sigmoid resection	2 (7%)	0	2 (25%)	
Total colectomy	1 (4%)	1 (6%)	0	
Neoadjuvant therapy				
Yes	18 (66%)	13 (68%)	5 (63%)	1
No	9 (33%)	6 (32%)	3 (37%)	
T stage				
T1	1 (4%)	0	1 (12%)	
T2	11 (40%)	9 (49%)	2 (25%)	
T3	10 (37%)	6 (31%)	4 (50%)	
T4	2 (7%)	2 (10%)	0	
T0	3 (11%)	2 (10%)	1 (12%)	

LARS low anterior resection syndrome, *TME* total mesorectal excision, *PME* partial mesorectal excision

benign adenoma), 1 for ulcerative colitis and 1 for diverticular disease. Eighteen patients received neoadjuvant therapy. In 24 patients, an end to end stapled anastomosis (colorectal or coloanal) was performed. In three patients the anastomosis was hand-sewn.

The median volume of water used for the irrigation was 450 ml (range 300–1000 ml).

The median number of daily bowel movements decreased significantly over time [at baseline 7 (range 0–14); at 6 months 1 (range 0–4); at 9 months 4 (range 0–13)].

The median LARS score fell from 35.1 (range 30–42) at baseline to 12.2 (range 0–21) at 6 months ($p < 0.0001$) (Table 2) and then rose again to 27 (range 5–39) at 9 months ($p < 0.0001$) despite the enema protocol.

Four components of the SF-36 assessment significantly improved (mental health, social functioning, emotional role functioning and bodily pain). No significant differences were reported in vitality, physical functioning, general health perceptions and physical role functioning (Fig. 3). QoL scores significantly decreased after the suspension of treatment.

The MSKCC results are shown in Fig. 4. In particular, a significant improvement in frequency items (Q5,8,9,10), urgency items (Q15,17,18), incomplete emptying (Q4) and clustering (Q6) was reported, and a non-significant improvement in dietary items, discrimination between gas and stool, and incontinence for flatus.

Twenty-three patients (85%) asked to resume the treatment with TAI before the end of 3 months of suspension, due to rapid recurrence of symptoms despite enema use. Neither age, sex, BMI, nor any tumor- or stoma-related features appeared to have any statistically significant influence on the effect of TAI (Table 3) and recurrence of symptoms. Moreover, no differences in outcome were found between patients that started TAI postoperatively

Table 2 Results of the LARS score at baseline and with the use of transanal irrigation evaluated for every item

	Range	Baseline	Using TAI	p*
Flatus control	0–7	5.1	2.5	0.005
Leakage of liquid stool	0–3	2.3	1	0.002
Bowel movements	0–5	3.7	0.9	<0.001
New bowel movement within 1 h	0–11	9.8	1.7	<0.001
Urgency	0–16	14.2	6.1	0.001
Total	0–42	35.1 (30–42)	12.2 (0–21)	<0.001

