



Anterior Resection Syndrome

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Low rectal tumors have increasingly been treated by sphincter-saving operations (SSO), but some patients with a low anterior resection (LAR) or a coloanal anastomosis (CAA), with or without (chemo)radiotherapy, may suffer from a defecation disorder called “anterior resection syndrome” (ARS)¹. Frequent bowel action, urgency, symptoms of fecal incontinence, that characterize anterior resection syndrome, may occur in 10 to 20% of patients after sphincter-

saving operations^{2,3}. Quality of life may thus be impaired but the outcome may still be preferable to life with a permanent abdominal stoma and the individual learns to live with the consequences of treatment⁴.

Therefore ARS must be considered a significant issue of rectal cancer surgery and colorectal surgeons should know about this syndrome from top to bottom: its pathophysiology, clinical events, diagnostic tools, and therapy.

Pathophysiology

All types of sphincter-saving operations may give rise to ARS. The proportion of patients who suffer from this syndrome seems to increase as the level of anastomosis approaches the anal sphincter. Urgency and leakage are significantly more common in patients who have an anastomosis 3 cm from the anal verge than in patients whose anastomosis is 6 cm or more from the anal verge⁵. Indeed ultralow anterior resection with straight coloanal anastomosis may be associated with the highest incidence of impaired continence (30%)⁶. In order to give a neorectal reservoir that aids bowel function a colonic J pouch (CJP)-anal anastomosis is used with the result that frequency of defecation, inability to delay defecation, and use of anti-diarrhea medication are less in patients with a J-pouch than in patients with a straight coloanal anastomosis⁷. Also frequency of fecal incontinence seems to be less in CJP patients, varying from 5.5%⁸ to 8.4%⁹. However a systematic review of randomized trials could not demonstrate that reservoir construction produces an improvement of ARS¹⁰. Similarly no data are available assessing the ability of neorectal reservoirs to mimic rectal continence mechanisms. Transverse colectomy and side-to-end anastomosis have been shown to have similar bowel function outcomes when compared to the CJP, as reported in small randomized

controlled trials^{11,12}. Laparoscopic sphincter-preserving surgery shows functional results equal to open surgery¹³.

Impaired fecal continence in SSO is usually provoked either by colonic dysmotility, by neorectal reservoir dysfunction, or by anal sphincter damage or by a combination of these factors.

Colonic dysmotility

Anterior resection for rectal cancer involves removal of the rectum, until a few centimeters from or up to the anal canal, and sigmoid colon. The descending colonic segment is used to construct a neo-rectum, by means of colorectal anastomosis or coloanal anastomosis.

Colonic transit time is shorter in SSO patients than in controls^{14,15}. It is conceivable that the operation itself removes the physiological brake, where there is a hyper-segmenting activity apt to slow colonic transit, that is believed to exist just above the rectum¹⁶. Colonic manometry may detect this behavior of colonic motility, revealing a reduction in contractile segmental activity and much more high-amplitude propagated contractions than those which occur in healthy subjects¹⁷. Experimental studies on rats suggest that mobilization of left colon and vasculature ligation result in a significant extrinsic denervation with destruction of inhibitory sympathetic

innervations and an increase in motility in the distal colon¹⁸.

Altered colonic motility and reduction in large intestine length may result in a more liquid effluent reaching the anal canal; therefore, frequent bowel action and liquid stool occur.

Rectal reservoir dysfunction

Most of the total rectal wall is removed during anterior resection and it is replaced with descending colon. Two events may take place in some patients¹⁹. When a remnant of the rectum is preserved, the procedure of total mesorectal excision can eliminate the connections between the remnant rectum and extrinsic autonomic nerves that originate from the pelvic plexus. This results in a denervated remnant rectum. Meanwhile also the descending colon used for constructing the neorectum may become a denervated segment because both the ascending nerves from the pelvic plexus and the descending nerves from the inferior mesenteric plexus may have been resected with coexisting arteries. Furthermore the neorectum may exhibit altered motility and irregular spastic waves which are closely correlated with major soiling, urgency, and multiple evacuations.