TAI transanal irrigation

*Wilcoxon

SF36 item	Phisical funct	Role physical	Bodily pain *	General health
pre-treatment	55	39	37	42
end of TAI	62	45	63	45
3 mts after TAI	57	47	47	39
SF36 item	Vitality	Social funct *	Role emotional *	Mental health *
pre-treatment	47	43	51	38
end of TAI	57	67	71	59
3 mts after TAI	53	49	57	53
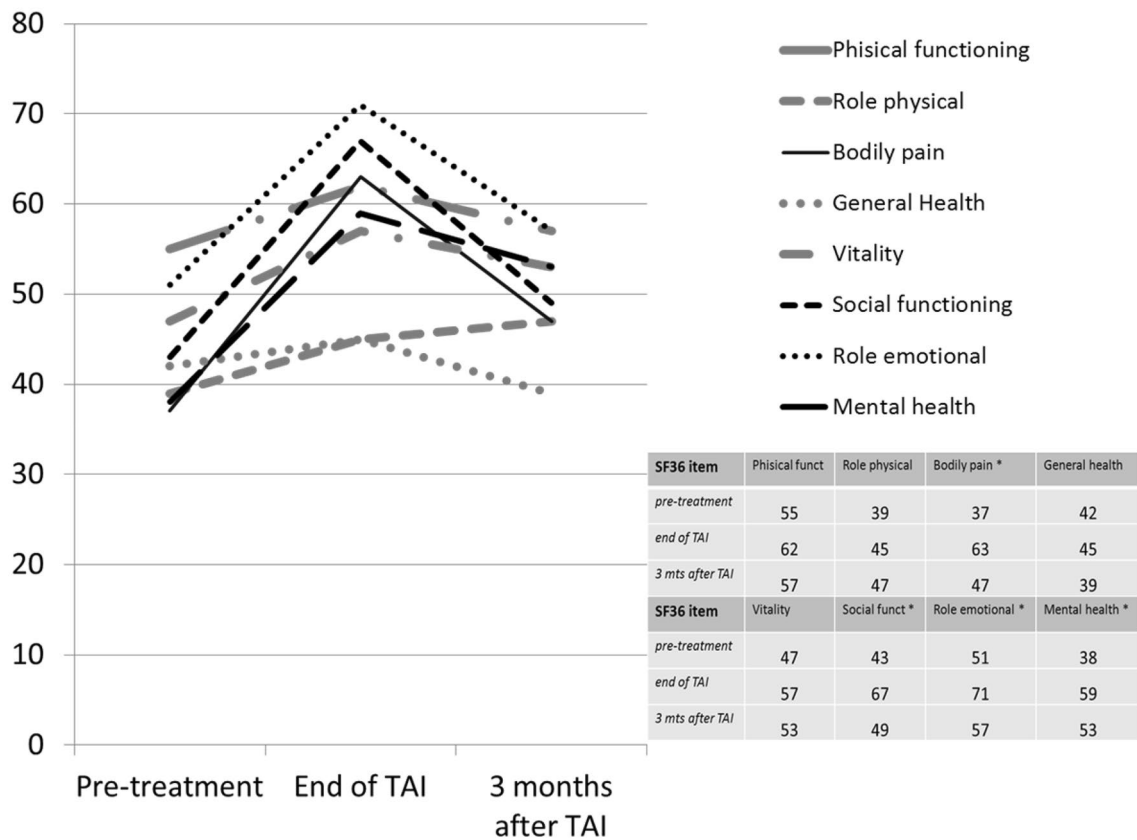
Fig. 3 Short form-36 results, *black line* significant improvement; *TAI* transanal irrigation
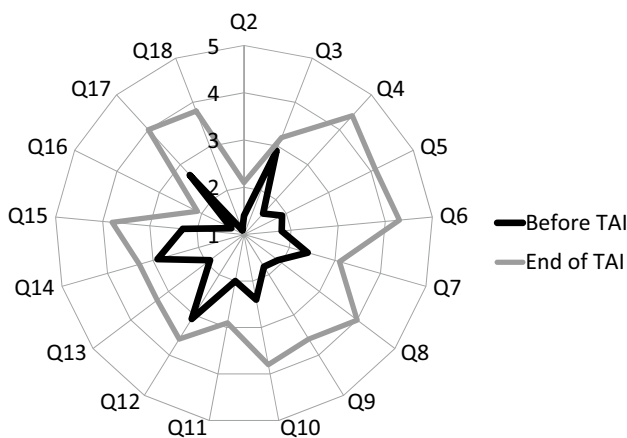

Fig. 4 The Memorial Sloan-Kettering Cancer Center Bowel Function Instrument score before and at the end of TAI (adapted: higher scores means better function for all the items); *TAI* transanal irrigation

(early LARS) or after some months, when the LARS symptoms were well established (chronic LARS). No significant differences were found between patients that continued or suspended TAI after the study period,

considering sex, age, surgical procedure, previous radio-therapy, previous stoma or time between surgery and TAI.

Discussion

Although dietary regimens, fiber, constipating agents and enemas may be considered a first-line conservative therapy for controlling LARS symptoms, their impact on patient satisfaction and QoL is doubtful and not supported by evidence. Conversely, transanal irrigation (TAI) has been reported to be a cheap and effective treatment for incontinence and frequent defecation associated with LARS [4, 5, 11, 12].

The effectiveness of TAI was previously reported for the treatment of symptoms induced by neurogenic bowel dysfunction [13, 14] or after dynamic graciloplasty [15] and the positive effects on transit time and continence were exploited in the management of patients with colostomy [16].

The effect of the irrigation is in part due to a simple mechanical wash-out effect, but studies of enema administration through colostomies have shown that irrigation with an enema > 250 ml generates colonic mass movements and other colonic functional responses [17, 18], suggesting that a regular management of bowel function through irrigation

Table 3 Response to transanal irrigation in sub-group analysis

	All patients 27	Baseline 35.1 (30–42)[a]	During TAI 12.2 (0–21)[a]	Score change	p
Sex					
Male	17	35.8 (32–42)	12.0 (4–16)	23.8	0.3
Female	10	33.9 (30–41)	12.7 (0–21)	21.2	
Age, years, *(median)*					
<70	16	35.2 (30–41)	12.0 (0–18)	23.2	0.6
>70	11	35.0 (32–42)	12.6 (4–21)	22.4	
Procedure					
TME	21	34.4 (30–40)	12.2 (4–21)	22.2	0.3
=thers	6	37.5 (33–42)	12.1 (0–18)	25.4	
Neoadjuvant					
Yes	18	34.7 (30–42)	12 (4–20)	22.7	0.8
No	9	35.8 (32–42)	12.7 (0–21)	23.1	
Stoma					
Yes	21	35.4 (30–42)	12.1 (4–20)	23.3	0.3
No	6	34.1 (30–38)	12.6 (0–21)	21.5	
Time between surgery and TAI					
<6 months	19	34.6 (30–42)	12.1 (4–20)	22.5	0.7
>6 months	8	36.5 (31–42)	12.6 (0–21)	23.9	

TAI transanal irrigation, *TME* total mesorectal excision

[a]median (range)

could have a rehabilitative effect on colonic motility. For the present study, the importance of performing TAI always at the same hour of the day, with the same time interval between tqo irrigations, without skipping any and maintaining a definite rhythm was explained to all the patients. After the 6 months of treatment with TAI, similar principles were followed during the enema regime, but the results of the present study failed to confirm a possible rehabilitative role of enema. The positive effect was usually maintained only during the TAI treatment phase.

Factors reported to correlate with a positive outcome for TAI include neurogenic bowel dysfunction and anal insufficiency as the underlying pathology, low rectal volume, low maximal rectal capacity and low anal squeeze pressure increment, factors that could be easily detected in patients with LARS [12].

Impaired bowel function and incontinence in LARS patients are usually related to a combination of colonic dysmotility, neorectal reservoir dysfunction and anal sphincter dysfunction. While neorectal reservoir function could benefit from anastomotic technique [19] or volumetric rehabilitation to enhance neorectal compliance and capacity, and sphincteric dysfunction could benefit from multimodal pelvic floor rehabilitation [20, 21], sacral neuromodulation [22, 23] or posterior tibial nerve stimulation [24], the problem of colonic dysmotility still remains unsolved. It may be the case that removal of the rectum and/or the rectosigmoid junction eliminates the physiological distal control center for

regulation of bowel transit, removing the negative feedback signals and leaving the bowel activity without a brake. In recent years, periodic (for the most part retrograde) motor phenomena have been documented in the rectum ("rectal motor complex", RMC) [25] and in the more distal colonic segments ("periodic colonic motor activity") [26]. The physiological significance of these phenomena is still under investigation, although for the RMC a continence-preserving mechanism (especially when sleeping) and negative feedback to transit and gastro/entero-colic reflexes have been hypothesized [27].

TAI may be the only treatment option that directly affects bowel dysmotility, mimicking the rectal pacemaker control and potentially giving a rhythm to bowel transit. Moreover, it has been shown that long-term TAI can increase urge rectal volume at manometric recording, suggesting a potential role of TAI in treating urgency [28].