Capacity and compliance are reduced in the neorectum, as compared with the rectum before resection²⁰. This means that greater pressures may be elicited in the neorectum than in the normal rectum using the same volumes. High neorectal pressures provoke a reduced ano-neorectal pressure gradient¹ and when this happens, particularly in cases of a malfunctioning anal sphincter, an episode of incontinence may result. This situation supports the idea that some patients who should undergo low anterior resection with coloanal anastomosis might benefit from the construction of a more capacious neorectal reservoir using a colonic pouch. Healed anastomotic leaks and radiotherapy, both neoadjuvant and adjuvant, seem to be predictive negative factors for neorectal function. Patients who have experienced anastomotic dehiscence show reduced neorectal capacity, more evacuation problems, and a tendency to more fecal urgency and incontinence than control patients²¹. Patients who have undergone postoperative radiotherapy have reduced neorectal capacity as demonstrated by impedance planimetry showing reduced neorectal distensibility²². Impaired neorectal capacity and decreased compliance are often found after short-term pre-operative radiotherapy but a recent study by Bakx et al.²³ suggests that a new pathophysiological mechanism contributes to the urgency for defecation: neorectal contractions develop in response to prolonged distension

instead of neorectal accommodation and a kind of neorectum "irritability" may occur.

These results prompt a unifying interpretation of malfunctioning neorectum in sphincter-saving operations. A filling of the neorectum with fecal material induces neorectal contractions, probably as result of the intrinsic property of the anastomosed colon characterized by innate motility and poor adaptation. This behavior worsens if capacity and compliance of the neorectum are impaired and, inevitably, stools are expelled.

Anal sphincter damage

Direct damage to the anal sphincter complex may result from anal stretching due to a transanally introduced stapling technique, as shown by anal sphincter defects detected by endoanal ultrasound²⁴. The damage is mainly confined to the internal sphincter: up to 18% of patients who underwent stapled low anterior resection had long-term evidence of internal anal sphincter injury²⁵. Internal anal sphincter function may also be compromised if the nerve supply to the sphincter is damaged²⁶. Sympathetic innervation, via hypogastric nerves, and parasympathetic supply, via pelvic nerves, are at risk if wide circumferential margins are resected, as in rectal cancer resection. Internal anal sphincter damage corresponds to a reduction in anal resting pressure²⁷. By contrast, the external sphincter is rarely directly or indirectly damaged with connotations for maximum squeeze pressure.

Preoperative radiation including the anal sphincters impairs anorectal function. More symptoms of fecal incontinence and more bowel movements per week are present in irradiated patients than in non-irradiated patients and endoanal ultrasound of irradiated patients shows more scarring of the anal sphincters²⁸. Also postoperative radiotherapy after anterior resection causes severe long-term anorectal dysfunction, which is mainly the result of a weakened anal sphincter and an undistensible rectum with reduced capacity²⁹. In order to protect the anal sphincter from the high dose field of irradiation, the modality known as 3D conformal radiotherapy (3DXRT) combined with full or partial sphincter block has been applied in the preoperative radiotherapy of patients considered candidates for sphincter-preserving surgery³⁰. Implementation of sphincter blocking using 3DXRT resulted in an 80% reduction in the mean dose distributed to the anal sphincter (from 33 to 6 Gy). In this way sphincter-preserving radiation therapy might improve the functional outcome of patients undergoing LAR.

Sometimes partial excision of the superior portion of the anal canal may be necessary for tumor

margin clearance in distal rectal cancer. This excision results in resections of varying magnitude of the internal anal sphincter and effects on fecal continence depend on anal portions that are sacrificed: continence is better in patients with coloanal anastomosis at 3.5-3 cm from anal verge than in patients with coloanal anastomosis at 3-2 cm from anal verge³¹. Impaired continence may be exacerbated by mucosal excision above the resected internal anal sphincter.

Anal sensation, obtained by typifying receptors in the anal mucosa particularly in the anal transition zone, allows discrimination of flatus from liquid or solid stool. Excisions of anal mucosa might impair anal sensation and therefore contribute to fecal soiling, as suggested by anal electrosensitivity studies performed in ileal J pouch-anal anastomoses³².

Clinical Outlines

Symptoms of ARS include a mix of high bowel frequency/day with liquid stools, at times multiple evacuations with multiple movements within a limited time period, urgency, and fecal incontinence. It is recommended to evaluate patients some months after the time of surgery. Immediately following low anterior resection almost all patients suffer from frequent bowel actions and soiling. These symptoms improve with time and most patients can enjoy almost normal daily life by the sixth postoperative month³³. Improvement of clinical symptoms is dependent upon the recovery of reservoir capacity and sensation of the neorectum. Therefore by the sixth month it may be correct to evaluate patients with impaired continence. The following step is to quantify the seriousness of illness. The Memorial Sloan-Kettering Cancer Center (MSKCC) bowel function instrument is a validated 18-item questionnaire, particularly referred to in the evaluation of bowel function after sphincter-preserving surgery³⁴. A total score may be calculated and factor analysis identifies 14 items that collapse into three subscales: frequency,

dietary, and soilage. In this way it is possible to evaluate simultaneously fecal continence, bowel frequency, and dietary restrictions used to reduce the number of bowel movements. The MSKCC instrument should be used to evaluate patient outcomes because electively it measures function after sphincter-saving operations.

Evaluation of quality of life (QOL) is the last but not least step that should be tackled to determine how the effects of an anterior resection impact on the psychosocial well-being of an individual⁴.

The European Organization for Research and Treatment of Cancer (EORTC) has designed a QOL questionnaire specific for colorectal cancer surgery (QLQ-CR38)³⁵.

Body image, future perspectives, sexual functioning, micturition problems, gastrointestinal dysfunction (symptoms related to the gastrointestinal tract) and problems with defecation are explored.

When applied to patients with sphincter-saving operations, problems with defecation are related to the lowest QOL scores and colonic J-pouch shows the worst results³⁶.

Diagnostic Tools

Following clinical evaluation the next step is to use diagnostic instruments that are useful to detect morphological lesions and functional disorders associated with ARS. Common diagnostic tools are defecography, endoanal ultrasound and anorectal manometry. Together these will provide accurate data for understanding of the pathophysiology of impaired continence. Defecography may detect the morphological features of defecatory disorder. Characteristic findings closely associated with incontinence are: 1) low volume of neorectum; 2) low evacuation fraction; 3) wide anorectal angle-posterior (> 110°); 4) barium shadow in the anal canal at rest³⁷. Using the reconstruction method, the

colonic J-pouch displays a larger volume than straight anastomosis and a significantly wider anorectal angle than high anterior resection. Judging from the morphological characteristics determined by cine-defecography, better postoperative defecatory function following sphincter-saving rectal resection is associated with reconstruction methods that are not too small in size, display high evacuation fraction, and offer an adequate anorectal angle that is not too wide. Endoanal ultrasound is the gold-standard technique to evaluate anal sphincters integrity because it can visualize defects, scarring, thinning and thickening, and other local alterations³⁸. The accuracy of demonstrating anorectal sphincter

injury is high and sensitivity and specificity reach almost 100%. For these reasons endoanal ultrasound has a basic position in the morphological diagnostic work-up of ARS, confirming or excluding anal sphincters damage. Anorectal manometry is of utmost importance because it may identify functional sphincter weakness, poor rectal compliance, and rectal sensation impairment. Routine diagnostic manometry can offer information about anal resting pressure, maximum squeeze pressure, rectoanal inhibitory reflex, threshold volumetric perception of fecal mass, threshold volume for urgency to defecate, and rectal compliance monitoring. Thanks to these intrinsic features anorectal manometry is capable of providing objective information about the mechanisms of fecal continence. When used in incontinent patients, manometric data suggest which continence mechanisms may be malfunctioning. A reduction in the mean anal resting pressure, expression of internal anal sphincter damage, and/or in the maximum squeeze pressure, expression of external sphincter dysfunction, may occur in ARS patients²⁶. Rectoanal inhibitory