In the present study, symptoms such as clustering or frequent bowel movements, strongly related to colonic dysmotility, were reported as highly disabling, together with urgency. Specialists tend to overestimate the impact of incontinence for liquid stool and frequent bowel movements, while underestimating the impact of urgency and clustering [29]. In fact, in previous studies about TAI in patients affected by LARS, only scores related to fecal incontinence were used for patient selection and evaluation of outcomes. This could create a significant bias. To the best of our knowledge, the present study is the first in

which patients were evaluated with dedicated validated scores for LARS. The MSKCC BFI and LARS scores are considered to be the best for assessing anorectal function after rectal cancer surgery [30]. For comprehensive and in-depth evaluation of LARS, the MSKCC BFI would be the questionnaire of choice. However, the MSKCC BFI's length (18 questions) and scoring method (which involves recoding, three subscale scores, a global score, and a total score) may limit its practicality. For rapid screening, the LARS score is preferable. Both instruments are valid, reliable, and able to detect clinically relevant differences.

The potential of TAI for treating LARS merits further investigation, although a cautious approach will be necessary to avoid the possibility of perforation in this at-risk group. In a collection of incidents caused by medical devices recorded by the European Community, the United States Food and Drug Association (FDA) and other national competent authorities, six perforations related to TAI were registered, and reported in a global audit on TAI-related bowel perforations[31].

This problem may be linked to the fact that the neorectum and the surroundings of the anastomosis have abnormal biomechanical properties that make the bowel wall more fragile. The same is probably true for other types of rectal surgery such as the stapled transanal rectal resection or ventral mesh rectopexy for obstructed defecation [32], and any kind of surgery for rectal prolapse.

While it is possible that the perforation rate observed in this cohort could be due to selection bias, the apparent increased risk in patients with prior rectal surgery emphasizes that pretreatment endoscopic evaluation of the rectum and of the integrity of the anastomosis are mandatory in such patients [33]. Furthermore, patients should be informed of the increased risk.

However, the weighted average risk of a bowel perforation was 6 per million (1:167.000) irrigation procedures [31]. In comparison, the standard quoted risk of perforation is 20 per million irrigation procedures (all irrigation systems) [12], 1:40.000 during flexible sigmoidoscopy [34], 1:1.000 during colonoscopy [35] and 1:10.000 during barium enema procedures [36]. In the present study, QoL and the LARS scores improved significantly. The majority of patients were able to empty their bowels with one to two bowel movements in 24–48 h, and they avoided the problem of night evacuation, which is probably a significant factor in improving QoL.

Unlike neurogenic patients, for whom the use of TAI represents a complex and often not autonomous maneuver with a high drop-out rate [37], a very low number of patients in the present study discontinued treatment. This is probably related to the simplicity of the procedure in self-sufficient trained and motivated patients, for whom TAI means a definite symptom-free period and a significant improvement of QoL.

A potential limitation of the present study could be the presence of patients with chronic LARS [median duration of functional impairment: 21 months (range 6–102 months)] as well as patients with early symptoms after rectal surgery. Some patients may notice that their symptoms resolve over time while others may continue to have symptoms and it is assumed that most patients clinically recover from functional impairments by 6–12 months after the operation. However, the only mechanisms that probably could be affected by time are neorectal reservoir dysfunction, (neorectal compliance and capacity could be recovered over time), and sphincteric muscular dysfunction (which can be partially recovered with training). Unfortunately, colonic dysfunction and nerve damage (due to surgery or adjuvant treatments) are strongly related to the main symptoms, and do not seem much influenced by time, often becoming permanent. In fact, long-term studies have reported the presence of relevant adverse symptoms up to 15 years after resection in about 50% of patients [2, 3]. No statistically significant differences were noted between the two groups in the present study.

However, the authors believe that early treatment of functional impairment after rectal surgery has the potential to enhance recovery and reduce the incidence of permanent dysfunctions [6].

Conclusions

The results of the present study confirm that TAI is an effective treatment of LARS and results in a marked improvement of continence scores and QOL. The rehabilitative role of TAI in the treatment of LARS still needs to be clarified and further studies are required to identify the best approach to correcting functional dysfunctions after rectal surgery.

Compliance with ethical standards

Informed consent Informed consent was obtained from all participants included in the study.

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