reflex (RAIR) may be abolished after anterior resection but it recovers in most cases by the end of the second postoperative year³⁹. Transection of the rectum which disrupts intramural neural pathways and regeneration of intramural autonomic nerves across the anastomotic scar might explain the reappearance of RAIR⁴⁰. The influence of RAIR loss on the symptoms of anterior resection syndrome is not well understood because only 33% of patients with incontinence does not have RAIR in one study⁴¹ and only 25% of 37 patients with absence of RAIR suffered from fecal incontinence in another study³⁹. In any case, the absence of RAIR means impairment of sampling reflex and this alteration might be important in those patients with suboptimal sphincter pressures or very diminished rectal capacity²⁶. Finally, low thresholds for perception of stool, low capacity of the neorectum, and altered compliance are the typical manometric reports in patients with inability to delay defecation. Therefore anorectal manometry offers irreplaceable diagnostic data for understanding the pathophysiology of ARS.

Therapy

The multifactorial pathophysiology of ARS should guide therapy whose primary aim should be to restore or significantly improve continence. Unfortunately, there is no therapeutic algorithm or gold standard treatment that may be used for fecal incontinence following sphincter-saving operations. Nevertheless, it is rational to use conservative therapy at first and then to deal with surgery.

There are many therapeutic agents for fecal incontinence (bulking agents and high fiber diet, valproate sodium, diazepam, topical phenylephrine, amitriptyline)⁴² but loperamide, an anti-diarrheal agent, is the preferred drug because it has also been observed to increase anal sphincter tone, leading to improved fecal continence in incontinent patients with and without diarrhea⁴³. The combination of loperamide with pelvic floor muscle exercises⁴⁴ or with methylcellulose⁴⁵ improves the positive response rate of fecal incontinence. However no reports are available on the application of drugs for ARS. When excessive stool frequency and incontinence after SSO are refractory to medical therapy, rehabilitative treatment may become a good option. Few reports have been published on the rehabilitation of patients affected by ARS, but results are encouraging. Biofeedback reduces daily stool frequency and incontinence

episodes^{3,46} and when combined with other rehabilitative techniques (“multimodal rehabilitation”), some patients become symptom-free (23.8%) and many experience improved incontinence (34.2%)⁴⁷.

The postrehabilitative results are worse in patients who have undergone irradiation; previous anal or pelvic surgery and pelvic organ prolapse may be considered impairing factors for rehabilitative treatment⁴⁷.

After failed rehabilitation, the therapeutic option might be sacral neuromodulation. Some experiences in a few patients have been published^{48,49} and results are promising. After device implant the number of incontinence episodes significantly drop and a significant improvement in fecal incontinence occurs. Further randomized controlled studies with many patients and long-term follow-up will be necessary to state the usefulness of this treatment.

When intractable fecal incontinence occurs, surgical treatment must be considered.

Surgical sphincter repair (sphincteroplasty), or sphincteric substitution (gracilis/gluteus transposition, artificial sphincter) may be tried before the radical approach of a stoma.

However, no reports are available on the application of these surgical techniques following sphincter-saving operations for rectal cancer.

Conclusions

Anterior resection syndrome may be a disabling condition which exerts a negative influence on the patient's quality of life.

An accurate clinical and instrumental evaluation is mandatory in order to understand the multifactorial picture of this pathophysiology.

Traditional therapeutic procedures for fecal incontinence are not always successful and new ways should be tried before resorting to more aggressive forms of treatment.

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